

# 2017 식·의약품 등 수사·분석사례집







## 발 간 사

최근 고령화 사회에 진입하면서 건강한 삶을 유지하기 위해 건강기능식품에 대한 관심과 수요가 점차 증가하고 있습니다. 이와 함께 식품이나 건강기능식품에 의약품 성분 등을 불법 혼입·제조하여 마치 발기부전치료, 근육강화 등에 특정한 효과가 있는 것처럼 판매함으로써 사회적 문제가 되고 있습니다. 또한, 매년 의약품 성분을 인위적으로 변경한 유사물질을 제조하여 불법으로 식·의약품에 혼입함으로써 검사망을 피하려는 시도가 다수 적발되는 등 그 수법도 더욱 지능화되는 추세에 있습니다.

신종 부정물질의 국내 유입차단 등 부정·불법 식·의약품에 대한 검사강화를 위하여 첨단분석팀은 다양한 첨단분석기기를 활용하여 새로운 분석법 개발과 함께 의약품성분의 화학적 구조를 변경한 신종 부정물질을 규명하고 있습니다. 이를통해 부정·불법 식·의약품의 유통을 선제적으로 차단함으로써 신속하고 정확한 분석을 수행할 수 있는 시스템을 적극적으로 구축하고 있습니다.

본 사례집은 '09년부터 식품의약품안전처 위해사범중앙조사단 등에서 분석 의뢰된 검체의 분석 결과를 중심으로 수사배경, 보도사례, 물질특성, 분석방법에 대한 내용을 수록하고 있으며, 이 사례집은 대검찰, 국과수, 시도보건환경연구원 등 일선 검사기관에 제공하여 정보를 공유하고 있습니다. 올해는 고지혈증치료제(25종), 등척 성분, 만병초 성분, 화장품(립스틱류) 중 타르색소(21종) 등이 신설 분석법으로 수록되었습니다. 또한, 국소마취관련성분(14종), 발기부전치료제와 그 유사성분(82종) 등 대상성분을 확대하여 분석법을 개정하였습니다.

본 사례집이 부정·불량식품의 유통 차단 및 의약품의 오남용 방지를 위한 과학적 시험분석 업무수행에 적극 활용되어 식·의약품의 사전·사후 안전관리에 기여할 뿐 아니라 소비자의 신뢰를 한층 더 제고할 수 있는 기회가 되기를 기대합니다.

2017년 12월

식품의약품안전평가원장 이 선 희



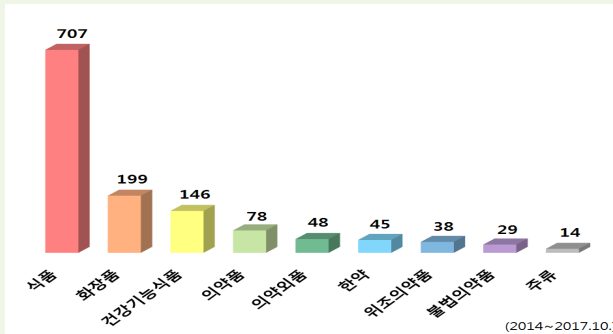
# 개요

“2017 수사·분석사례집”은 고지혈증치료제(25종), 등취 성분, 만병초 성분, 화장품(립스틱류) 중 타르색소(21종) 등에 대한 시험법을 새롭게 확립하여 수재하였으며, 국소마취 관련성분(14종), 발기부전치료제와 그 유사성분(82종) 등 기존 다성분 동시분석법에 신규 물질 성분을 추가하여 발간하게 되었습니다.

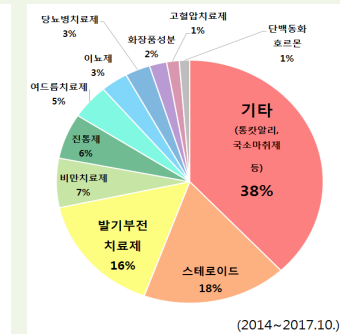
## 연도별 위해사범중앙조사단 의뢰건수

연도	2009~2013	2014	2015	2016	2017.10
건수	2114	291	219	238	149

## 검체 유형별 의뢰건수



## 의뢰된 성분 비율



## 신종부정물질규명현황

(세계최초 12종, 국내최초 7종)

구분	화학물명	규명년도	비고
발기부전 치료제 유사물질	Desmethylpiperazinyl propoxysildenafil <sup>1)</sup>	2017	SCI(SJ) <sup>6)</sup> 투고
	Desulfonylchlorosildenafil <sup>2)</sup>	2017	-
	Isopropylnortadalafil <sup>1)</sup>	2016	SCI(FAC) <sup>3)</sup> 등재
	Descarbonsildenafil <sup>2)</sup>	2016	-
	Bisprenortadalafil <sup>1)</sup>	2015	SCI(FAC) <sup>3)</sup> 등재
	Bisprehomotadalafil <sup>1)</sup>	2014	SCI(JPBA) <sup>4)</sup> 등재
	Bisprecyclopentyltadalafil <sup>1)</sup>	2014	SCI(JPBA) <sup>4)</sup> 등재
	trans-Cyclopentyltadalafil <sup>1)</sup>	2014	SCI(JPBA) <sup>4)</sup> 등재
	Cyclopentyltadalafil <sup>1)</sup>	2014	SCI(JPBA) <sup>4)</sup> 등재
	Bisprehomotadalafil <sup>1)</sup>	2014	SCI(JPBA) <sup>4)</sup> 등재
	Homotadalafil <sup>2)</sup>	2013	-
	Propoxyphenyl thiohydroxyhomosildenafil <sup>2)</sup>	2013	-
	Propoxyphenyl thiosildenafil <sup>2)</sup>	2013	-
	Propoxyphenyl thioildenafil <sup>1)</sup>	2013	SCI(FAC) <sup>3)</sup> 등재
Propoxyphenyl thiohomosildenafil <sup>1)</sup>	2013	SCI(FAC) <sup>3)</sup> 등재	
Acetaminotadalafil <sup>1)</sup>	2011	SCI(FAC) <sup>3)</sup> 등재	
발모성분	Triaminodil <sup>2)</sup>	2017	SCI(FAC) <sup>3)</sup> 등재
마약류	APINAC <sup>1)</sup>	2016	SCI(JFT) <sup>5)</sup> 등재
	MDMB-FUBINACA <sup>2)</sup>	2016	SCI(JFT) <sup>5)</sup> 등재
체중감량성분	Chlorosibutramine <sup>1)</sup>	2013	SCI(FAC) <sup>3)</sup> 등재

1) 신종부정물질 세계최초규명사례      2) 식품에서 검출된 국내 최초사례  
 3) FAC : Food Additives and Contaminants      4) JPBA : Journal of Pharmaceutical and Biomedical Analysis  
 5) JFT : Journal of Forensic Toxicology      6) SJ : Science & Justice



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# I-1 < 고지혈증치료제(25종) 분석법

## ■ 배경

- 홍콩 및 홍콩/폴리코사놀 복합제제, 콜레스테릭스 제품에서 고지혈증 치료제 메바코의 활성성분인 ‘로바스타틴’ 검출('07, 미국)
- 홍콩쌀 식이보충제에서 고지혈증 치료제인 ‘로바스타틴’이 검출되어 회수 조치('14, 미국)

FDA 건강식품 '홍콩' 불법 의약품 성분 함유



【서울=메디칼투데이/뉴스시스】

미국 FDA가 판매되고 있는 세 종의 홍콩(red yeast rice)제품에 대해 구입 및 섭취를 금한다고 발표하면서 이들 제품에 건강에 해로울 수 있는 미승인 약 성분이 함유돼 있다고 밝혔다.

홍콩은 콜레스테롤 수치를 낮추는 식품 보조제로 판매되고 있다.

이번 지적을 받은 제품은 홍콩 및 홍콩/폴리코사놀 복합제제 (스완슨 건강식품회사 판매, 네이처스 헬프사 및 와이코사 제품), 콜레스테릭스 (센바스드 마인스가닉 판매)였으며 이 FDA 조사결과 이 제품들에서 미국 내에서 콜레스테롤 조절 처방제로 승인된 난 대마균의 활성성분인 로바스타틴이 발견됐다.

FDA는 소비자가 로바스타틴의 부작용을 인식하지 못할 경우 더 위험할 수 있고 다른 약품과 함께 복용시 해로울 수 있다고 밝혔다.

이들 홍곡제품에 포함된 로바스타틴은 심각한 근육질환에서부터 신장손상 등 부작용이 보고 되고 복용량이 많은 경우와 다른 약품과 함께 복용 시 더욱 심각한 부작용을 초래할 수 있다.

합제 복용에선 안 되는 약품으로는 항우울제인 니파조론, 및 항생제, 세균감염 및 HIV 감염 치료제 그리고 콜레스테롤 조절제제 등이 있다.

FDA는 미식약청은 스완슨과 센바스드 마이닝가닉 사에 경고장을 발행 이들 제품의 수입 및 판매를 금지시켰으며 경고에 따르지 않을 경우 이행명령이나 불법제품 압류 등 강제 조치를 도할 수 있다고 밝혔다.

FDA는 홍곡제품을 섭취 후 이상증세가 있는 소비자는 즉시 병원을 방문할 것을 권했다.

Red Yeast Rice by Doctor's Best: Recall - Undeclared Lovastatin

**ADVICE:** Consumers  
**WARNING:** Doctor's Best is voluntarily recalling lot 3121000 (120 bottles) of Best Yeast Rice dietary supplement, 600 mg Capsules, 120 count bottles to the retail level. Doctor's Best Best Yeast Rice has been found to contain undeclared lovastatin, a previously approved drug indicated for the treatment of high cholesterol, making this an unapproved new drug.  
 Consumers who use supplements found to contain lovastatin in rare cases could result in serious muscle injury, paralysis, fatigue with proximal "grip" such as incontinence, incontinence, or incontinence. Pregnant women could prematurely get their unborn child at risk by using the product with undeclared lovastatin. Patients with pre-existing liver disease may be at an increased risk for liver injury following chronic use of statins.  
**BACKGROUND:** Doctor's Best Best Yeast Rice was distributed nationwide through retail and internet outlets. Doctor's Best Best Yeast Rice is marketed as a dietary supplement for lowering cholesterol and is packaged in white plastic bottles with an orange flip-top cap and a clear tamper-evident outer seal. UPC code: 75300081193, Lot 3121000 and expires February 2017.  
**RECOMMENDATION:** Consumers/retailers/subscribers that have Best Yeast Rice which is being recalled should discontinue usage and return the amount portion to their place of purchase. Doctor's Best is notifying its distributors and customers to stop use and arranging the return of all recalled products.  
 Consumers with questions regarding this recall can contact Doctor's Best at 1-888-717-2100 Monday through Friday, 9am to 5pm PST, and contact their physician or healthcare provider if they have experienced any problems that may be related to taking or using this drug product.  
 Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.  
 • Complete and submit the report Order: [www.fda.gov/medwatch](http://www.fda.gov/medwatch)  
 • Download form or call 1-800-352-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-541-0715.  
 (3121000) - (Press Release - Doctor's Best)  
 (Phyto) Product Labels



## ■ 특성

- 고지혈증치료제는 크게 HMG-CoA 저해제, Fibrate 유도체 등이 있음
  - HMG-CoA 저해제: 세포의 초저밀도지질단백질(LDL) 수용체 합성 증가, 혈장의 콜레스테롤을 세포내로 이동시켜 혈관 염증을 완화시킴 (ex) Atorvastatin, Lovastatin, Simvastatin 등
  - Fibrate 유도체: 말초조직 및 혈청의 lipoprotein lipase 활성을 촉진하여 중성지방(TG) 수치 저하, 초저밀도지질단백질(VLDL) 분해 증가 및 고밀도지단백질(HDL)을 상승시킴 (ex) Bezafibrate, Clofibrate, Etofibrate 등
- 부작용: 장기 복용 시 당뇨병을 유발할 수 있으며 임신부가 복용 시 최기형성(선천기형)이 있을 수 있고, 다른 약물과 상호작용에 의해 근육 관련 독성이 문제가 될 수 있음

## ■ 분석사례

- 건강식품 & 한약 관련 제품: Bezafibrate 5 mg/g 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

- 표준액 조제 : 표준액 1\* Pitavastatin calcium 등 18종  
 표준액 2\* Pravastatin sodium salt hydrate 등 7종  
 → 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10~50 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용
- \* 표준액 1 : Pitavastatin calcium, Benfluorex, D-Thyroxine, Cerivastatin codium salt hydrate, Triparanol, Rosuvastatin calcium, Lomitapide, Clofibrac acid, Bezafibrate, Ezetimibe, Etofibrate, Ciprofibrate, Atorvastatin calcium salt trihydrate, Fenofibrac acid, Lapaquistat acetate, Gemfibrozil, Fenofibrate, Anacetrapib
- \* 표준액 2 : Pravastatin sodium salt hydrate, Fluvastatin sodium, Mevastatin, Lovastatin, Simvastatin, Lovastatin hydroxy acid sodium salt, simvastatin hydroxy acid ammonium salt

#### ○ Analytical conditions of HPLC

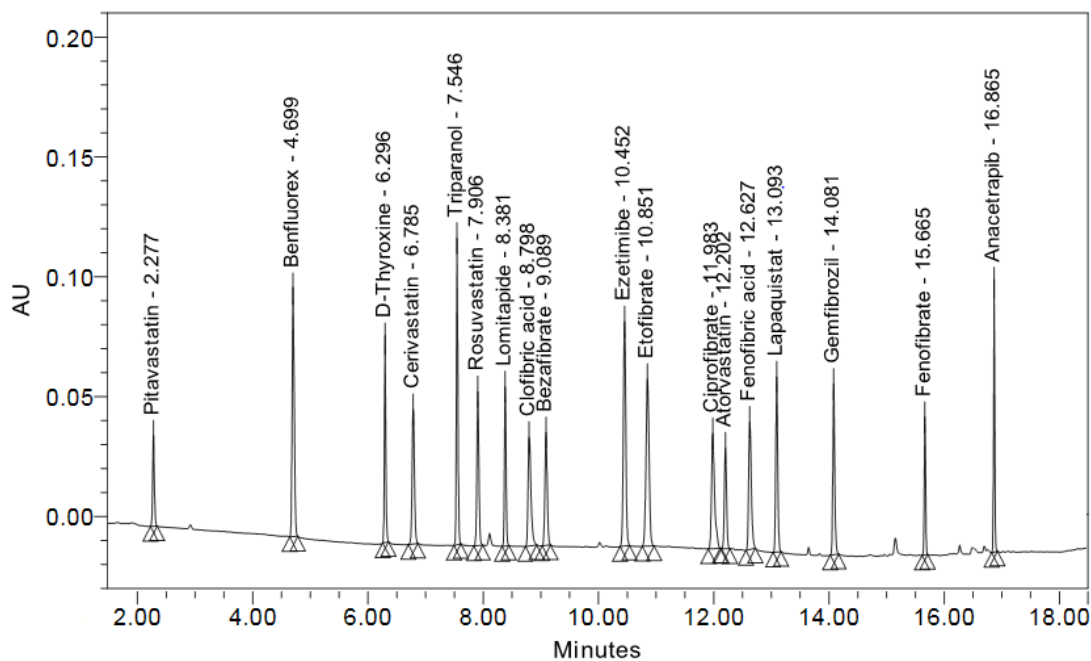
- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC CSH C18 (2.1 mm × 150 mm, 1.7 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1 mM dipotassium phosphate (pH 2.0, phosphoric acid)  
(B) 100% Acetonitrile

Time (min)	A (%)	B (%)
0.0	70	30
2.0	70	30
4.0	60	40
8.0	50	50
9.0	50	50
11.0	40	60
14.0	10	90
16.0	0	100
18.0	0	100
19.5	70	30
24.0	70	30

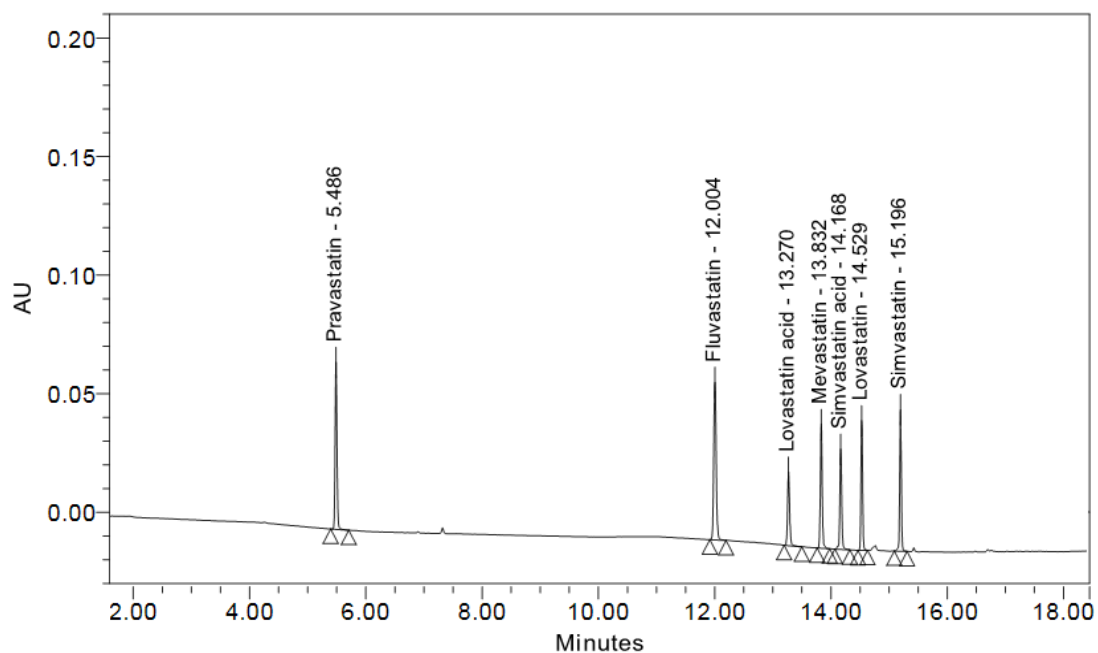
- Flow Rate 0.3 mL/min
- Inj. Volume 1 µL
- UV Detection 표준액 1 : 200 nm  
표준액 2 : 235 nm
- PDA Range 190~400 nm



○ Chromatogram



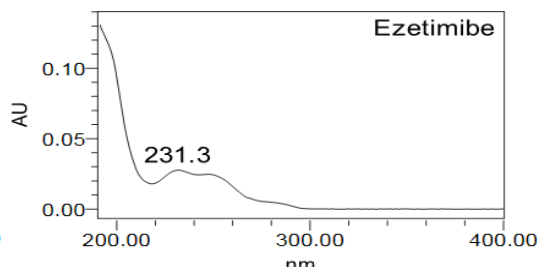
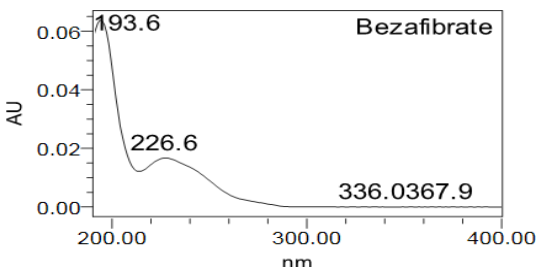
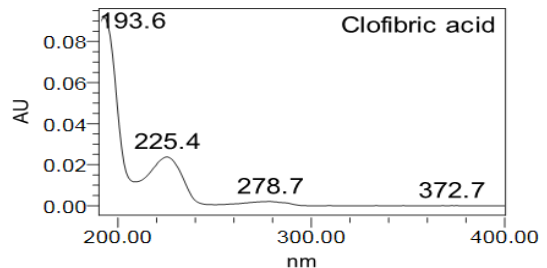
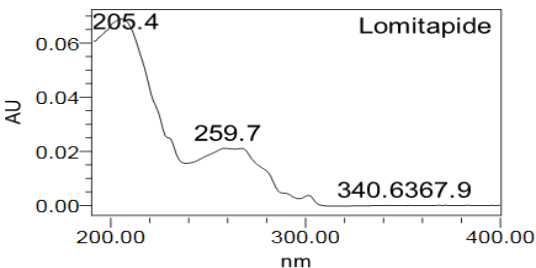
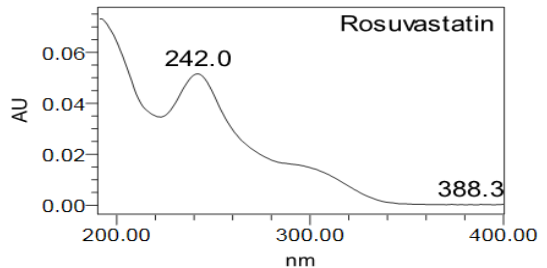
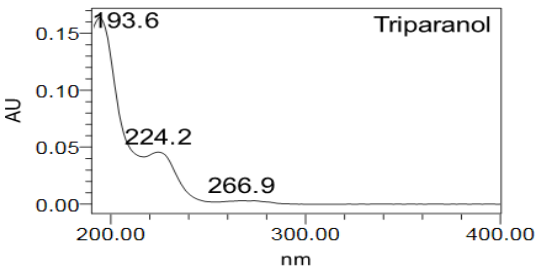
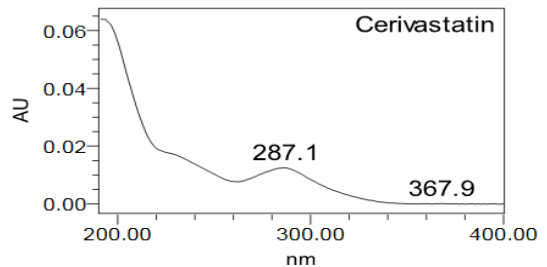
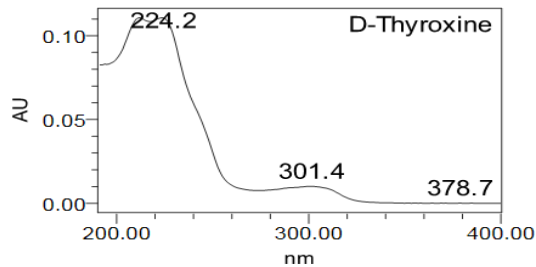
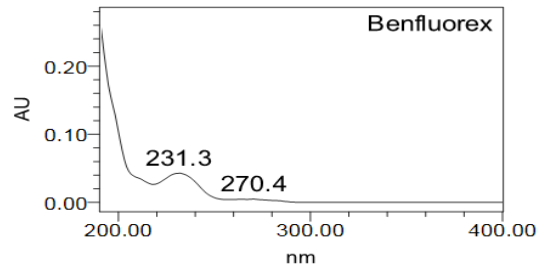
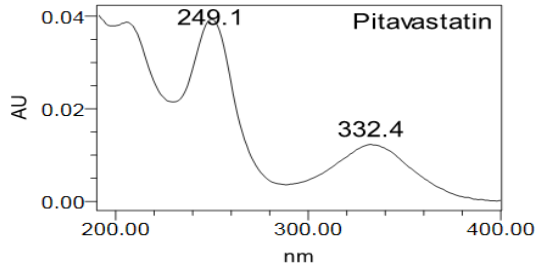
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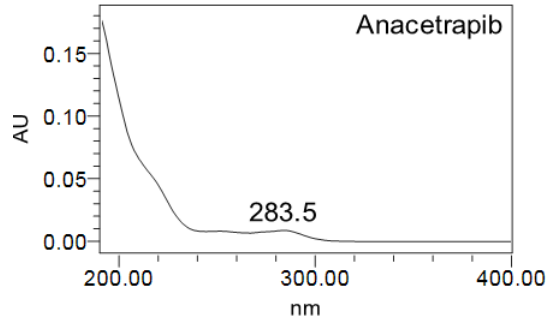
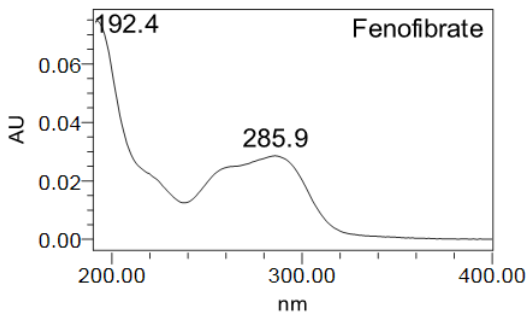
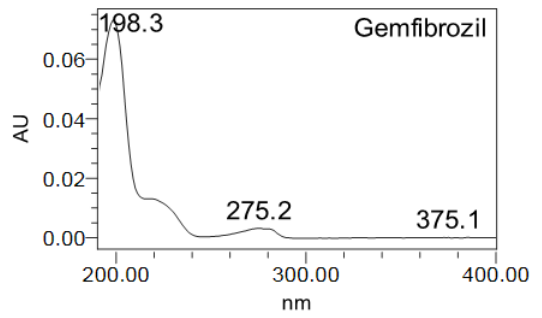
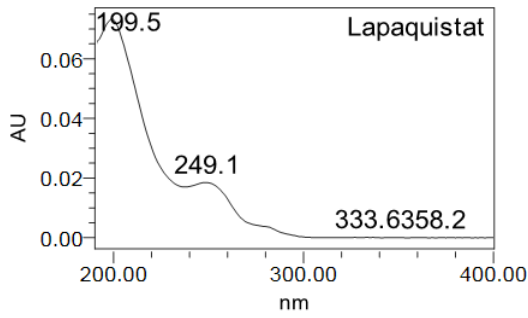
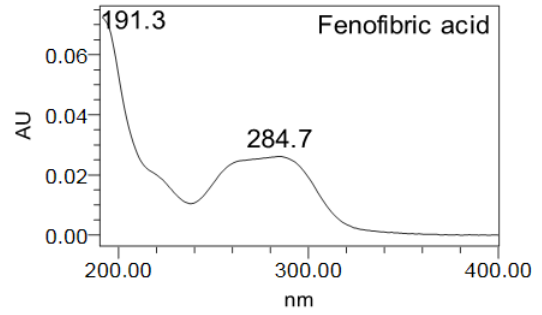
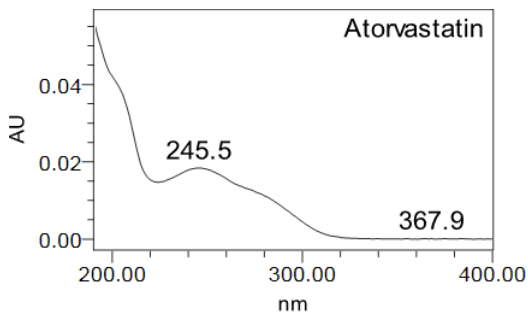
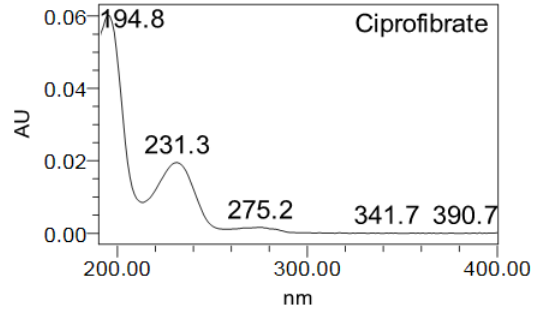
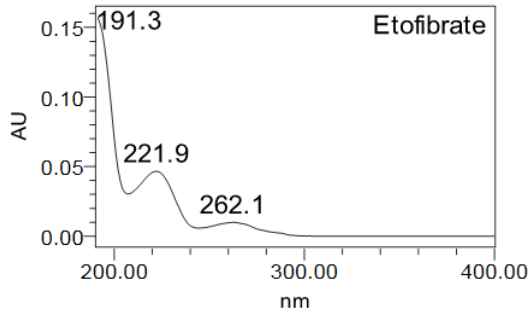


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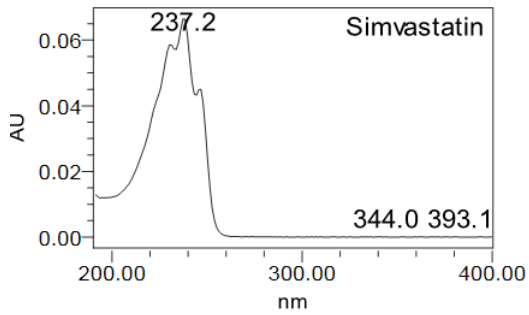
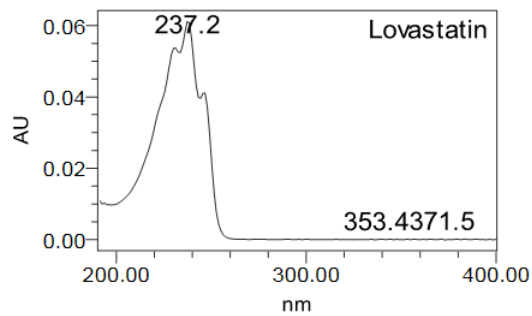
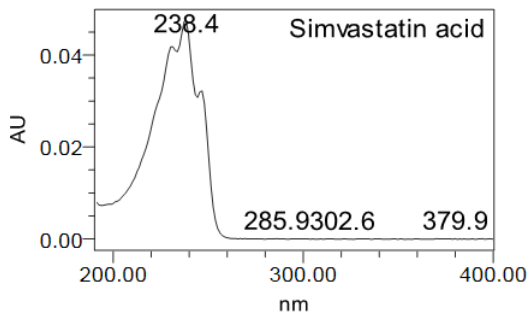
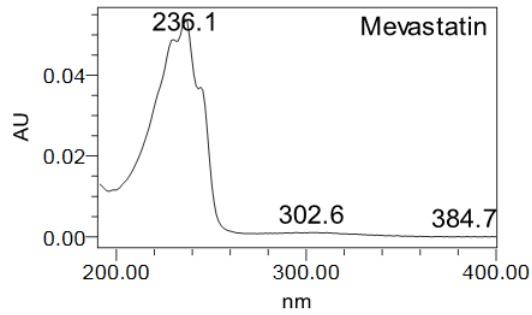
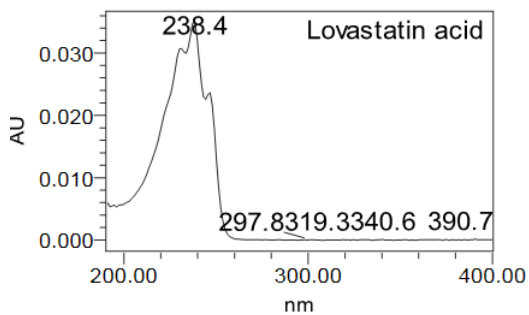
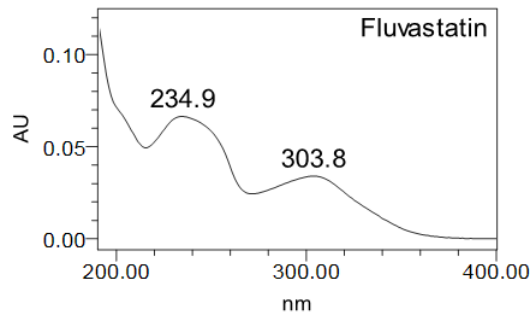
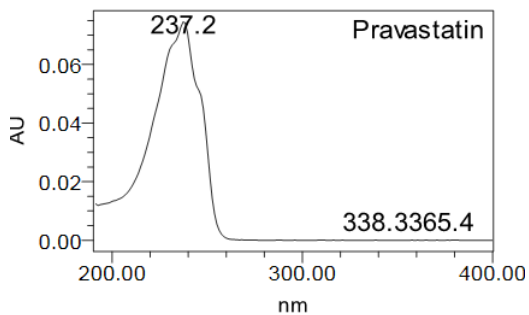
## ○ PDA Spectrum

\* 표준액 1





\* 표준액 2



## 2. LC-MS/MS

### ○ Analytical conditions of HPLC

• Instrument	Agilent DE/1200 HPLC		
• Column	Atlantis dC18 (2.0 mm × 100 mm, 3.0 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	1.0	95	5
	2.0	40	60
	8.0	10	90
	11.0	0	100
	13.0	0	100
	14.0	95	5
	18.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	AB sciex API 4000	
• Ionization Mode	ESI (+)	ESI (-)
• Curtain Gas	25 psi	25 psi
• Collision Gas	5 psi	5 psi
• Ion Voltage	5500 V	4500 V
• Ion Source Gas 1	50 psi	50 psi
• Ion Source Gas 2	50 psi	50 psi
• Source Temp.	500°C	500°C

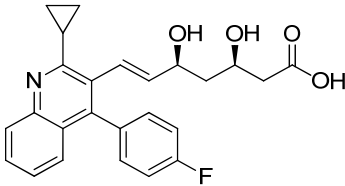
○ Analyte MS/MS transition

Compound	Ion mode	Precursor ion (m/z)	DP (V)	Product ion	CE (V)	CXP (V)
Pitavastatin	+	422.1	116	290.2	39	18
				318.2	43	22
				260.1	69	18
Benfluorex	+	352.2	86	230.2	25	16
				159.2	27	10
				149.1	47	8
D-Thyroxine	+	777.7	51	731.8	39	44
				633.9	37	30
				604.8	49	32
Cerivastatin	+	460.4	121	356.2	49	24
				324.2	65	22
				280.2	81	18
Triparanol	+	438.2	106	100.2	39	20
				213.2	41	14
				418.2	22	11
Rosuvastatin	-	480.2	45	340.1	32	9
				298.0	42	7
				249.2	65	16
Lomitapide	+	694.3	161	429.3	53	30
				179.2	75	12
				126.9	18	9
Clofibric acid	-	212.9	45	84.9	14	5
				274.0	24	7
				153.8	40	11
Bezafibrate	-	360.0	60	85.0	30	5
				271.0	22	7
				118.9	66	7
Ezetimibe	-	408.1	55	132.0	56	9
				150.1	25	8
				114.1	37	22
Etofibrate	+	364.1	81	124.1	47	24
				84.9	18	5
				200.8	14	9
Ciprofibrate	-	286.9	45			

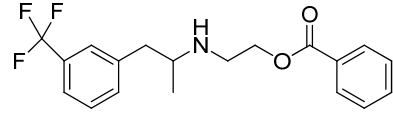
표준액  
1

Compound	Ion mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (V)	CXP (V)
Atorvastatin	-	557.2	100	397.1	40	9
				278.1	60	7
				453.1	32	13
Fenofibric acid	+	319.1	86	233.1	23	14
				139.1	39	14
				121.1	69	22
Lapaquistat	+	645.3	96	502.3	31	14
				404.2	39	28
				214.2	47	14
Gemfibrozil	-	249.1	50	120.9	18	7
				126.7	16	7
Fenofibrate	+	361.1	81	233.1	25	16
				138.9	37	8
Anacetrapib	+	638.3	121	121.0	51	24
				283.2	31	18
Pravastatin	-	423.1	70	268.2	63	18
				255.1	59	16
Fluvastatin	-	410.1	70	321.0	22	7
				303.0	24	7
Lovastatin acid	-	421.3	95	100.9	42	5
				348.0	22	9
Mevastatin	+	391.2	81	209.8	38	15
				319.0	24	7
Simvastatin acid	-	435.4	85	100.9	42	7
				158.8	30	7
Lovastatin	+	405.3	81	185.2	19	12
				229.3	19	14
Simvastatin	+	419.3	86	159.2	35	10
				318.9	24	7
Simvastatin	+	419.3	86	115.0	36	7
				159.0	32	7
Simvastatin	+	419.3	86	285.2	17	18
				199.2	17	12
Simvastatin	+	419.3	86	225.1	29	14
				285.3	15	18
Simvastatin	+	419.3	86	199.2	17	12
				303.3	17	16

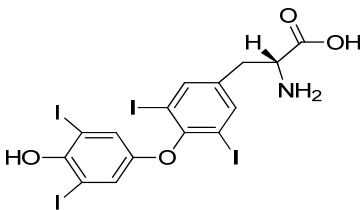
■ 구조식



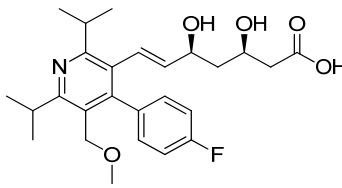
Pitavastatin  
[C<sub>25</sub>H<sub>24</sub>FNO<sub>4</sub>]



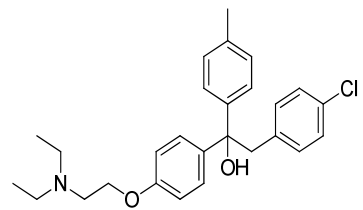
Benfluorex  
[C<sub>19</sub>H<sub>20</sub>F<sub>3</sub>NO<sub>2</sub>]



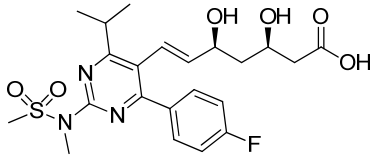
D-Thyroxine  
[C<sub>15</sub>H<sub>11</sub>I<sub>4</sub>NO<sub>4</sub>]



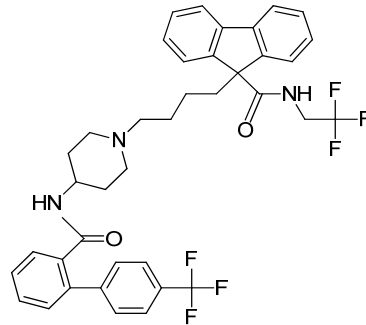
Cerivastatin  
[C<sub>26</sub>H<sub>34</sub>FNO<sub>5</sub>]



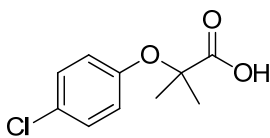
Triparanol  
[C<sub>27</sub>H<sub>32</sub>ClNO<sub>2</sub>]



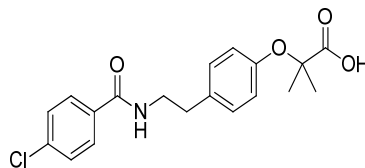
Rosuvastatin  
[C<sub>22</sub>H<sub>28</sub>FN<sub>3</sub>O<sub>5</sub>S]



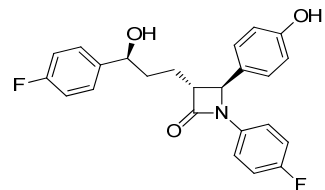
Lomitapide  
[C<sub>38</sub>H<sub>37</sub>F<sub>6</sub>N<sub>3</sub>O<sub>2</sub>]



Clofibric acid  
[C<sub>10</sub>H<sub>11</sub>ClO<sub>3</sub>]

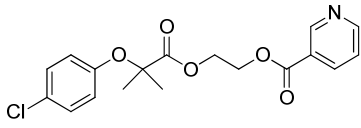


Bezafibrate  
[C<sub>19</sub>H<sub>20</sub>ClNO<sub>4</sub>]

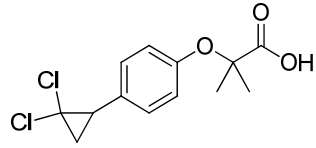


Ezetimibe  
[C<sub>24</sub>H<sub>21</sub>F<sub>2</sub>NO<sub>3</sub>]

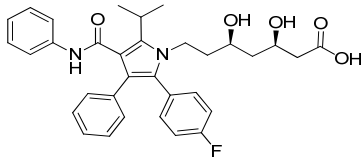




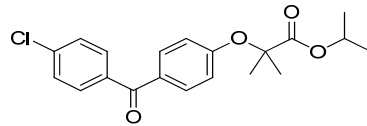
Etofibrate  
[C<sub>18</sub>H<sub>18</sub>ClNO]



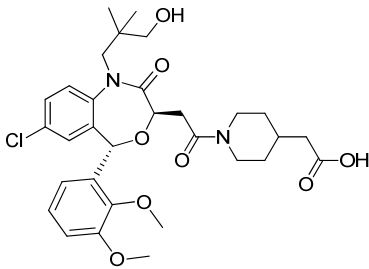
Ciprofibrate  
[C<sub>13</sub>H<sub>14</sub>Cl<sub>2</sub>O<sub>3</sub>]



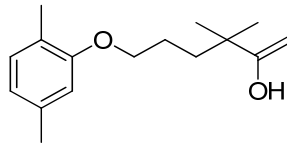
Atorvastatin  
[C<sub>33</sub>H<sub>34</sub>FN<sub>2</sub>O<sub>5</sub>]



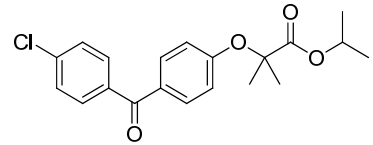
Fenofibric acid  
[C<sub>17</sub>H<sub>15</sub>ClO<sub>4</sub>]



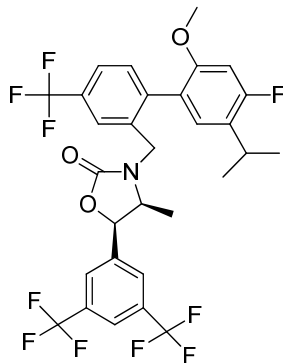
Lapaquistat  
[C<sub>31</sub>H<sub>39</sub>ClN<sub>2</sub>O<sub>8</sub>]



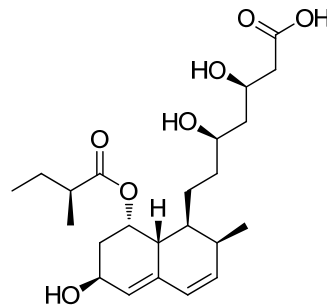
Gemfibrozil  
[C<sub>15</sub>H<sub>22</sub>O<sub>3</sub>]



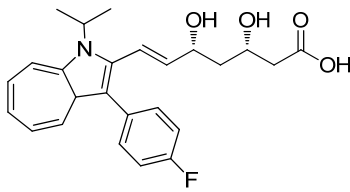
Fenofibrate  
[C<sub>20</sub>H<sub>21</sub>ClO<sub>4</sub>]



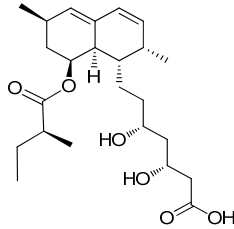
Anacetrapib  
[C<sub>30</sub>H<sub>25</sub>F<sub>10</sub>NO<sub>3</sub>]



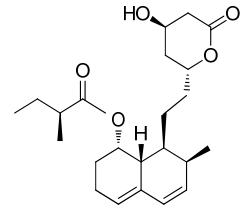
Pravastatin  
[C<sub>23</sub>H<sub>36</sub>O<sub>7</sub>]



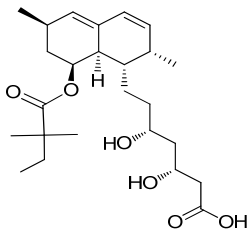
Fluvastatin  
[C<sub>24</sub>H<sub>26</sub>FNO<sub>4</sub>]



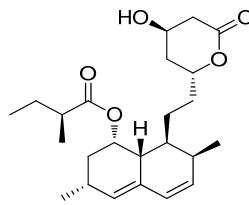
Lovastatin acid  
[C<sub>24</sub>H<sub>38</sub>O<sub>6</sub>]



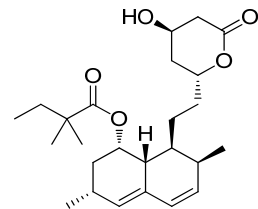
Mevastatin  
[C<sub>23</sub>H<sub>34</sub>O<sub>5</sub>]



Simvastatin acid  
[C<sub>25</sub>H<sub>40</sub>O<sub>6</sub>]



Lovastatin  
[C<sub>24</sub>H<sub>36</sub>O<sub>5</sub>]



Simvastatin  
[C<sub>25</sub>H<sub>38</sub>O<sub>5</sub>]

## ■ 참고문헌

1. Bin Guo, Meiling Wang, Yanyan Liu, Jing Zhou, Hua Dai, Zhiqiang Huang, Lingling Shen, Qingsheng and Bo Chen. Wide-Scope Screening of illegal Adulterants in Dietary and Herbal Supplements via Rapid Polarity-Switching and Multistage Scurate Mass Confirmation Using an LC-IT/TOF Hybrid Instrument. *Journal of Agricultural and Food Chemistry*. 63, 6954-6967 (2015)
2. Qingxia Zhu, Mengyun Chen, Lu Han, Yongfang Yuan, Feng Lu. High efficiency screening of nine lipid-lowering adulterants in herbal dietary supplements using thin layer chromatography coupled with surface enhanced Raman spectroscopy. *Analytical Methods*. 9, 1595-1602 (2017)
3. Tomohide Fukiwake, Takashi Hasegawa, Kazunaga Takahashi, Masaaki Saiko and Masanori Hamana, Simultaneous determination of statins in dietary supplements by ultra-performance liquid chromatography. *Food hygiene safety science Japan*. 55(2), 94-102 (2014)

# 1-2 등취 성분 분석법

## 배 경

- 신장 손상과 발암 위험이 높아 식·의약품에 사용할 수 없는 ‘등취’를 ‘통초’로 둔갑시켜 약령시장이자 인터넷을 통해 판매한 일당 적발(‘16. 10.)
- 산후조리 중 ‘통초’가 아닌 ‘등취’이 들어간 한약재를 먹은 산모가 급성 신부전, 말기 신장질환으로 신장 이식 받음(‘17. 01.)



## 특 성

- 등취(*Aristolochia manshuriensis* Kom.)은 쥐방울과 식물의 덩굴줄기로서 관목통으로 불리며 예전부터 통초로 잘못 사용되어 왔고, 특히 발암물질인 아리스틀로크산(Aristolochic acid)이 함유되어 사용이 금지됨
- 주요성분: Aristolochic acid A~D

■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 표준액 조제 : Aristolochic acid A 등 5종\*  
→ 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 1 µg/mL)
- 검액 조제 : 약 1 g 취함 → 100% 메탄올 가함 → 30분 진탕 → 50 mL 정용  
SPE(Solid Phase Extraction, C<sub>8</sub>, 500 mg, 6 cc)  
→ Conditioning(100% 메탄올, 5 mL) → Equilibration(물, 5 mL)  
→ Loading(SPE용 검액, 2 mL) → Elution(100% 메탄올, 10 mL)  
→ 100% 메탄올 가함 → 20 mL 정용

\* 표준액 : Aristolochic acid A, Aristolochic acid B, Aristolochic acid C, Aristolochic acid D

○ Analytical condition of HPLC

- Instrument Agilent DE1200
- Column Shiseido Capcell Pak C<sub>18</sub> MGII (2.0 mm × 100 mm, 3 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1% Formic acid in Water  
(B) 0.1% Formic acid in Acetonitrile

Time (min)	A (%)	B (%)
0.0	85	15
1.0	45	55
2.0	45	55
2.5	35	65
4.0	35	65
5.0	10	90
7.0	10	90
7.1	85	15
10.0	85	15

- Flow Rate 0.25 mL/min
- Inj. Volume 5 µL

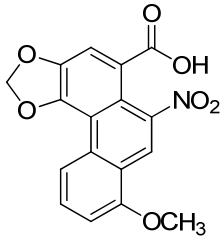
## ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX QTRAP 5500
• Ionization Mode	ESI (+)
• Curtain Gas	30 psi
• Collision Gas	9 psi
• Ion Voltage	5500 V
• Ion Source Gas 1	50 psi
• Ion Source Gas 2	50 psi
• Source Temp.	500℃

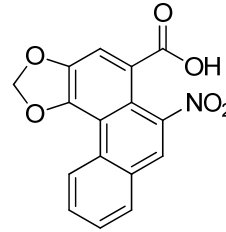
## ○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion ( <i>m/z</i> )	DP (V)	Product ion ( <i>m/z</i> )	CE (V)	CXP (V)
Aristolochic acid A	+	359.0 [M+NH <sub>4</sub> ] <sup>+</sup>	61	298.0	17	12
				324.0	19	20
				268.1	15	16
Aristolochic acid B	+	329.0 [M+NH <sub>4</sub> ] <sup>+</sup>	31	238.0	25	18
				221.0	35	18
				284.0	17	16
Aristolochic acid C	+	345.1 [M+NH <sub>4</sub> ] <sup>+</sup>	51	267.0	31	18
				312.0	19	20
				358.0	9	28
Aristolochic acid D	+	375.0 [M+NH <sub>4</sub> ] <sup>+</sup>	76	297.0	45	14

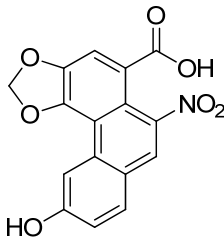
## ■ 구조식



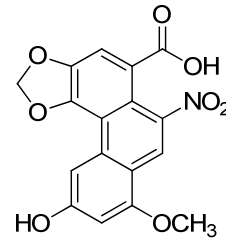
Aristolochic acid A  
[C<sub>17</sub>H<sub>11</sub>NO<sub>7</sub>]



Aristolochic acid B  
[C<sub>16</sub>H<sub>9</sub>NO<sub>6</sub>]



Aristolochic acid C  
[C<sub>17</sub>H<sub>9</sub>NO<sub>7</sub>]



Aristolochic acid D  
[C<sub>17</sub>H<sub>11</sub>NO<sub>8</sub>]

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2. Chiu-Yu Huang, Mu-Chuan Tseng and Jer-Huei Lin. Analyzing aristolochic acids in Chinese herbal preparations using LC/MS/MS. *J Food Drug Anal*, 13(2), 125-131 (2005)
3. Lukas Vaclavik, Alexander J Krynitsky and Jeanne I. Rader. Quantification of aristolochic acids I and II in herbal dietary supplements by ultra-high-performance liquid chromatography-multistage fragmentation mass spectrometry. *Food Addit Contam A*, 31(5), 784-791 (2014)

## I-3 만병초 성분 분석법

### ■ 배경

- 동아시아에서 주로 서식하는 만병초는 국내에서 그 잎을 술에 담가 마시거나, 물에 끓여 차로 마신 후 중독증상을 일으켜 응급실에 내원하는 사례가 꾸준히 발생함(2002, 2006, 2015)
- 식품 원료로 사용할 수 없는 만병초는 가공식품 중 혼입을 확인할 수 있는 분석법이 마련되어 있지 않으며, 유사한 중독증상을 일으키는 벌꿀 중 Grayanotoxin III 분석법만 식품공전에 등재됨



### ■ 특성

- 만병초 잎에 함유된 Grayanotoxin을 과량 섭취하였을 경우 저혈압과 구토, 과도한 타액분비, 오심, 무력감, 의식 소실, 시야장애, 경련 등 유발. 고혈압 및 심장질환자 등은 사망에 이를 수 있음
- 만병초 차 또는 담금주를 섭취한 후 긴급 후송되는 사례 발생
- 주요성분: Grayanotoxin I, Grayanotoxin III, Rhodioloside

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Grayanotoxin I, Grayanotoxin III, Rhodiolioside  
→ 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 1 µg/mL)
- 검액 조제 : 약 1 g 취함 → 100% 메탄올 가함 → 30분 진탕 → 50 mL 정용  
SPE(Solid Phase Extraction, HLB, 500 mg, 6 cc)  
→ Conditioning(100% 메탄올, 5 mL) → Equilibration(물, 5 mL)  
→ Loading(SPE용 검액, 2 mL) → Elution(100% 메탄올, 10 mL)  
→ 100% 메탄올 가함 → 20 mL 정용

\* 표준액 : Grayanotoxin I, Grayanotoxin III, Rhodiolioside

#### ○ Analytical condition of HPLC

- Instrument Agilent DE1200
- Column Shiseido Capcell Pak C<sub>18</sub> MGII (2.0 mm × 100 mm, 3 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1% Formic acid in Water  
(B) 0.1% Formic acid in Methanol

Time(min)	A(%)	B(%)
0.0	95	5
4.0	60	40
6.5	30	70
7.0	30	70
7.5	5	95
8.0	5	95
8.1	95	5
10.0	95	5

- Flow Rate 0.25 mL/min
- Inj. Volume 5 µL



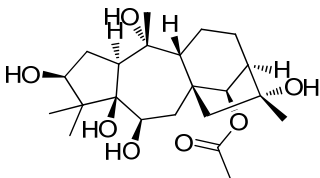
## ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX QTRAP 5500	
• Ionization Mode	ESI (+)	ESI (-)
• Curtain Gas	30 psi	20 psi
• Collision Gas	9 psi	9 psi
• Ion Voltage	5500 V	4500 V
• Ion Source Gas 1	50 psi	50 psi
• Ion Source Gas 2	50 psi	50 psi
• Source Temp.	450°C	450°C

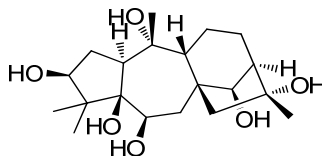
## ○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion ( $m/z$ )	CV (V)	Product ion ( $m/z$ )	CE (V)	CXP (V)
Grayanotoxin I	+	435.2 [M+Na] <sup>+</sup>	81	375.2	31	14
				357.0	35	20
Grayanotoxin III	+	335.0 [M+H-2H <sub>2</sub> O] <sup>+</sup>	30	317.2	17	14
				299.0	19	21
Rhodiolide	-	299.0	25	119.0	18	17
				58.8	46	29
				88.8	18	13

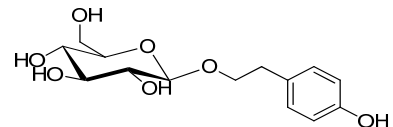
## ■ 구조식



Grayanotoxin I  
[C<sub>22</sub>H<sub>36</sub>O<sub>7</sub>]



Grayanotoxin III  
[C<sub>20</sub>H<sub>34</sub>O<sub>6</sub>]



Rhodiolide  
[C<sub>14</sub>H<sub>20</sub>O<sub>7</sub>]

## ■ 참고문헌

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## I -4 부테아수페르바 성분 분석법

### 배 경

- 부테아 수페르바(*Butea superba*)는 남성 성기능 개선과 관련한 원료로 태국 등지에서 천연 발기부전치료제로서 사용되어 왔으나, 안전성이 확보되지 않아 국내에서 수입 및 유통·판매가 금지됨. 그러나 남성 성기능 강화에 효과가 있다는 광고를 내세워 독성 및 안전성이 확보되지 않은 제품이 인터넷 쇼핑몰(해외직구) 등을 통해 수입·판매되고 있음
- 안전성이 확보되지 않은 부테아 수페르바의 유통관리 필요

제품명	NO-BOMB	
원산지	미국	
제조사	MHP	
검출물질/사용금지원료	검출물질: Butea superba 검출량: 사용금지원료: 검출물질: Forsythia suspensa extract/frut 사용금지원료	
등록일	2016.01.19	조희수



### 특 성

- 태국 등지에서 부테아 수페르바가 남성 성기능 향상에 도움이 된다고 알려져 사용하여 왔고, 구강섭취를 통한 혈중 테스토스테론 수치 변화와 발기부전환자의 성기능 향상이 보고됨
- 동물실험에서 과량 섭취 시 유전독성평가에서 안전하지 못하거나 사람과 동물에게 독성을 일으킬 수 있으며, 건강한 남성이 꾸준히 섭취하였을 경우 성욕증가와 함께 남성 호르몬 수치가 상승하는 등 고안드로젠 혈증을 나타냄
- 주요성분 : Butesuperin A, Butesuperin B

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Butesuperin A, Butesuperin B  
→ 일정량 취합 → 100% DMSO 가함 → 최종 농도(약 1 µg/mL)
- 검액 조제 : 약 1 g 취합 → 100% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* DMSO : Dimethyl sulfoxide

#### ○ Analytical condition of HPLC

- Instrument Agilent DE1200
- Column Agilent Pursuit XRs Ultra C<sub>18</sub> (2.1 mm × 100 mm, 2.8 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1% Formic acid in Water  
(B) 0.1% Formic acid in Acetonitrile

Time(min)	A(%)	B(%)
0.0	90	10
2.0	90	10
2.5	45	55
3.5	45	55
4.5	35	65
6.5	35	65
7.0	0	100
10.0	0	100
10.1	90	10
12.0	90	10

- Flow Rate 0.25 mL/min
- Inj. Volume 2 µL

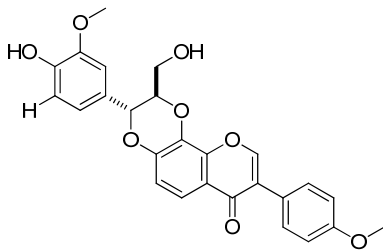
#### ○ Analytical conditions of LC-MS/MS

- Instrument AB SCIEX QTRAP 5500
- Ionization Mode ESI (+)
- Curtain Gas 30 psi
- Collision Gas 9 psi
- Ion Voltage 5500 V
- Ion Source Gas 1 50 psi
- Ion Source Gas 2 50 psi
- Source Temp. 450°C

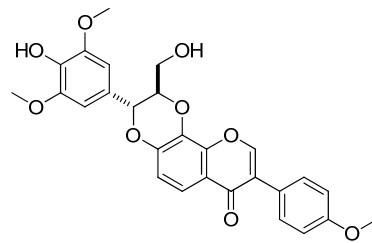
## ○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion ( $m/z$ )	DP (V)	Product ion ( $m/z$ )	CE (V)	CXP (V)
Butesuperin A	+	463.0	50	255.1	47	18
				445.1	29	14
				283.0	37	22
Butesuperin B	+	493.2	41	255.0	51	12
				283.0	39	12
				475.1	29	14

## ■ 구조식



Butesuperin A  
[C<sub>26</sub>H<sub>22</sub>O<sub>8</sub>]



Butesuperin B  
[C<sub>27</sub>H<sub>24</sub>O<sub>9</sub>]

## ■ 참고문헌

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2. A Pongpanparadons, S Aritajat and K Saenphet. The toxicology of *Butea superba* Robx. *Southeast Asian J Trop Med Public Health*. 33(3), 155-158 (2002).
3. Kamon Chaiyasit and Viroj Wiwnaitkit. Hyperandrogenemia due to ingestion of *Butea superba*. *Indian J Endocrinol Metabol*. 16(3), 485-486 (2012).

## 2. 유전자 분석법

### ○ PCR을 위한 주형유전자의 준비

#### - 유전자추출키트(DNeasy Mini Kit) 이용하여 추출

(재현성 및 검출효율 등을 고려하여 QIAGEN DNA Mini Kits 또는 동등 이상의 제품 사용 가능)

- 
- 검액 조제 : ① 약 100 mg을 취함
  - ② 400  $\mu$ L의 Buffer AP1, 4  $\mu$ L의 RNase A를 가함  
→ Vortex Mixer를 사용하여 균질화  
→ 65°C incubator에 2시간 방치
  - ③ 130  $\mu$ L의 Buffer AP2 가함  
→ Vortex Mixer를 사용하여 균질화  
→ 5분간 ice에 방치
  - ④ 원심분리(14,000 rpm, 8분) → 상층액을 취함  
→ IAshredder spin column에 넣음  
→ 원심분리(14,000 rpm, 2분)
  - ⑤ Column을 통과한 액을 새로운 tube에 옮김  
→ 이의 1.5배의 Buffer AP3/E를 가하고 균질화
  - ⑥ 650  $\mu$ L를 취함  
→ DNeasy Mini spin column에 넣음  
→ 원심분리(8,000 rpm, 1분)  
→ 통과한 액을 버림
  - ⑦ ⑥ 반복
  - ⑧ Spin column을 새로운 2 mL collection tube에 넣음  
→ 500  $\mu$ L의 Buffer AW를 가함  
→ 원심분리(8,000 rpm, 1분)  
→ 통과한 액을 버림
  - ⑨ ⑧번 반복
  - ⑩ Column을 새로운 1.5 mL 또는 2 mL microcentrifuge tube에 옮김  
→ 60  $\mu$ L의 증류수 가함  
→ 15분간 실온에서 방치
  - ⑪ 원심분리(8,000 rpm, 1분)  
→ 통과된 액을 취함
-

- **농도 확인** : DNA 원액을 TE 완충액(pH 8.0) 또는 멸균증류수로 적절히 희석
  - 분광광도계를 사용하여 260 nm에서 흡광도(Absorbance, A) 측정
  - 그 값이 1일 때 DNA 농도가 50 ng/μL인 것으로 하여 계산

- **순도 확인** : 230, 260, 280 nm에서 흡광도를 각각 측정
  - $A_{260}/A_{280}$ 과  $A_{260}/A_{230}$ 이 1.7~2.0일 경우 PCR에 적합한 DNA로 판단
  - ※ 단, 가공식품의 경우 이러한 순도 적용이 어려운 경우가 있으므로 반드시 적용되는 것은 아님
  - ※  $A_{260}/A_{280}$ 이 낮아 단백질 유래 불순물의 혼입이 우려되는 경우
    - 단백질 분해효소(protease)로 처리한 후 DNA 회수
  - ※  $A_{260}/A_{230}$ 이 낮을 경우
    - 전분 분해효소(amyase)로 처리한 후 DNA를 회수하여 PCR에 사용

○ Real-time PCR을 위한 프라이머(primer) 및 PNA 프로브(probe) 염기서열

유전자	구분	염기서열(5'-3')	중폭산물 크기(bp)	비고
<i>matK</i>	프라이머	CTACGTAACAAATCCTCTCAG	456	Forward
		CCGGCTTACTAATGGGATGACC		Reverse
	프로브	TCTGATTAGTTCATTGG		형광-FAM
		AATAGAACATCTTGTAGA		형광-TxR
AS2	프라이머	CAACACCAACTTCGCCAGCTTC	82	Forward
		AGGCCGTGGCCGCAGATTCG		Reverse
	프로브	TTGTGCCAAATCAGA	형광-HEX	

### ○ PCR 반응액 조제

- ① 1.5 mL tube에 주형 DNA를 제외한 시약들을 아래와 같은 양을 섞어 반응액을 제조한다. 한번에 여러 시료를 동시에 실시할 경우에는 각각의 시약에 시료의 수만큼 배수로 반응액을 제조한다(반응액 분주시 부족하지 않도록 여유 있게 준비해야하며, 음성대조군을 포함하여 제조한다).

성분	1회 용량(μL)
주형 DNA	5
2X qPCR PreMix	10
Detection mixture	5

- ② 제조한 반응액을 15 μL씩 Real-Time PCR용 plate에 분주하고 추출한 주형 DNA 5 μL를 나중에 넣는다.
- ③ 제외한 반응액과 DNA를 담은 plate는 microplate 전용 원심분리기에서 spin down하여 내용물을 아래쪽으로 모으고 불필요한 공기방울을 제거한다.
- ④ 반응액과 DNA를 담은 plate는 microplate 전용 원심분리기에서 spin down하여 내용물을 아래쪽으로 모으고 불필요한 공기방울을 제거한다.

### ○ Real-time PCR 반응조건

구분	온도	시간	반복 수
초기변성(Initial denaturation)	95℃	10 min	1
변성(Denaturation)	95℃	30 sec	45
결합(Annealing)	58℃	30 sec	
신장(Extension)	72℃	1 min	
PNA hybridization step	95℃	5 min	1
	75℃	1 min	1
	55℃	1 min	1
	45℃	30 sec	1
Melting step (Plate read step)	25~85℃	increment 1℃ 5 sec hold*	1

\* 25℃에서부터 1℃씩 올리며 5 sec 기다린 후 형광 검출 과정 수행

### ○ 결과 확인

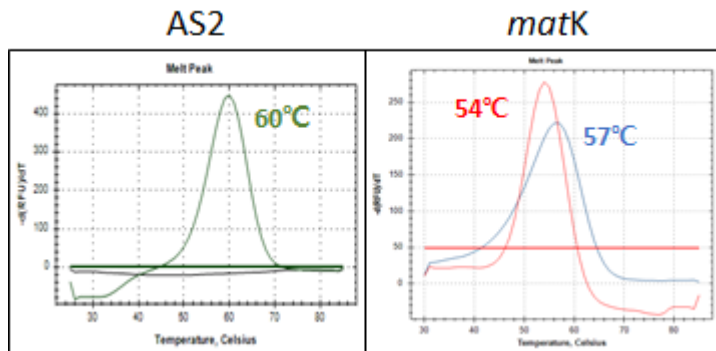
- **결과 확인** : Real-time PCR 장비의 Melt peak 탭에서 melt peak의 T<sub>m</sub> 확인



## ○ 실시간 유전자 증폭산물의 결과 판정

## - Melt peak Tm 확인

: 종 특이 프라이머(Species-specific primer) 및 프로브(PNA probe)를 사용한 Real-time PCR 결과 표적 산물의 생성유무를 판단하기 위하여 melt peak의 Tm을 확인하여 제시한 판정표에 따라 부테아 수페르바의 혼입여부를 판별



Target	Gene	Fluorescence	Species
<i>B. superba</i> detection	<i>matK</i> Melt peak Tm	FAM	<i>B. superba</i> 55~59°C
<i>P. lobate</i> , <i>P. mirifica</i> 구분용	<i>matK</i> Melt peak Tm	TxR	<i>P. lobata</i> 63~67°C
<i>B. superba</i> detection	AS2 Melt peak Tm	HEX	<i>B. superba</i> 58~62°C

부테아 수페르바 PNA 프로브를 이용한 Real-time PCR 결과

< Melt peak Tm을 이용한 부테아 수페르바 혼입판별 판정표 >

I-5

## 알러지질환 항히스타민제(36종) 분석법

### 배 경

- 인천공항 비만치료제, 항우울제, 이뇨제, 항히스타민제 등 위해성분이 함유된 불법다이어트 약품 밀수입 여행객 적발('12. 7.)
- 서울시 특별사법경찰(특사경)은 위조, 부정 의약품을 판매한 성인용품점 23개 적발, 수면제(독실아민), 진정제(디펜히드라민), 항히스타민(클로르페니라민) 성분 등 불법 의약품을 싼 가격으로 구입하여 폭리를 취함 ('13. 2.)



### 특 성

- 알레르기 염증 때 분비되는 많은 화학매개체중 히스타민이 가장 중요한 매개체가 되며 알레르기 비염 등 여러 증상을 일으킴. 분비된 히스타민은 히스타민 수용체와 결합하여 혈관을 확장시키고 혈관 투과력을 증가시키며 부교감신경을 자극하여 분비선의 분비를 증가시키고 감각신경의 말단을 자극하여 가려움증, 재채기, 분비물 증가를 일으킴
- 1세대 항히스타민제는 졸음 때문에 치명적인 자동차 사고의 원인이 될 수 있으며 마약이나 최면제보다 작업장 사고의 위험이 높고 소아에서는 학습 수행능력을 감소시킴
- 2세대 항히스타민제는 중추신경계로의 침투력이 거의 없어 진정작용이 없거나 낮음

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

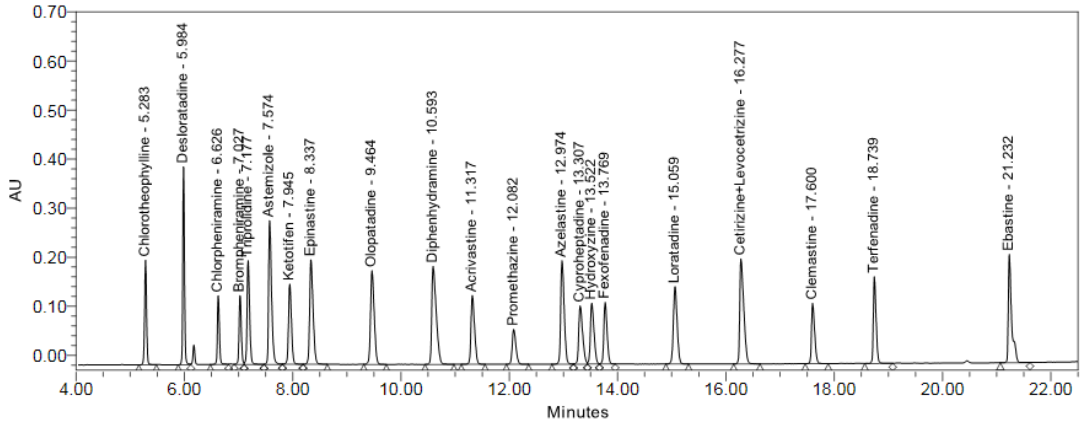
- 표준액 조제 : 표준액 1\* Dimenhydrinate 등 22종  
표준액 2\* Azatadine 등 14종  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 5~20 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

- \* 표준액1 : Dimenhydrinate (Chlorotheophylline+Diphenhydramine), Desloratadine, Chlorpheniramine maleate, Brompheniramine maleate, Triprolidine hydrochloride, Astemizole, Ketotifen fumarate salt, Epinastine hydrochloride, Olopatadine hydrochloride, Diphenhydramine hydrochloride, Acrivastine, Promethazine hydrochloride, Azelastine hydrochloride, Cyproheptadine hydrochloride sesquihydrate, Hydroxyzine hydrochloride, Fexofenadine hydrochloride, Loratadine, Cetirizine hydrochloride, Levocetirizine dihydrochloride, Clemastine fumarate salt, Terfenadine, Ebastine
- \* 표준액2 : Azatadine, Dimetindene, Tripelennamine, Rupatadine, Carbinoxamine, Dexbrompheniramine, Mizolastine, Cyclizine, Diphenylpyraline, Pimethixene, Oxatomide, Mequitazine, Thiethylperazine, Deptropine

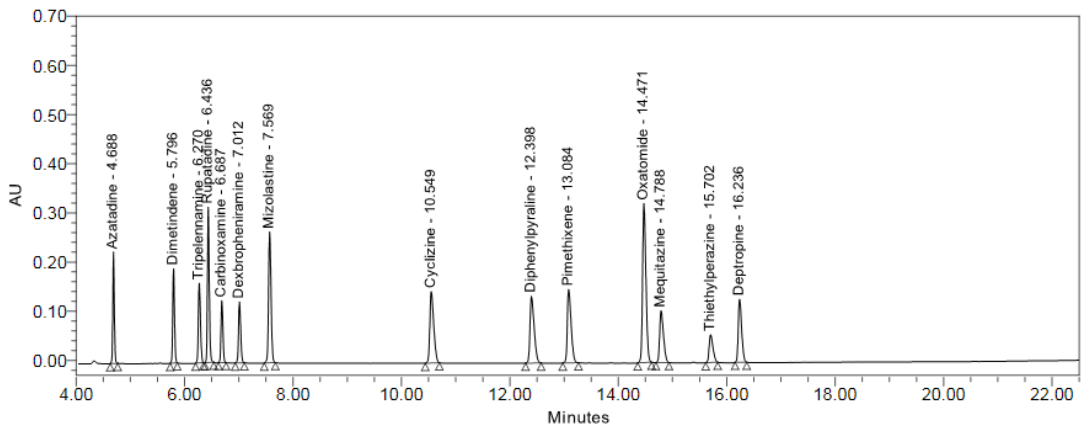
#### ○ Analytical condition of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 150 mm, 1.7 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 5 mM Sodium phosphate in Water (pH 2.3, H <sub>3</sub> PO <sub>4</sub> ) (B) 90% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	0.8	80	20
	3.5	65	35
	6.0	65	35
	12.8	50	50
	17.8	25	75
	20.0	0	100
	24.0	0	100
	24.1	90	10
	27.0	90	10
• Flow Rate	0.13 mL/min		
• Inj. Volume	2 µL		
• UV Detection	205 nm		
• PDA Range	190~400 nm		

### ○ Chromatogram

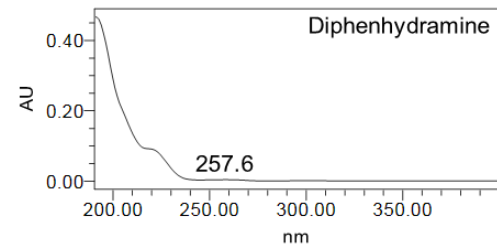
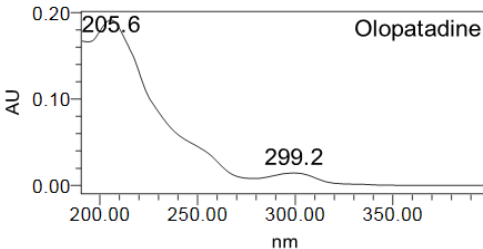
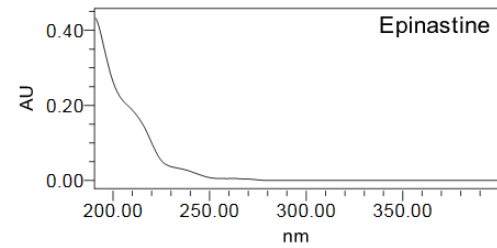
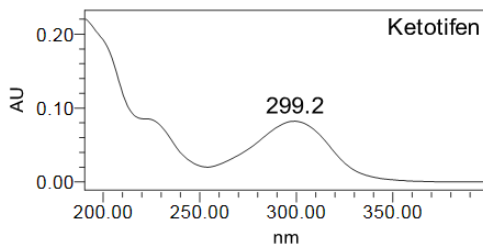
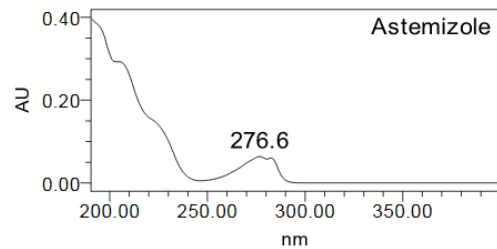
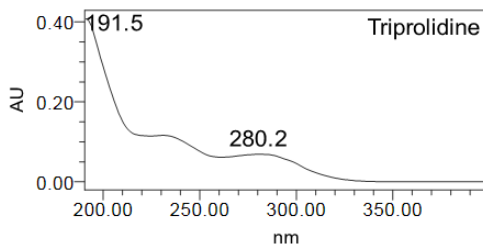
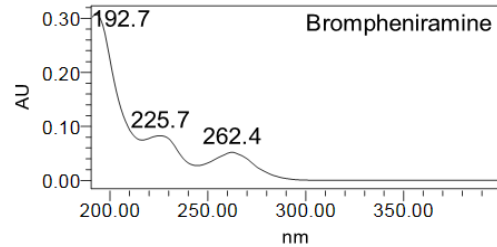
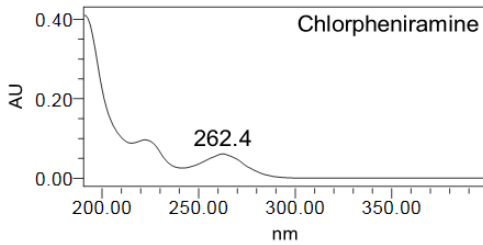
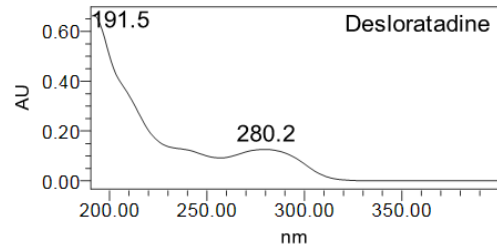
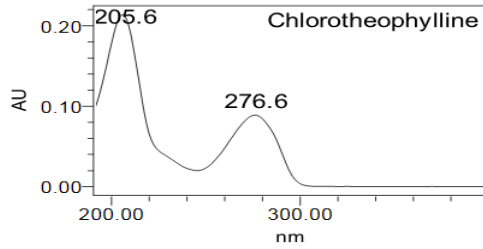


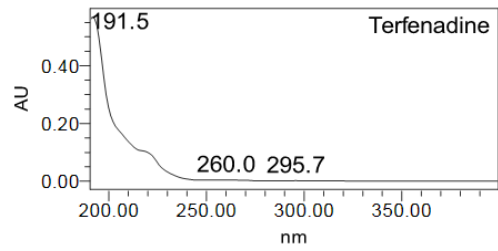
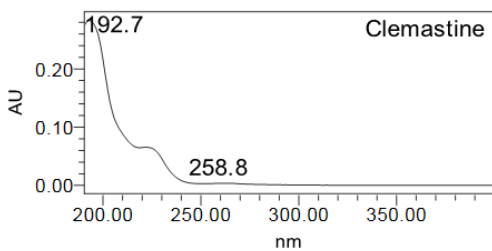
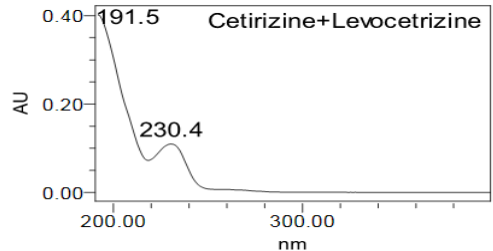
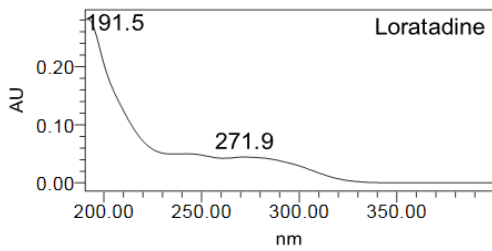
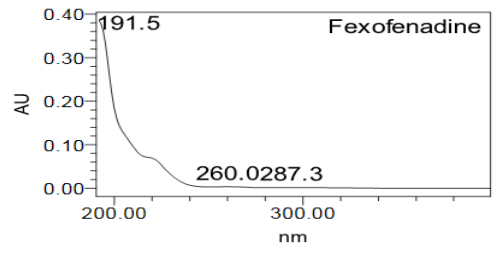
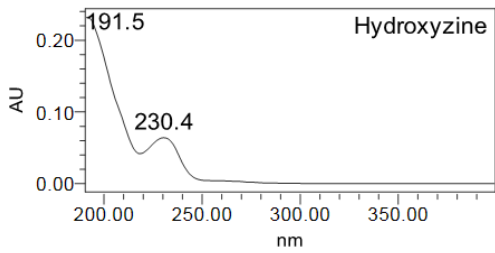
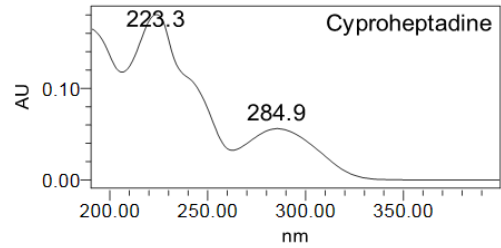
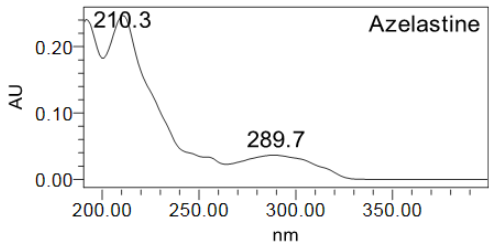
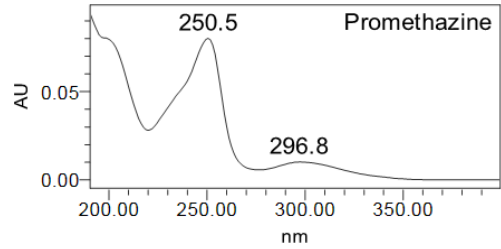
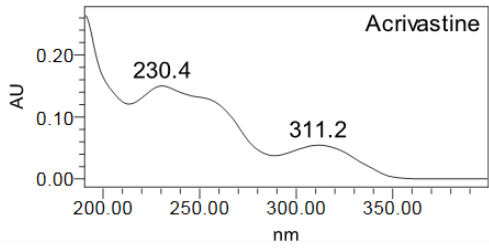
[표준액 1]



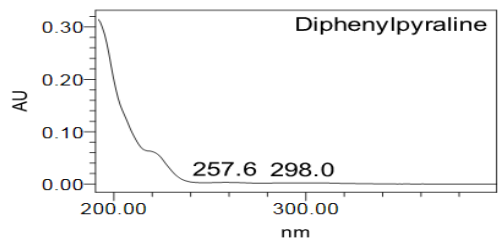
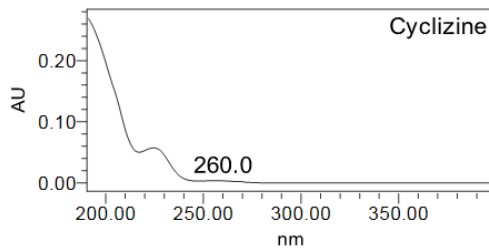
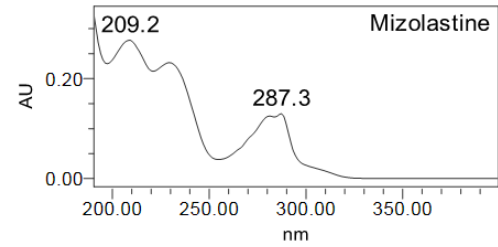
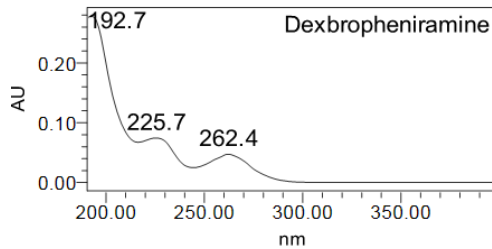
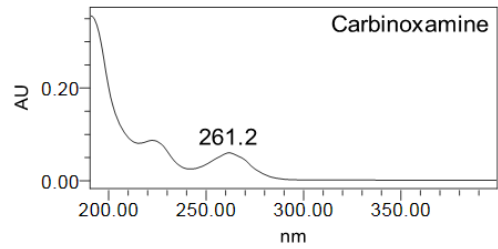
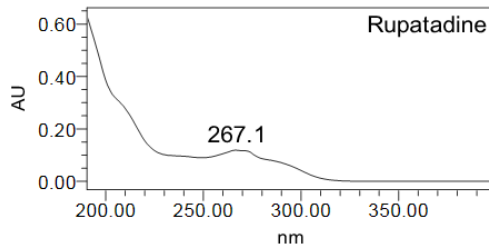
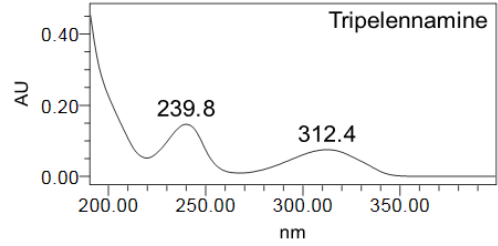
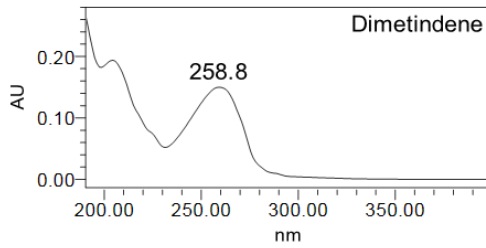
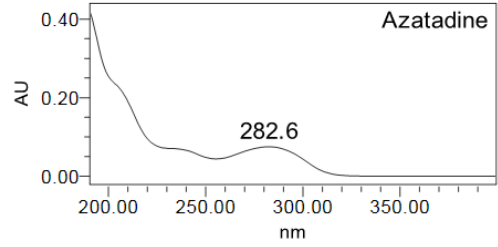
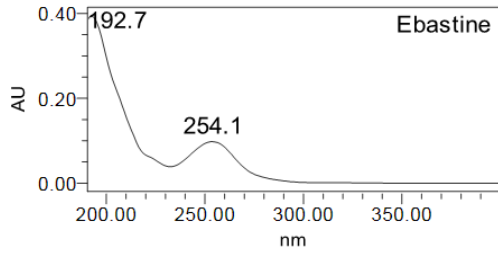
[표준액 2]

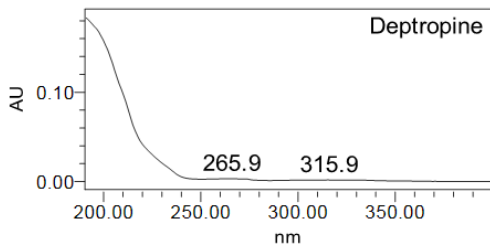
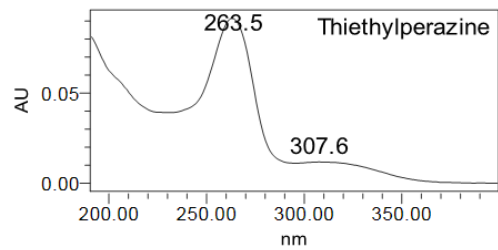
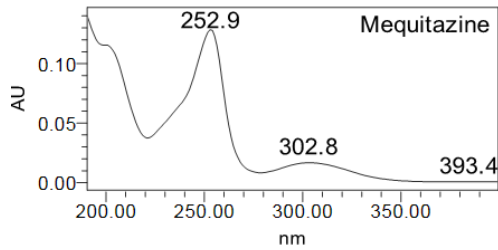
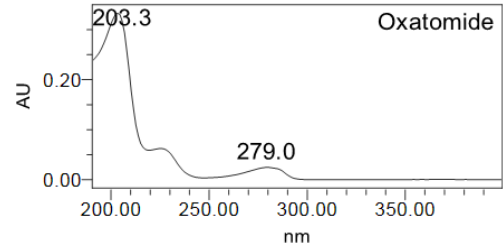
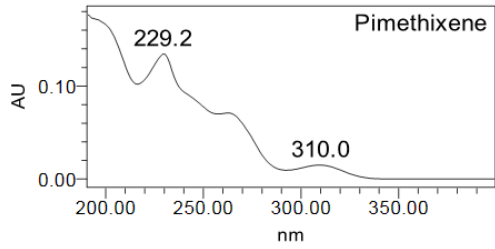
○ PDA Spectrum





I -5. 알러지질환 항히스타민제(36종) 분석법







## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	2.0	95	5
	3.0	80	20
	10.0	55	45
	11.0	0	100
	12.0	0	100
	12.5	95	5
	15.0	95	5
• Flow Rate	0.25 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	3.5 kV
• Desolvation Temp.	200°C
• Desolvation Gas Flow	500 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Prodeuct Ion ( $m/z$ )	CE (eV)
Chlorotheophylline	+	214.90	35	157.92	20
				196.80	15
				152.06	35
Dimen hydrinate	+	256.22	18	165.13	35
				167.08	17
				259.01	30
Desloratadine	+	311.05	15	281.93	30
				293.95	35
				167.06	37
Chlorpheniramine	+	275.13	25	201.00	34
				230.05	14
				167.06	42
Brompheniramine	+	319.22	25	245.20	38
				274.12	21
				167.07	44
Triprolidine	+	279.29	35	193.09	34
				208.17	19
				135.03	40
Astemizole	+	459.35	40	218.15	25
				308.20	25
				96.02	20
Ketotifen	+	310.23	30	213.11	32
				130.99	34
				193.15	34
Epinastine	+	250.16	50	208.17	27
				141.06	30
				165.11	26
Olopatadine	+	338.29	40	247.16	24
				232.15	36
				260.17	26
Acrivastine	+	349.29	25	278.18	16

표준액 1

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Prodeuct Ion ( $m/z$ )	CE (eV)
Promethazine	+	285.22	25	86.05	16
				198.06	22
				240.17	20
Azelastine	+	382.30	30	112.05	24
				159.06	36
				271.15	30
Cyproheptadine	+	288.29	40	191.12	32
				202.17	52
				215.17	42
Hydroxyzine	+	375.32	20	165.05	50
				166.06	40
				201.08	20
Fexofenadine	+	502.46	38	171.15	40
				466.47	30
				484.50	35
Loratadine	+	383.29	38	259.13	36
				267.06	36
				337.21	30
Cetirizine	+	403.05	25	165.97	30
				200.93	25
				367.01	25
Levocetirizine	+	389.00	25	164.98	55
				200.93	20
				130.05	10
Clemastine	+	344.27	20	180.02	33
				215.01	17
				262.10	30
Terfenadine	+	472.32	40	436.20	25
				454.22	20
				167.00	35
Ebastine	+	470.32	35	203.08	30
				302.12	20

표준액 1

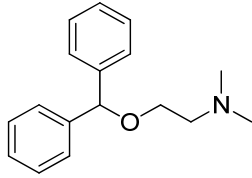
Compound	Ion mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Azatadine	+	291.10	25	164.95	45
				232.99	30
				248.00	20
Dimetindene	+	293.10	30	105.95	30
				140.95	35
				247.99	20
Tripeleennamine	+	256.10	20	90.95	30
				118.95	30
				211.01	15
Rupatadine	+	416.05	35	105.98	40
				259.00	30
				282.00	20
				308.98	20
Carbinoxamine	+	291.05	20	71.98	20
				166.94	30
				201.92	15
Dexbrompheniramine	+	319.05	20	117.98	40
				166.95	40
				245.86	30
				273.92	20
				108.95	40
Mizolastine	+	433.07	40	199.00	30
				253.97	30
				308.03	25
				114.95	45
Cyclizine	+	267.08	20	151.94	35
				166.97	15
				97.98	30
Diphenylpyraline	+	282.10	35	166.98	25
				78.96	35
				93.98	30
Pimethixene	+	294.00	35	236.96	20
				262.98	20
				151.97	45
				166.98	20
Oxatomide	+	427.11	30	259.02	15

표준액 2

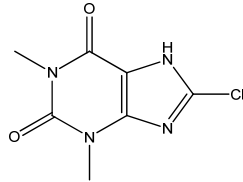
Compound	Ion mode	Precursor Ion ( <i>m/z</i> )	CV (V)	Product Ion ( <i>m/z</i> )	CE (eV)
Mequitazine	+	323.05	35	78.98	45
				110.00	30
				123.99	25
Thiethylperazine	+	400.05	30	113.04	30
				141.03	20
				237.90	40
				299.90	20
				114.95	40
Deptropine	+	334.10	35	140.00	25
				177.96	45
				193.00	30

표준액 2

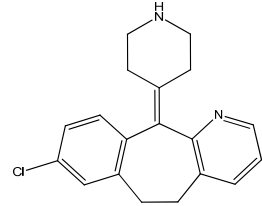
■ 구조식



① Diphenhydramine  
[C<sub>17</sub>H<sub>21</sub>NO]

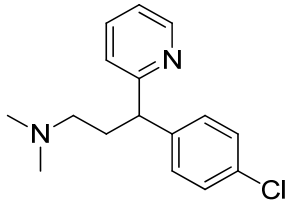


② Chlorotheophylline  
[C<sub>7</sub>H<sub>7</sub>ClN<sub>4</sub>O<sub>2</sub>]

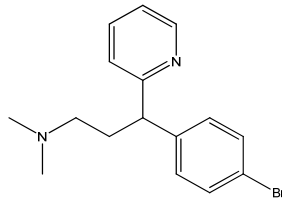


Desloratadine  
[C<sub>19</sub>H<sub>19</sub>ClN<sub>2</sub>]

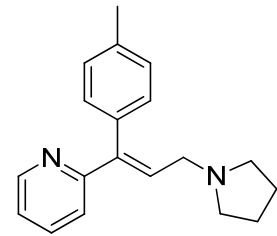
Dimenhydrinate  
[①+②]



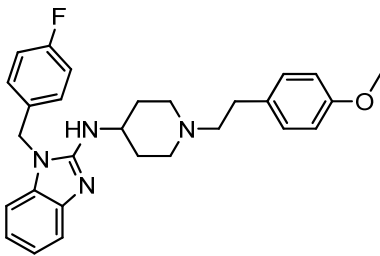
Chlorpheniramine  
[C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>]



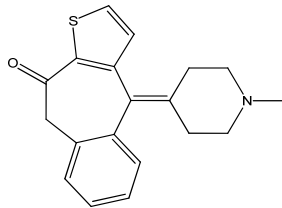
Brompheniramine  
[C<sub>16</sub>H<sub>19</sub>BrN<sub>2</sub>]



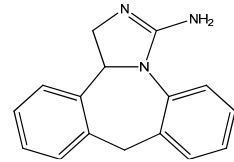
Triprolidine  
[C<sub>19</sub>H<sub>22</sub>N<sub>2</sub>]



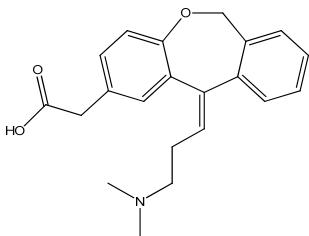
Astemizole  
[C<sub>28</sub>H<sub>31</sub>FN<sub>4</sub>O]



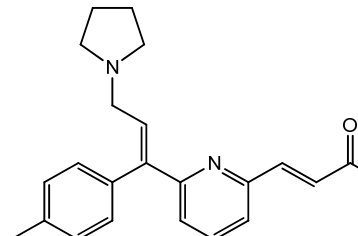
Ketotifen  
[C<sub>19</sub>H<sub>19</sub>NOS]



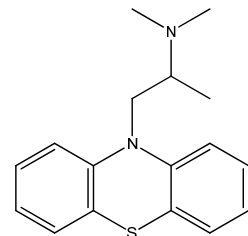
Epinastine  
[C<sub>16</sub>H<sub>15</sub>N<sub>3</sub>]



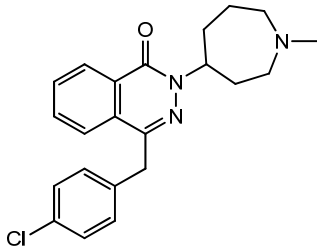
Olopatadine  
[C<sub>21</sub>H<sub>23</sub>NO<sub>3</sub>]



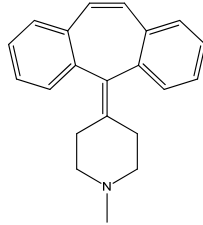
Acrivastine  
[C<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>]



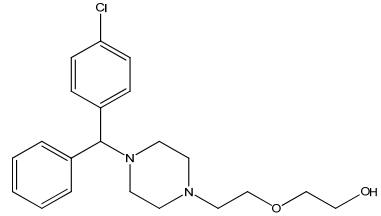
Promethazine  
[C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>S]



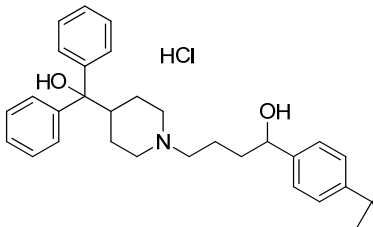
Azelastine  
[C<sub>22</sub>H<sub>24</sub>ClN<sub>3</sub>O]



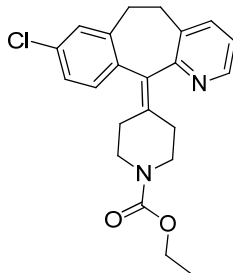
Cyproheptadine  
[C<sub>21</sub>H<sub>21</sub>N]



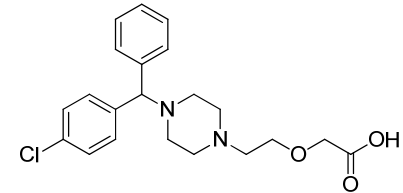
Hydroxyzine  
[C<sub>21</sub>H<sub>27</sub>ClN<sub>2</sub>O<sub>2</sub>]



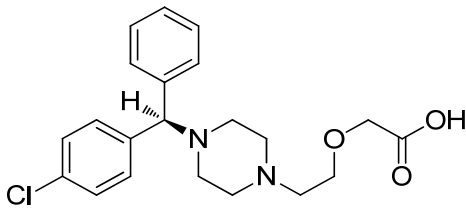
Fexofenadine  
[C<sub>32</sub>H<sub>39</sub>NO<sub>4</sub>]



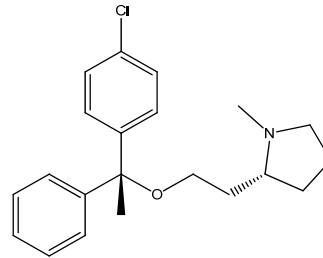
Loratadine  
[C<sub>22</sub>H<sub>23</sub>ClN<sub>2</sub>O<sub>2</sub>]



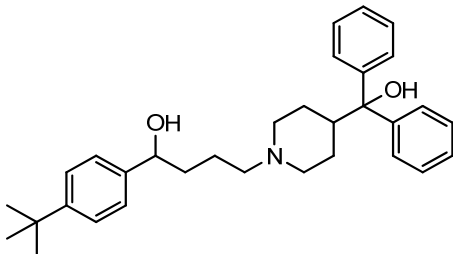
Cetirizine  
[C<sub>21</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>3</sub>]



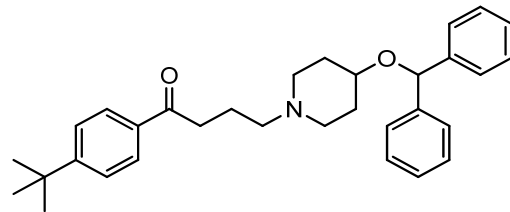
Levocetirizine  
[C<sub>21</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>3</sub>]



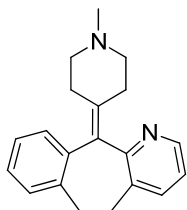
Clemastine  
[C<sub>21</sub>H<sub>28</sub>ClNO]



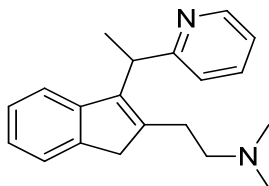
Terfenadine  
[C<sub>32</sub>H<sub>41</sub>NO<sub>2</sub>]



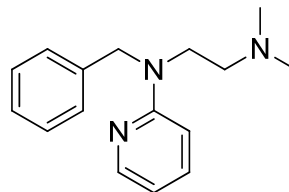
Ebastine  
[C<sub>32</sub>H<sub>39</sub>NO<sub>2</sub>]



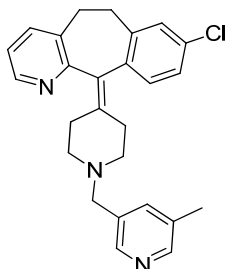
Azatadine  
[C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>]



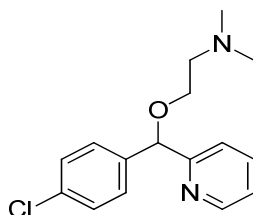
Dimetindene  
[C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>]



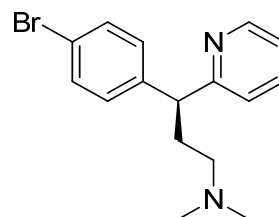
Tripelennamine  
[C<sub>16</sub>H<sub>21</sub>N<sub>3</sub>]



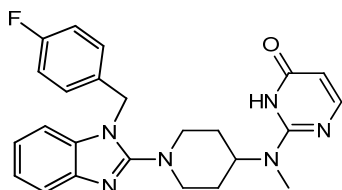
Rupatadine  
[C<sub>26</sub>H<sub>26</sub>ClN<sub>3</sub>]



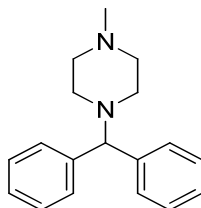
Carbinoxamine  
[C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>O]



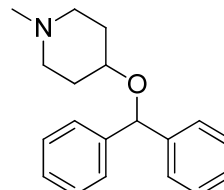
Dexbromopheniramine  
[C<sub>16</sub>H<sub>19</sub>BrN<sub>2</sub>]



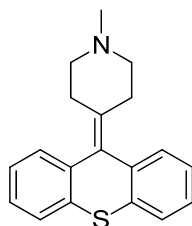
Mizolastine  
[C<sub>24</sub>H<sub>25</sub>FN<sub>6</sub>O]



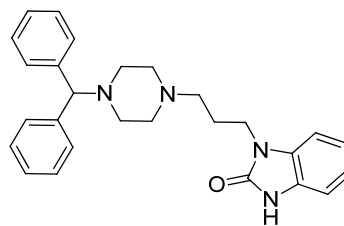
Cyclizine  
[C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>]



Diphenylpyraline  
[C<sub>19</sub>H<sub>23</sub>NO]

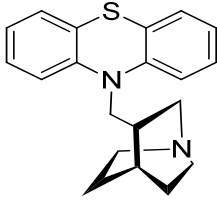


Pimethixene  
[C<sub>19</sub>H<sub>19</sub>NS]

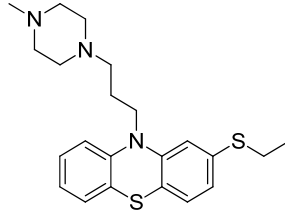


Oxatomide  
[C<sub>27</sub>H<sub>30</sub>N<sub>4</sub>O]

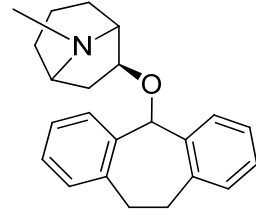




Mequitazine  
[C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>S]



Thiethylperazine  
[C<sub>22</sub>H<sub>29</sub>N<sub>3</sub>S<sub>2</sub>]



Deptropine  
[C<sub>23</sub>H<sub>27</sub>NO]

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## 1-6 주류 중 Potassium aluminium silicate 분석법

### ■ 배경

- 국내에서 식용으로 사용할 수 없는 식품첨가물인 Potassium aluminium silicate이 함유된 주류제품 (일명: 우주술)을 불법제조 및 인터넷 블로그나 중고거래 인터넷을 통해 몰래 판매한 일당이 적발('15. 10.)
- 허용되지 않는 식품첨가물을 사용한 수입 과실주 회수 조치('17. 2.)



### ■ 특 성

- Potassium aluminium silicate는 식품 중 착색보조의 목적으로 사용되는 첨가물로서, Titanium dioxide와 Iron oxide의 코팅에 따라 3가지로 분류 (Type 1: Titanium dioxide, Type 2: Iron oxide, Type 3: Titanium dioxide와 Iron oxide)
- 현재 국내에서는 식품첨가물로 지정되지 않음(일본, 중국에서도 허용금지)

### ■ 분석사례

- L;CURE (무허가제조): Potassium aluminium silicate 검출
- PLATINUM, MAVAM (수입과일주): Potassium aluminium silicate 검출

■ 분석법

1. XRF, XRD법

○ 전처리 방법

- 시료 채취 : 주류 전량 취함 → 여과지(Whatman No.1)로 감압 여과 → 30분 건조 (105°C)  
→ XRF: 여과된 건조물을 시료대 위에 올림
- → XRD: 여과된 건조물을 샘플홀더 위에 올림

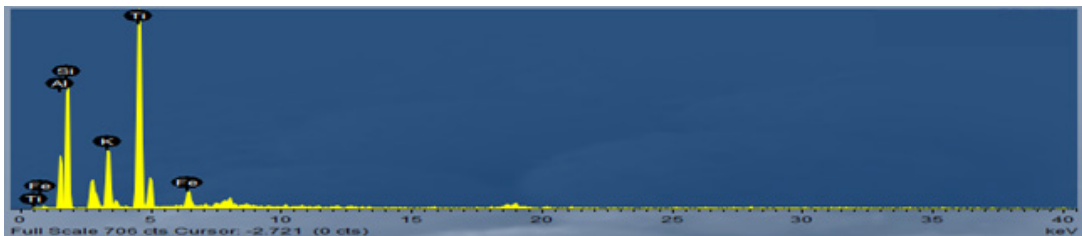
○ Analytical condition of XRF

• Instrument	Horiba Scientific, XGT-7200
• Acquisition Time	300 s
• XGT Diameter	10 μm
• X-ray tube voltage	50 kV
• Current	1,000 mA
• Analysis object range	<sup>11</sup> Na ~ <sup>92</sup> U (K, Al, Si)

- X-선 발생기 확인 조건

구분	Cu-Kα (ROI:7.82~8.25 keV)		Al-Kα (ROI:1.33~1.63 keV)	
	Vaccum	VAC C (Chamber)	VAC C (Chamber)	VAC P (Probe)
XGT		50 kV, 1 mA(10 μm)/ 0.5 mA(100 μm)	50 kV, 1 mA	50 kV, 1 mA
	Power			
	Cond.	100 sec / P3		
10 μm	허용범위	> 2,000 cps/mA	> 100 cps/mA	> 50 cps/mA
100 μm	허용범위	> 12,000 cps/mA	> 1,000 cps/mA	> 500 cps/mA

- 대표적인 XRF 스펙트럼



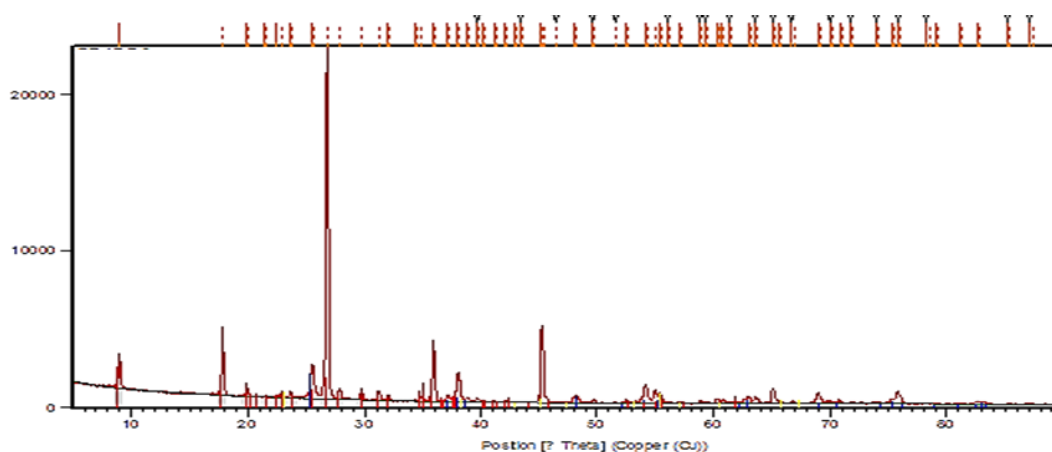
### ○ Analytical condition of XRD

• Instrument	NL/X'Pert PRO MPD, PANalytical
• Configuration	Spinner Stage
• Anode Material	CuK $\alpha$ ,
• Generator Voltage	40 kV
• Tube Current	40 mA
• Scan Axis	Gonio
• Filter	Ni
• Scan step size	0.017°
• Time per step	50 s
• Diffraction Degree	5° ~ 90°

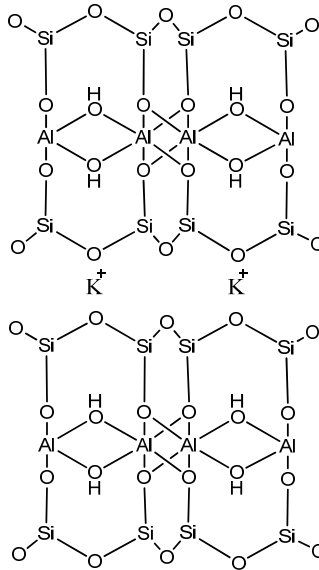
#### - Potassium aluminium silicate의 대표적인 회절피크

No.	d [Å]	2 $\theta$ [°]	허용범위[°]
1	10.02320	8.815	± 0.2°
2	5.00031	17.723	
3	3.33111	26.741	
4	2.49798	35.922	
5	1.99766	45.362	

#### - 대표적인 XRD 스펙트럼



## ■ 구조식



Potassium aluminium silicate  
 $\text{KAl}_2[\text{AlSi}_3\text{O}_{10}](\text{OH})_2$

## ■ 참고문헌

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2. Guggenheim, S., Chang, Y.-H., Koster-van Groos, A.F., Muscovite dehydroxylation: High temperature studies, *American Mineralogist*. 72, 537-550 (1987)

## 1-7 화장품(립스틱류) 중 타르색소(21종) 분석법

### 배 경

- 발암논란 타르색소인 적색 2호, 적색 102호 2종 영유아 화장품에 사용 금지 ('16.02.)
- 일부 국내 기업 타르색소 사용으로 해당품목 판매업무정지, 광고업무 정지 등 행정처분 ('14.01.)
- 미국산 립밤에서 사용 금지된 타르 색소 '적색 225호'가 검출되어 판매 금지 및 회수 조치 ('12.09.)

**발암논란 타르색소 2종 영유아 화장품 사용금지**

(서울=연합뉴스) 서한기 기자 = 적색 2호와 적색 102호 등 타르 색소 2종은 영유아용 화장품에 사용하지 못한다.

식품의약품안전처는 이런 내용의 '화장품의 색소 종류와 기준 및 시험방법'을 일부 개정해 고시하고, 3월부터 시행한다고 25일 밝혔다.

식약처 화장품정책과는 "영유아는 손 빨기 등을 통해 이들 타르 색소를 먹을 우려가 있는 등 안전성 논란이 있어 안전관리 강화차원에서 영유아용 제품에는 사용 금지하기로 했다"고 설명했다.

**아름다운화장품 6개월 판매업무정지 행정처분**

식약처, 미고시 타르색소 사용 제품 수입 적발

01나리 기자 nalliee@co.sinkorea 기사 입력 2014-01-06 14:50

[코스인코리아닷컴 이나리 기자] 식품의약품안전처(처장 경순)은 아름다운화장품, 화이, 라비다, 리핀코스메틱, 광덕신약, 피토스 등 6개 기업을 화장품법 위반으로 판매업무정지, 광고업무정지 등 행정처분을 공표했다.

**식품의약품안전처 화장품 행정처분 내용**

업체명	소재지	제품명	위반내용	처분처분내용
주(아름다운) 화장품	충남 진안 시	레블론 프로페셔널 이케이트 볼룬드 디팬글링 립 컨디셔너	○ '화장품의 타르색소와 기준 및 시험방법'에 따라 고시된 타르색소인 'CI 42520(Basic Violet 2)'이 사용된 수입화장품 '레블론 프로페셔널 이케이트 볼룬드 디팬글링 립 컨디셔너'를 2012.10.19. 수입하여 판매함	해당 품목판매업무 정지 6개월
(주)화이	경주광역시 동구	노도리 보습크림	의약품으로 요인할 수 있는 문구인 '이토의 거장 NO. 1'에 기재된 문구(이토의 거장)가 화장품의 안전 여재되어 전체 화장품의 안전성을 보장할 수 없다. 등의 광고를 하여 판매한 사실이 있음	해당품목 광고업무 정지 3개월

▲ 자료 출처 : 식품의약품안전처.

### 특 성

- 화장품에 사용할 수 있는 타르색소는 총 81종으로 화장품의 유형별 또는 사용부위에 따라 제한적으로 사용할 수 있도록 기준을 정하고 있음 [고시 제2016-49호] 화장품의 색소 종류와 기준 및 시험방법
- 이 중 눈 주위 및 입술에 사용 금지 및 염모용 화장품에만 사용할 수 있는 색소 등 54종이 사용제한 품목으로 지정되어 있음

## ■ 분석법

### 1. UPLC법

#### ○ 전처리 방법

- 표준액 조제 : 표준액 1\* Pyranine conc 등 15종

→ 각각 일정량 취함 → 100% 증류수 가함(1,000 µg/mL)

→ 20% 메탄올을 가함 → 최종 농도(약 5~30 µg/mL)

표준액 2\* Tetrabromofluorescein 등 6종

→ 각각 일정량 취함 → 100% 클로로포름 가함(1,000 µg/mL)

→ 100% 메탄올을 가함 → 최종 농도(약 5~15 µg/mL)

- 검액 조제 : ① 약 0.2 g 취함 → 20% 메탄올:100% 클로로포름(9:1) 50 mL 가함

→ 30분 진탕 → 원심분리(3,000 rpm, 5분)

② 「①」의 메탄올층 전량을 취함, 약 45 mL → 20% 메탄올을 가함

→ 50 mL 정용 → 실린지필터(0.2 µm PDVE) 여과

→ 최종검액(A)(표준액 1로 분석)

③ 「①」의 클로로포름층, 약 5 mL

→ SPE(Solid Phase Extraction, HLB C<sub>18</sub> 500 mg)

→ Conditioning(증류수, 5 mL) → Equilibration(100% 메탄올, 5 mL)

→ Loading(「①」의 클로로포름층, 약 5 mL)

→ Elution(메탄올:아세토니트릴(1:1), 45 mL)

→ 메탄올:아세토니트릴(1:1) 가함 → 50 mL 정용

→ 실린지 필터(0.2 µm PDVE) 여과

→ 최종검액(B)(표준액 2로 분석)

\* 표준액 1 : Pyranine conc, Tartrazine, Amaranth, Indigo carmine, New cocchine, Naphthol yellow S, Sunset yellow FCF, Fast acid magenta, Allura red AC, Uranine, Ponceau SX, Brilliant blue FCF, Eosine YS, Orange II, Alizurool purple

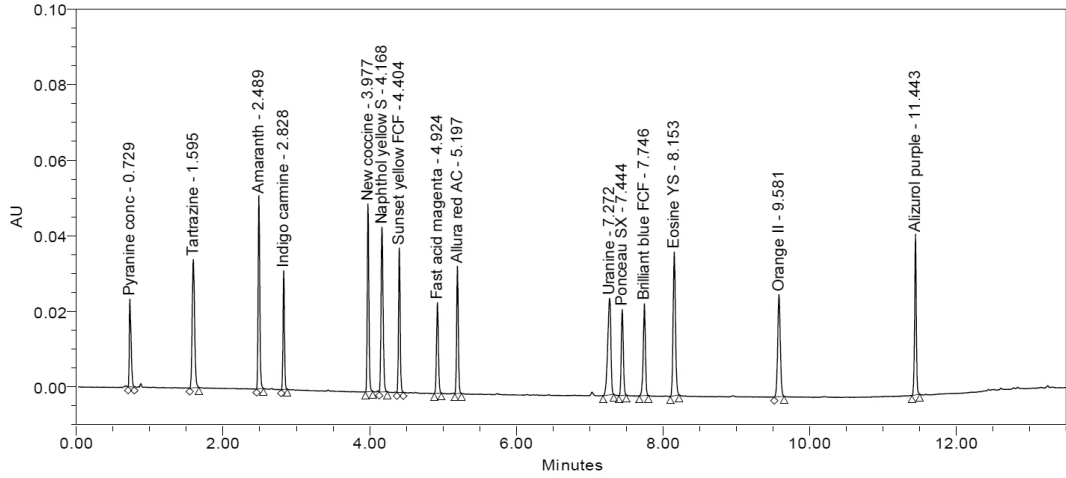
\* 표준액 2 : Tetrabromofluorescein, Tetrachlorotetrabromofluorescein, Quinoline yellow SS, Alizurine purple SS, Sudan III, Quinizarine green SS

○ Analytical conditions of HPLC

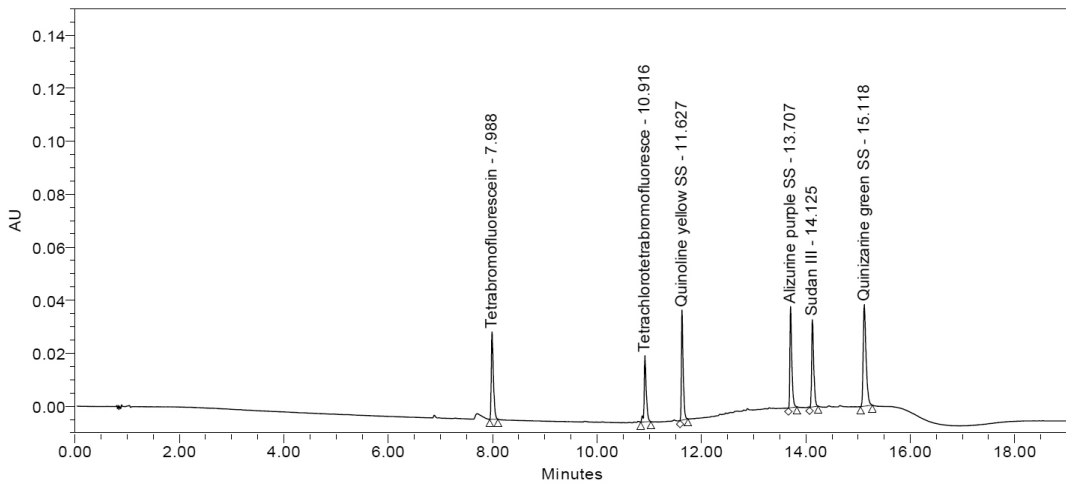
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	40℃		
• Mobile Phase	(A) 10 mM Ammonium formate in Water (B) Acetonitrile : Methanol = 1 : 1		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	6.0	60	40
	9.0	45	55
	11.0	5	95
	14.0	5	95
	16.0	95	5
	19.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 μL		
• UV Detection	254 nm		
• PDA Range	190~700 nm		



○ Chromatogram

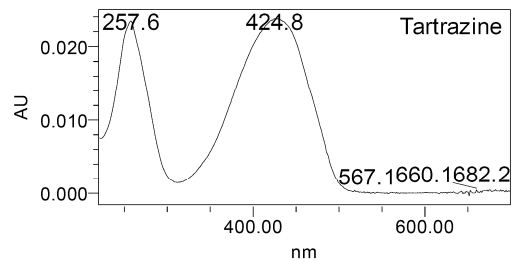
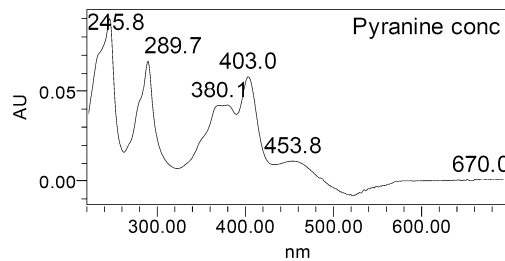


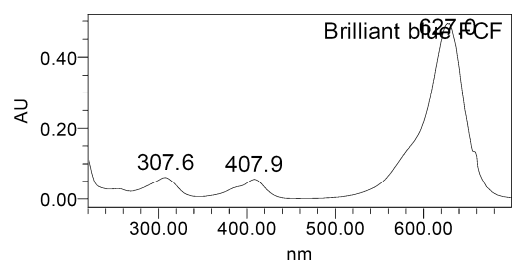
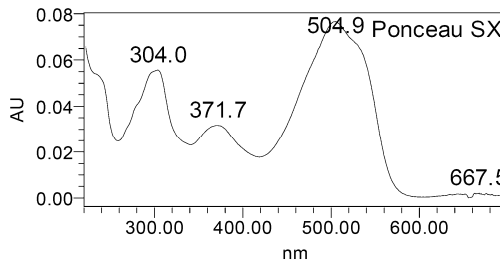
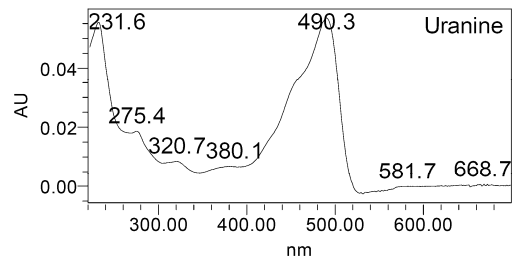
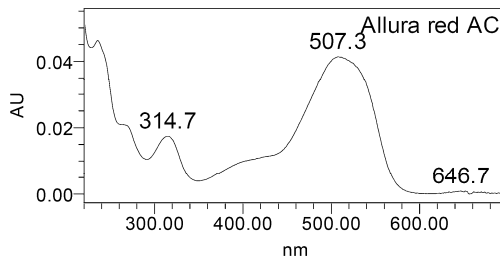
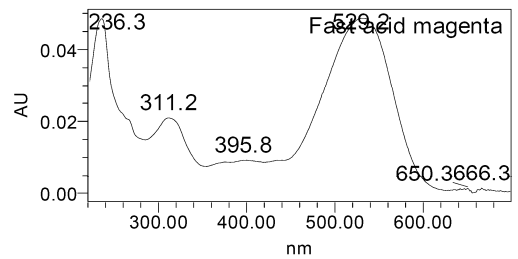
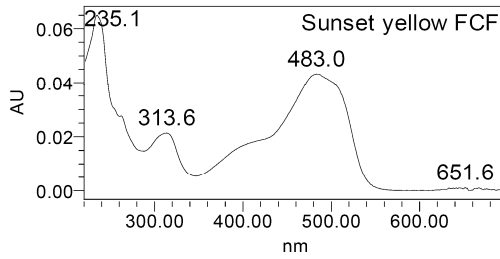
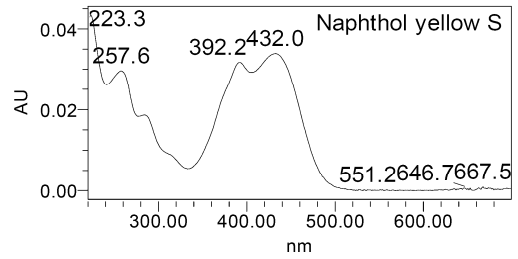
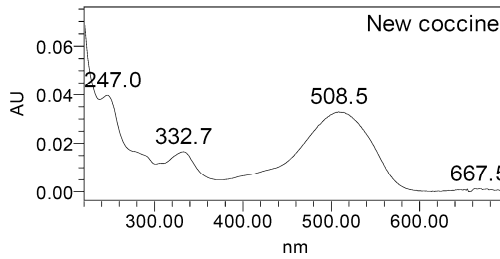
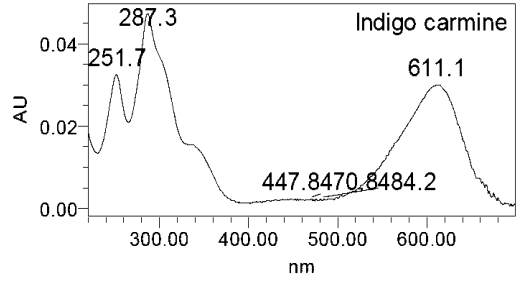
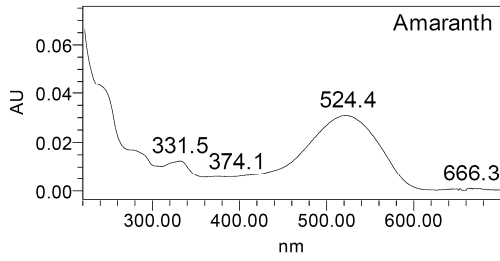
[표준액 1]



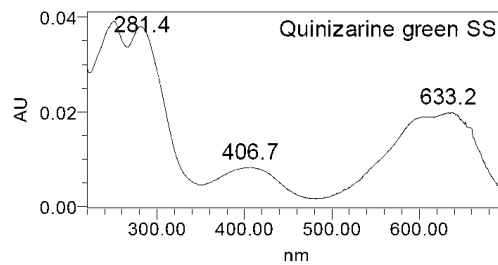
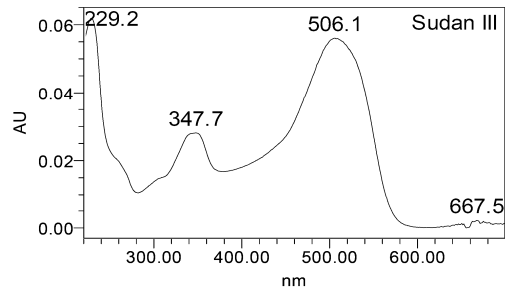
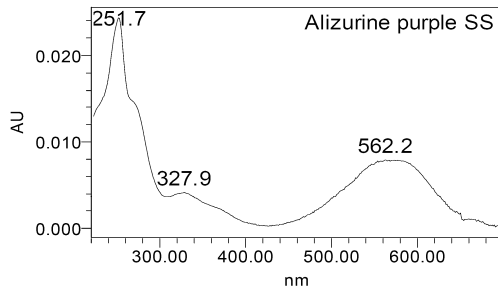
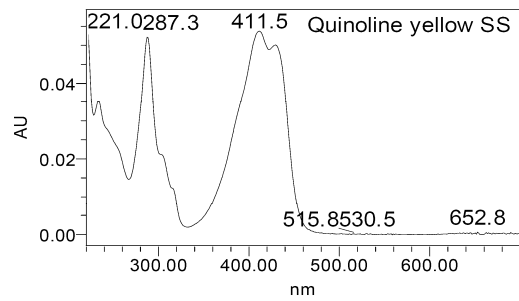
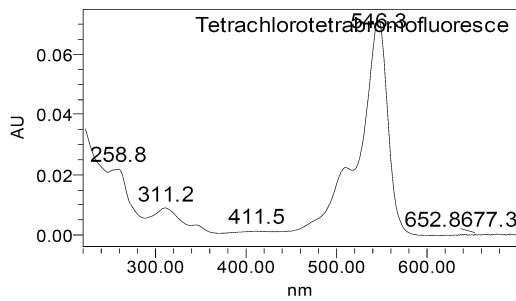
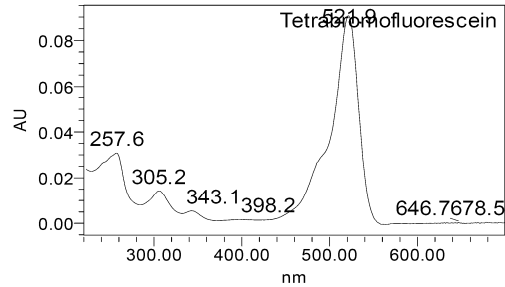
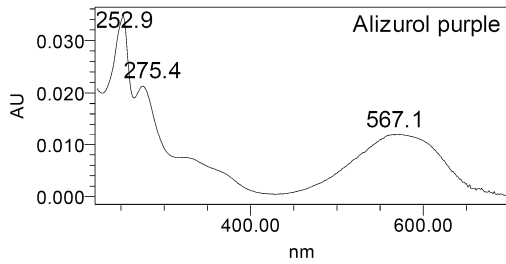
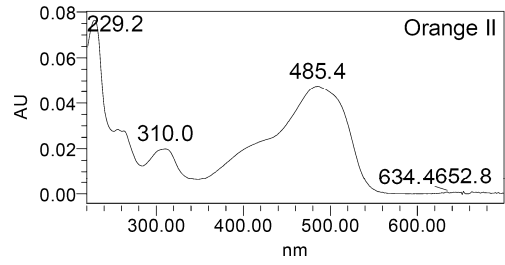
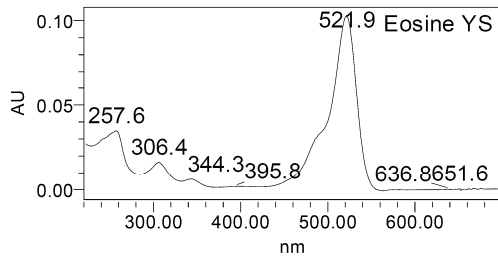
[표준액 2]

○ PDA Spectrum





I -7. 화장품(립스틱류) 중 타르색소(21종) 분석법



## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	UPLC Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 10mM Ammonium formate in Water (B) Acetonitrile : Methanol = 1 : 1		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	4.0	60	40
	6.0	30	70
	8.0	5	95
	10.0	5	95
	12.0	95	5
	15.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+), (-)
• Capillary Voltage	2.6 kV
• Desolvation Temp.	400°C
• Desolvation Gas Flow	800 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	0 L/Hr (N <sub>2</sub> )

## ○ Analyte MS/MS transition

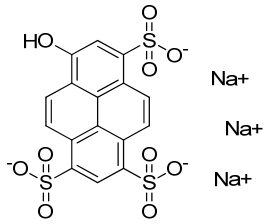
Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (V)
Pyranine conc	-	227.89 <sup>a)</sup>	20	79.89	20
				187.97	15
Tartrazine	-	232.96 <sup>a)</sup>	10	79.89	30
				197.95	15
				141.99	35
Amaranth	-	267.94 <sup>a)</sup>	25	205.99	20
				233.99	15
				261.21	35
Indigo carmine	-	421.19 <sup>b)</sup>	40	277.21	35
				341.21	25
				157.95	25
New coccine	-	267.93 <sup>a)</sup>	15	205.98	10
				221.98	20
				171.06	35
Sunset yellow FCF	-	407.22 <sup>b)</sup>	40	207.10	30
				327.21	25
				173.09	30
Naphthol yellow S	-	313.14 <sup>b)</sup>	40	233.14	25
				296.13	20
				185.12	35
Fast acid magenta	-	422.23 <sup>b)</sup>	35	249.14	25
				317.12	25
				207.10	30
Allura red AC	-	451.24 <sup>b)</sup>	35	371.26	25
				170.08	40
				199.11	35
Ponceau SX	-	435.24 <sup>b)</sup>	30	355.28	20
				170.06	55
				561.39	45
Brilliant blue FCF	-	747.49 <sup>b)</sup>	40	202.20	50
				231.22	40
				287.27	35
Uranine	+	333.29 <sup>e)</sup>	50	441.14	35
				519.07	30
Eosine YS	-	643.02 <sup>b)</sup>	35		

표  
준  
액  
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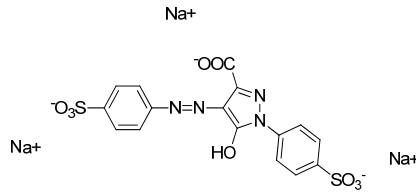
	Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (V)
표준액 1	Orange II	-	327.21 <sup>b)</sup>	35	156.04	30
					171.07	25
					247.23	20
	Alizuroil purple	-	408.28 <sup>b)</sup>	40	185.11	30
					310.26	30
					328.29	25
표준액 2	Tetrabromofluorescein	+	645.06 <sup>e)</sup>	40	487.16	45
					538.09	40
	Tetrachlorotetrabromo fluorescein	-	780.89 <sup>d)</sup>	35	656.94	30
					700.92	25
	Quinoline yellow SS	+	274.28 <sup>e)</sup>	35	217.23	35
					228.23	30
					256.24	25
	Alizurine purple SS	+	330.34 <sup>e)</sup>	35	210.17	30
					238.20	25
					312.31	25
	Sudan III	-	351.31 <sup>d)</sup>	40	197.17	25
					218.19	25
313.31					30	
Quinizarine green SS	+	419.42 <sup>e)</sup>	45	328.34	35	
				404.39	30	

<sup>a)</sup> [(M-nNa+nH)-H]<sup>2-</sup>, <sup>b)</sup> [(M-nNa+nH)-H]<sup>-</sup>, <sup>c)</sup> [(M-nNa+nH)+H]<sup>+</sup>, <sup>d)</sup> [M-H]<sup>-</sup>, <sup>e)</sup> [M+H]<sup>+</sup>

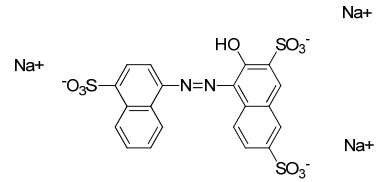
■ 구조식



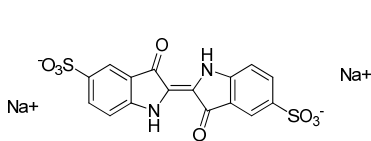
Pyranine conc  
[C<sub>16</sub>H<sub>7</sub>Na<sub>3</sub>O<sub>10</sub>S<sub>3</sub>]



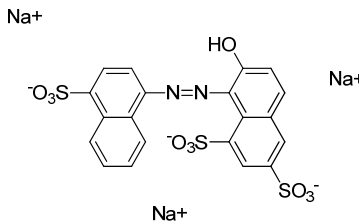
Tartrazine  
[C<sub>16</sub>H<sub>9</sub>N<sub>4</sub>Na<sub>3</sub>O<sub>9</sub>S<sub>2</sub>]



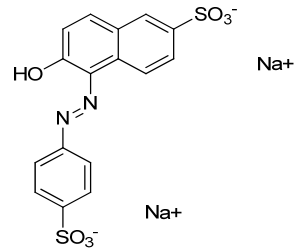
Amaranth  
[C<sub>20</sub>H<sub>11</sub>N<sub>2</sub>Na<sub>3</sub>O<sub>10</sub>S<sub>3</sub>]



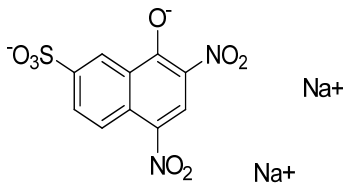
Indigo carmine  
[C<sub>16</sub>H<sub>8</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>8</sub>S<sub>2</sub>]



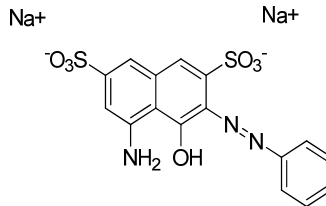
New cocchine  
[C<sub>20</sub>H<sub>11</sub>N<sub>2</sub>Na<sub>3</sub>O<sub>10</sub>S<sub>3</sub>]



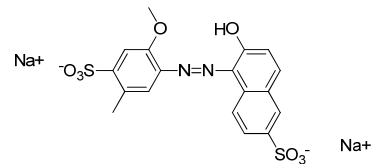
Sunset yellow FCF  
[C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>7</sub>S<sub>2</sub>]



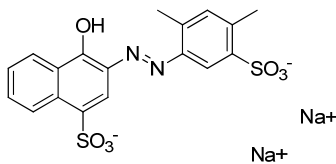
Naphthol yellow S  
[C<sub>10</sub>H<sub>4</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>8</sub>S]



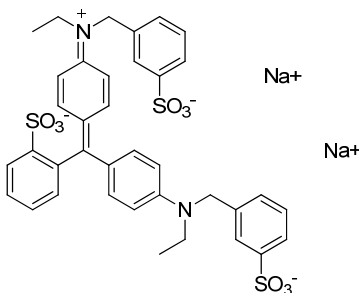
Fast acid magenta  
[C<sub>18</sub>H<sub>11</sub>N<sub>3</sub>Na<sub>2</sub>O<sub>7</sub>S<sub>2</sub>]



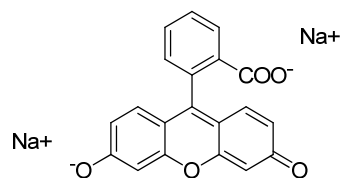
Allura red AC  
[C<sub>18</sub>H<sub>14</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>8</sub>S<sub>2</sub>]



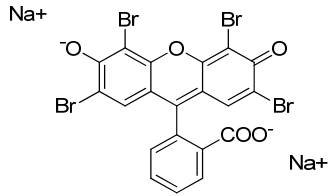
Ponceau SX  
[C<sub>18</sub>H<sub>14</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>7</sub>S<sub>2</sub>]



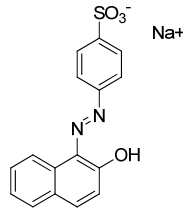
Brilliant blue FCF  
[C<sub>37</sub>H<sub>34</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>9</sub>S<sub>3</sub>]



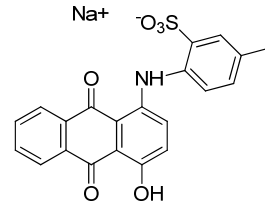
Uranine  
[C<sub>20</sub>H<sub>10</sub>Na<sub>2</sub>O<sub>5</sub>]



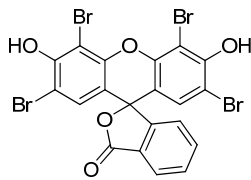
Eosine YS  
[C<sub>20</sub>H<sub>8</sub>Br<sub>4</sub>Na<sub>2</sub>O<sub>5</sub>]



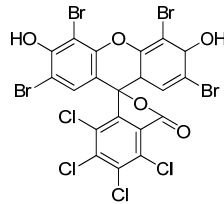
Orange II  
[C<sub>16</sub>H<sub>11</sub>N<sub>2</sub>NaO<sub>4</sub>S]



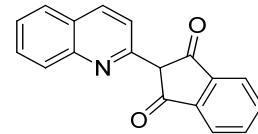
Alizarul purple  
[C<sub>21</sub>H<sub>14</sub>NNaO<sub>6</sub>S]



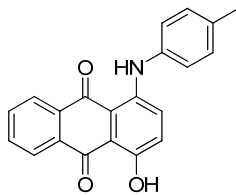
Tetrabromofluorescein  
[C<sub>20</sub>H<sub>8</sub>Br<sub>4</sub>O<sub>5</sub>]



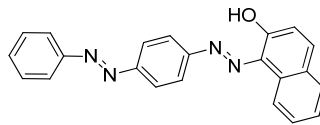
Tetrachlorotetrabromofluorescein  
[C<sub>20</sub>H<sub>6</sub>Br<sub>4</sub>Cl<sub>4</sub>O<sub>5</sub>]



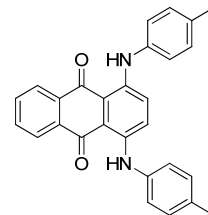
Quinoline yellow SS  
[C<sub>18</sub>H<sub>11</sub>NO<sub>2</sub>]



Alizarine purple SS  
[C<sub>21</sub>H<sub>15</sub>NO<sub>3</sub>]



Sudan III  
[C<sub>22</sub>H<sub>16</sub>N<sub>4</sub>O]



Quinizarine green SS  
[C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>]

## ■ 참고문헌

1. Yanping Xian, Yuluan Wu, Xindong Guo, Yujing Lu, Haiying Luo, Donghui Luo, Yiguang Chen. Simultaneous determination of 11 restricted dyes in cosmetics by ultra high-performance liquid chromatography/tandem mass spectrometry. *Anal. Methods*. 5, 1965-1974 (2013)
2. Xiu Qin Li, Qing He Zhang, Kang Ma, Hong Mei Li, Zhen Guo. Identification and determination of 34 water-soluble synthetic dyes in foodstuff by high performance liquid chromatography-diode array detection-ion trap time-of-flight tandem mass spectrometry. *Food Chemistry*. 182, 316-326 (2015)
3. Chia-Fen Tsai, Ching-Hao Kuo, Daniel Yang-Chin Shin. Determination of 20 syntetic dyes in chili powders and syrup-preserved fruits by liquid chromatography/ tandem mass spectrometry. *J. Food Drug Anal.* 23, 453-462 (2015)



## II-1 국소마취관련성분(14종) 분석법

### 배 경

- 리도카인이 함유된 무허가 의약외품(STALLION)이 불법 판매된 사례 발생('13. 1.)
- 국소마취제(사정지연제) 1000만 개를 불법으로 제조, 판매한 일당 검거('15. 3.)
- 수술 앞두고 마취 크림 발랐는데... 호흡곤란으로 중환자실행('17. 7.)



### 특 성

- 리도카인은 표면마취나 촉각을 둔감하게 할 수 있어 남성 사정지연 및 조루억제 효과가 있을 수 있음
- 문제된 제품은 정상적인 품질관리 절차를 거쳐 제조된 것이 아니므로 과량 사용 시 국소 피부질환, 발기부전, 성욕감퇴 등 발생할 수 있으며, 의사 처방 없이 사용하면 쇼크현상과 심장기능에 부작용이 있을 수 있음

### 분석 사례

- STALLION: Menthol 0.031 mg/포 검출  
2-Phenoxyethanol 0.212 mg/포 검출  
Lidocaine 2.81 mg/포 검출
- 금당2호 주사약: Procaine 2.29 mg/g 검출

## ■ 분석법

### 1. GC

#### ○ 전처리 방법

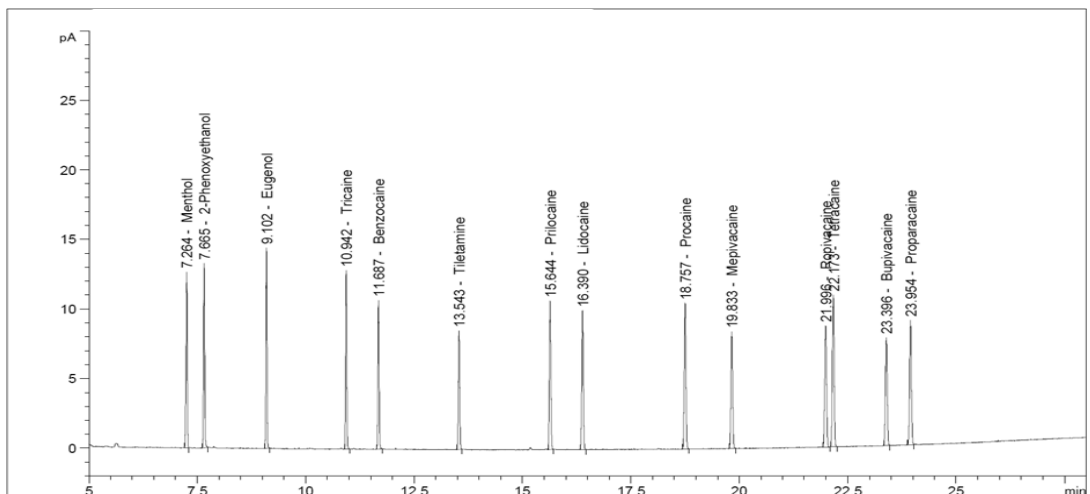
- 표준액 조제 : Menthol 등 14종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종농도(약 20~40 µg/mL)
- 검액 조제 : 약 1 g 취함 → 100% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Menthol, 2-Phenoxyethanol, Eugenol, Ethyl 3-aminobenzoate methanesulfonate (Tricaine mesylate), Benzocaine, Tiletamine hydrochloride, Prilocaine hydrochloride, Lidocaine, Procaine hydrochloride, Mepivacaine hydrochloride, Ropivacaine, Tetracaine hydrochloride, Bupivacaine hydrochloride, Proparacaine hydrochloride

#### ○ Analytical conditions of GC

• Instrument	Agilent, 7890A, GC
• Column	J&W DB-5 (50 m × 0.25 mm, 0.25 µm)
• Temp.	100°C → 15°C/min → 200°C → 5°C/min → 300°C (8 min)
• Inj. Temp.	250°C
• Inj. Mode	Split ratio (10:1)
• Carrier Gas	N <sub>2</sub> , 1.0 mL/min
• Inj. Volume	1 µL
• Det. Temp.	300°C

#### ○ Chromatogram



## 2. GC/MS 법

### ○ Analytical conditions of GC

• Instrument	Agilent, 7890A
• Column	Agilent HP 5MS (30 m × 0.25 mm, 0.25 μm)
• Oven Temp.	100°C → 15°C/min → 200°C → 10°C/min → 300°C (8 min)
• Inj. Temp.	250°C
• Transfer Line	280°C
• Inj. Mode	Split ratio (10:1)
• Carrier Gas	He, 1 mL/min
• Inj. Volume	1 μL

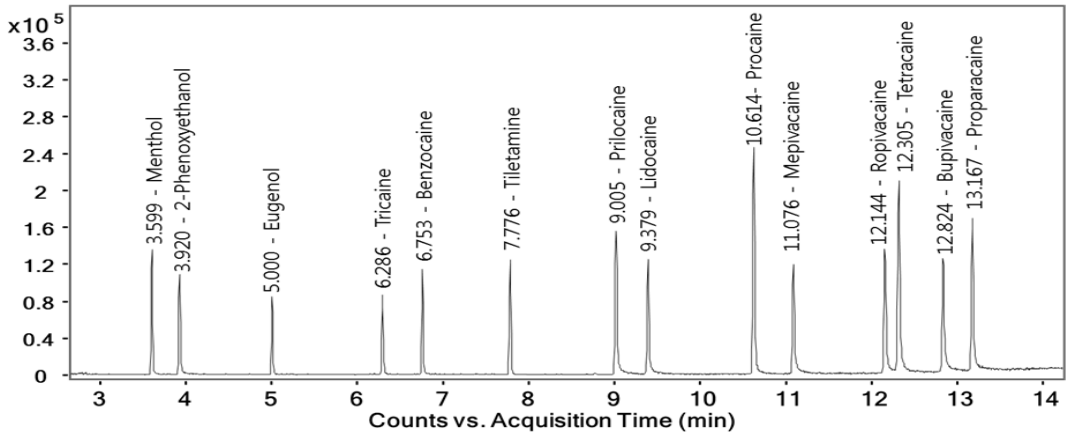
### ○ Analytical condition of GC/MS : SIM and Scan

• Instrument	Agilent, GC/MSD, 5975C
• Ionization Mode	EI
• Ionization Energy	70 eV
• Source Temp.	230°C
• Quad Temp.	150°C
• Mass Mode	SIM and Scan
• Scan Range	50~500 amu
• SIM Dwell Time	100 ms

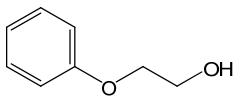
- SIM ions

Compound	Ion (m/z)		
Menthol	71	81	95
2-Phenoxyethanol	94	77	138
Eugenol	164	149	131
Tricaine mesylate	120	165	92
Benzocaine	120	165	92
Tiletamine	166	110	195
Prilocaine	86	106	77
Lidocaine	86	58	87
Procaine	86	99	120
Mepivacaine	98	70	42
Ropivacaine	126	84	56
Tetracaine	58	71	176
Bupivacaine	140	141	84
Proparacaine	86	99	136

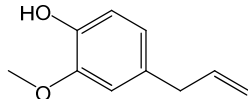
### ○ Chromatogram



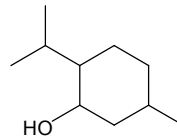
### ■ 구조식



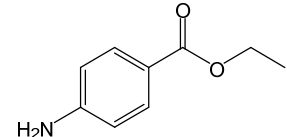
2-Phenoxyethanol  
[C<sub>8</sub>H<sub>10</sub>O<sub>2</sub>]



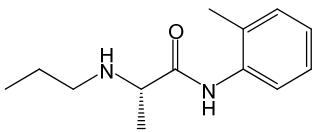
Eugenol  
[C<sub>10</sub>H<sub>12</sub>O<sub>2</sub>]



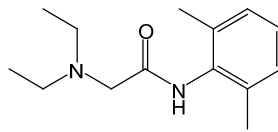
Menthol  
[C<sub>10</sub>H<sub>20</sub>O]



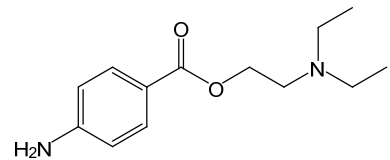
Benzocaine  
[C<sub>9</sub>H<sub>11</sub>NO<sub>2</sub>]



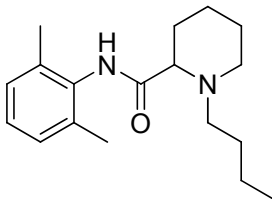
Prilocaine  
[C<sub>13</sub>H<sub>20</sub>N<sub>2</sub>O]



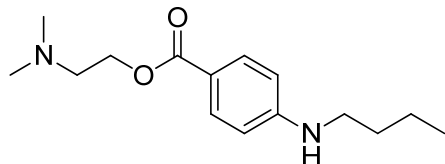
Lidocaine  
[C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>O]



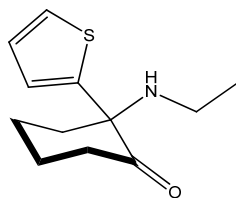
Procaine  
[C<sub>13</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>]



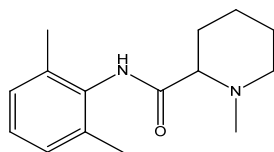
Bupivacaine  
[C<sub>18</sub>H<sub>28</sub>N<sub>2</sub>O]



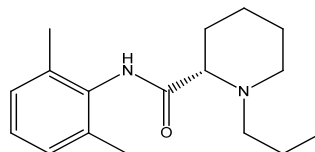
Tetracaine  
[C<sub>15</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>]



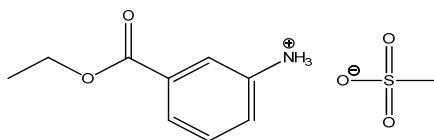
Tiletamine  
[C<sub>12</sub>H<sub>17</sub>NOS]



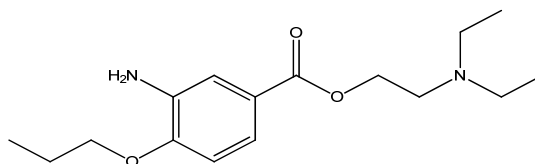
Mepivacaine  
[C<sub>15</sub>H<sub>22</sub>N<sub>2</sub>O]



Ropivacaine  
[C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O]



Tricaine mesylate  
[C<sub>10</sub>H<sub>15</sub>NO<sub>5</sub>S]



Proparacaine  
[C<sub>16</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>]

## ■ 참고문헌

1. Determination and quantification of nine adulterant local anaesthetics in illegal treatments for male premature ejaculation by GC-FID and GC-MS. Ji Hyun Lee, So Hyun Cho, Jung Yeon Kim, Hyoung Joon Park, Jung-Ah Do, and Sunyoung Baek. *International Journal of Pharmacy and Pharmaceutical Sciences*, 8, 135-140 (2016)
2. Mihaela, B., Costel, V. M., Sanda & M. P. Chromatographic analysis of local anesthetics in biological samples. *J Pharmaceu Biomed Anal.* 54, 1-12 (2011)
3. Mohamed A. R. New trend in sample preparation: on-line microextraction in packed syringe for liquid and gas chromatography applications I. Determination of local anaesthetics in human plasma samples using gas chromatography-mass spectrometry. *J Chromatography B.* 801, 317-321 (2004)
4. Tohru O., Tatsunori T. Simultaneous determination of local anesthetics including ester-type anesthetics in human plasma and urine by gas chromatography-mass spectrometry with solid-phase extraction. *J Chromatography B.* 726, 185-194 (1999)

## II-2 단백질동화스테로이드류(28종) 분석법

### 배 경

- 근육 만들기용 불법 의약품 밀조·밀수 일당 적발('14. 2.)
- 단백질동화스테로이드제 밀수한 헬스트레이너들 적발('15. 5.)
- 헬스보충제, 단백질 보충제 등에 근육증강을 목적으로 단백질동화스테로이드를 불법으로 첨가할 우려가 있음
- 불법적으로 근육을 키우고 근력을 증강시키는 데 사용되어 미국올림픽위원회 등 대부분 스포츠단체에서는 단백질동화스테로이드의 사용을 금지



### 특 성

- 단백질동화스테로이드는 단백질동화를 촉진시키는 합성약물로 테스토스테론과 유사한 구조를 가지고 있음
- 남용될 경우에는 심장병, 간암, 성장방해, 섭식장애 등 심각한 부작용을 일으킬 수 있음

### 분석사례

- D-BOL : 메탄디에논(M) 29.7  $\mu\text{g/g}$  검출  
볼데논 27.4  $\mu\text{g/g}$  검출  
메탄드로스테놀론 68.8 mg/g 검출

■ 분석법

1. LC-MS/MS법

○ 전처리 방법

• 표준액 조제 : 1-Androstenedione 등 28종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10 µg/L)

• 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : 1-Androstenedione, 19-Norandrostenedione, Bolasterone, Boldenone, Boldione, Calusterone, Clostebol, Fluoxymesterone, Metenolone, Methylnortestosterone, Mibolerone, Nandrolone, Norbolethone, Norclostebol, Norethandrolone, Oral-turinabol(M), Nandrolone(MI), Nandrolone(M2), Methandienone(M), Boldenone(M), Danazol(M), Formebolone(M), Nandrolone decanoate, Testosterone, Testosterone-17-valerate, Testosterone-17-propionate, Methandrostenolone, Drostanolone propionate

○ Analytical conditions of HPLC

• Instrument	Water ACQUITY UPLC																								
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 µm)																								
• Column Temp.	35°C																								
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile																								
	<table border="1"> <thead> <tr> <th>Time (min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0.0</td> <td>80</td> <td>20</td> </tr> <tr> <td>3.0</td> <td>80</td> <td>20</td> </tr> <tr> <td>13.0</td> <td>40</td> <td>60</td> </tr> <tr> <td>17.0</td> <td>0</td> <td>100</td> </tr> <tr> <td>20.0</td> <td>0</td> <td>100</td> </tr> <tr> <td>20.1</td> <td>80</td> <td>20</td> </tr> <tr> <td>25.0</td> <td>80</td> <td>20</td> </tr> </tbody> </table>	Time (min)	A (%)	B (%)	0.0	80	20	3.0	80	20	13.0	40	60	17.0	0	100	20.0	0	100	20.1	80	20	25.0	80	20
Time (min)	A (%)	B (%)																							
0.0	80	20																							
3.0	80	20																							
13.0	40	60																							
17.0	0	100																							
20.0	0	100																							
20.1	80	20																							
25.0	80	20																							
• Flow Rate	0.25 mL/min																								
• Inj. Volume	2 µL																								

○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	2.7 kV
• Desolvation Temp.	500°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

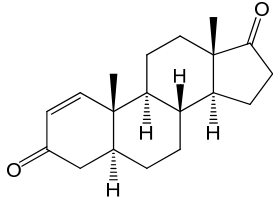
Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
19-Norandrostenedione	+	273.16	26	109.15	26
				197.21	18
				255.31	18
1-Androstenedione	+	287.22	26	143.13	28
				185.22	20
				203.26	16
Bolasterone	+	317.03	30	107.29	20
				123.24	34
				121.15	22
Boldenone	+	287.16	20	135.21	14
				269.26	10
				105.14	34
Boldenone(M)	+	289.20	22	187.22	20
				271.30	12
				121.15	26
Boldione	+	285.16	18	147.21	12
				151.17	14
				123.15	24
Calusterone	+	317.10	32	132.93	22
				203.23	16
				131.13	22
Clostebol	+	323.16	24	143.12	26
				157.13	30
				105.14	28
Danazol(M)	+	313.16	28	109.15	24
				123.16	30
				105.14	40
Fluoxymesterone	+	337.16	32	131.20	32
				281.27	22
				147.15	30
Formebolone(M)	+	347.22	17	281.26	14
				329.25	15



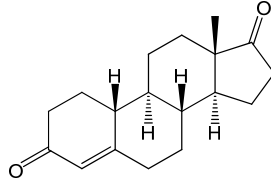
Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Metylnortestosterone	+	289.22	28	109.15	26
				253.28	16
				271.26	14
Mibolerone	+	303.29	32	107.08	30
				121.08	24
				177.24	22
Metenolone	+	303.29	30	131.15	30
				187.14	22
				205.21	16
Methandienone(M)	+	317.16	10	121.14	26
				281.30	12
				299.28	8
Nandrolone	+	275.16	24	109.15	24
				239.24	16
				257.28	14
Nandrolone(M1)	+	277.22	12	145.20	20
				241.29	12
				259.27	8
Nandrolone(M2)	+	277.22	12	145.14	22
				241.29	16
				259.27	8
Norbolethone	+	317.22	26	109.15	28
				245.28	20
				299.34	16
Norclostebol	+	309.10	26	117.13	30
				143.12	30
				291.23	16
Norethandrolone	+	303.22	26	109.15	28
				267.31	16
				285.30	16
Oral-turinabol(M)	+	351.16	12	147.20	16
				155.11	32
				333.23	8

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Nandrolone decanoate	+	429.06	30	239.06	20
				257.07	20
				275.09	20
Testosterone	+	289.25	35	96.98	23
				109.00	20
				253.17	20
Testosterone 17-valerate	+	373.24	30	97.00	25
				109.00	25
Testosterone 17-propionate	+	345.22	28	97.00	20
				109.00	20
				253.15	25
Methandrostenolone	+	301.55	35	149.26	25
				121.18	15
Drostanolone propionate	+	361.38	30	173.11	20
				215.15	20
				269.25	15

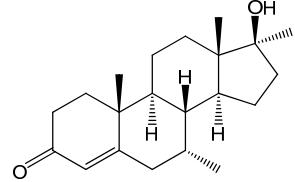
■ 구조식



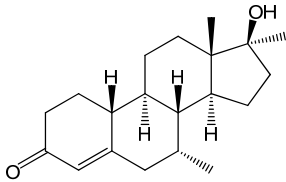
1-Androstenedione  
[C<sub>19</sub>H<sub>26</sub>O<sub>2</sub>]



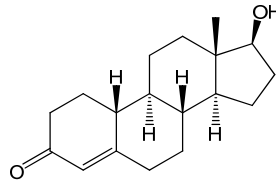
19-Norandrostenedione  
[C<sub>18</sub>H<sub>24</sub>O<sub>2</sub>]



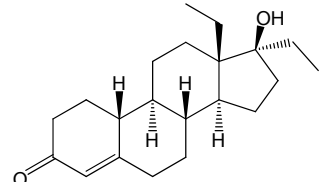
Bolasterone  
[C<sub>21</sub>H<sub>32</sub>O<sub>2</sub>]



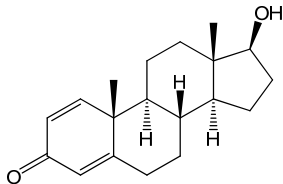
Mibolerone  
[C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>]



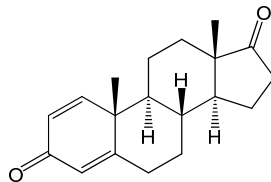
Nandrolone  
[C<sub>18</sub>H<sub>26</sub>O<sub>2</sub>]



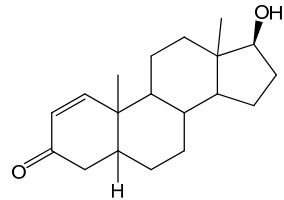
Norbolethone  
[C<sub>21</sub>H<sub>32</sub>O<sub>2</sub>]



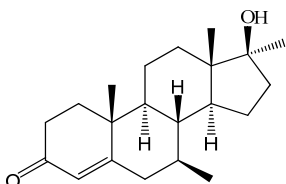
Boldenone  
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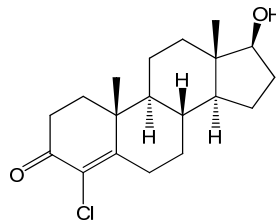
Boldione  
[C<sub>19</sub>H<sub>24</sub>O<sub>2</sub>]



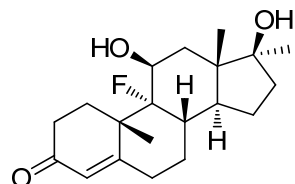
Boldenone(M)  
[C<sub>19</sub>H<sub>28</sub>O<sub>2</sub>]



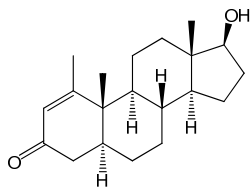
Calusterone  
[C<sub>21</sub>H<sub>32</sub>O<sub>2</sub>]



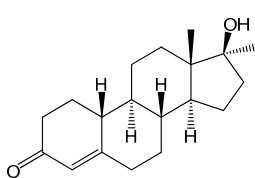
Clostebol  
[C<sub>19</sub>H<sub>27</sub>ClO<sub>2</sub>]



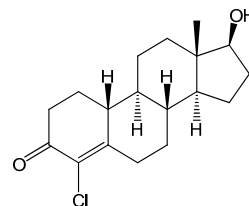
Fluoxymesterone  
[C<sub>20</sub>H<sub>29</sub>FO<sub>3</sub>]



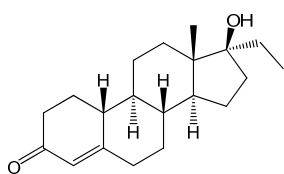
Metenolone  
[C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>]



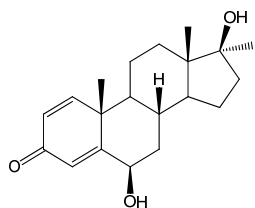
Methylnortestosterone  
[C<sub>19</sub>H<sub>28</sub>O<sub>2</sub>]



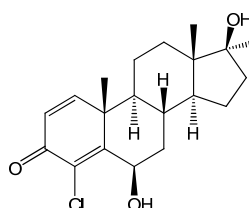
Norclostebol  
[C<sub>18</sub>H<sub>25</sub>ClO<sub>2</sub>]



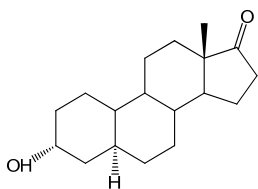
Norethandrolone  
[C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>]



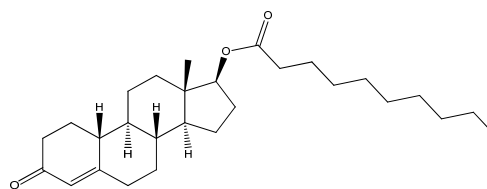
Methandienone(M)  
[C<sub>20</sub>H<sub>28</sub>O<sub>3</sub>]



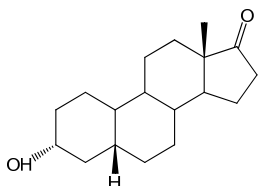
Oral-turinabol(M)  
[C<sub>20</sub>H<sub>27</sub>ClO<sub>2</sub>]



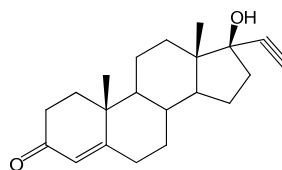
Nandrolone(M1)  
[C<sub>18</sub>H<sub>28</sub>O<sub>2</sub>]



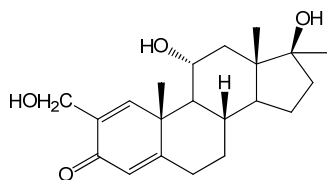
Nandrolone decanoate  
[C<sub>28</sub>H<sub>44</sub>O<sub>3</sub>]



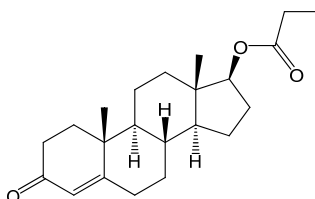
Nandrolone(M2)  
[C<sub>18</sub>H<sub>28</sub>O<sub>2</sub>]



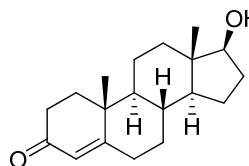
Danazol(M)  
[C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>]



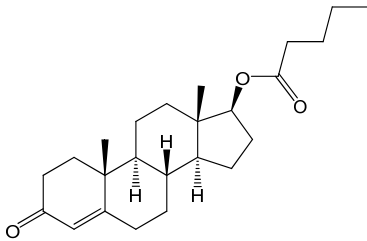
Formebolone(M)  
[C<sub>21</sub>H<sub>30</sub>O<sub>4</sub>]



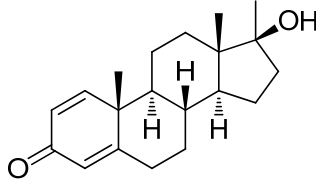
Testosterone 17-propionate  
[C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>]



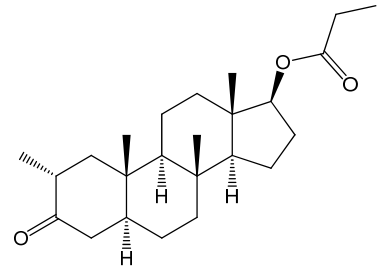
Testosterone  
[C<sub>19</sub>H<sub>28</sub>O<sub>2</sub>]



Testosterone 17-valerate  
[C<sub>24</sub>H<sub>36</sub>O<sub>3</sub>]



Methandrostenolone  
[C<sub>20</sub>H<sub>28</sub>O<sub>2</sub>]



Drostanolone propionate  
[C<sub>23</sub>H<sub>36</sub>O<sub>3</sub>]

## ■ 참고문헌

1. So-Hyun Cho, Hyoung Joon Park, Ji Hyun Lee, Jung-Ah Do, seok Heo, Jeong Hwa Jo, Sooyeul Cho. Determination of anabolic-androgenic steroid adulterants in counterfeit drug by UHPLC-MS/MS, *Journal of Pharmaceutical and Biomedical Analysis*. 111 (2015) 138 - 146
2. Theron, H. B., Coetzee, C., Sutherland, F. C., Wiesner J. L. & Swart, K. J. Selective and sensitive liquid chromatography-tandem mass spectrometry method for the determination of levonorgestrel in human plasma. *J Chromatogr B Analyt Technol Biomed Life Sci*. 813(1-2), 331-336 (2004)
3. Van Poucke, C., Detavernier C., Van Cauwenberghe, R. & Van Peteghem, C. Determination of anabolic steroids in dietary supplements by liquid chromatography-tandem mass spectrometry. *Anal Chim Acta*. 586(1-2), 35-42 (2007)
4. Shahidi, N. T. A review of the chemistry, biological action, and clinical applications of anabolic-androgenic steroids. *Clin Ther*. 23(9), 1355-1390 (2001)

## II-3 마약류(42종) 분석법

### ■ 배 경

- 식·의약품 중 불법 마약 성분 검출의 증가에 따른 지속적인 안전관리 필요함
- 인체 시료를 이용한 분석법은 많으나, 식품 등에 마약류를 검출하는 분석법은 거의 없는 실정임
- 마약 성분 ‘대마 쿠키’ 밀반입 적발('09. 7.)  
다이어트제 속 마약 성분 검출('10. 5.),  
마약 성분 함유한 대마씨 오일 판매 적발('11. 9.),  
마약류 ‘공부 잘하는 약’으로 판매('11. 11.),  
몸짱 보충제에서 유사마약 성분 검출('13. 7.)  
해외 사이트 판매 식품에서 유사마약성분 검출('15. 9.)



### ■ 특 성

- 마약류란 「마약류 관리에 관한 법률」 제2조제2호부터 제4호까지에 따른 마약, 향정신성의약품 및 대마를 말함

### ■ 분석 사례

- 향미유 :  $\delta$ -9-Tetrahydrocannabinol 검출
- 대마씨유 :  $\delta$ -9-Tetrahydrocannabinol 2081mg/kg 검출

■ 분석법

1. UPLC법

○ 전처리방법

- 표준액 조제 : 표준액 1\* Dihydrocodeine bitartrate 등 19종  
 표준액 2 Codeine phosphate hydrate 등 11종  
 표준액 3 Alprazolam 등 12종  
 → 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 25 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

- \* 표준액 1 : Dihydrocodeine bitartrate, Ephedrine hydrochloride, Amphetamine, Phendimetrazine tartrate, Phentermine hydrochloride, α-Pyrrolidinopentiothiophenone(alpha-PVT), Methylphenidate hydrochloride, 5-MeO-Dipt hydrochloride, Mazindol, Bromazepam, Fentanyl citrate, Flurazepam hydrochloride, AM2233, Estazolam, Lorazepam, Methaqualone, Flunitrazepam, Clobazam, Diazepam
- \* 표준액 2 : Codeine phosphate hydrate, MDMA hydrochloride, Ketamine hydrochloride, Cocaine hydrochloride, 2C-I hydrochloride, Pentazocine, Fenfluramine hydrochloride, Modafinil, Sufentanyl citrate, Triazolam, Temazepam
- \* 표준액 3 : Alprazolam, AM2201, A-834735, JWH250, JWH073, XLR11, JWH018, JWH081, JWH122, JWH019, Tetrahydrocannabinol(THC), APINAC

○ Analytical condition of HPLC (표준액 1, 2)

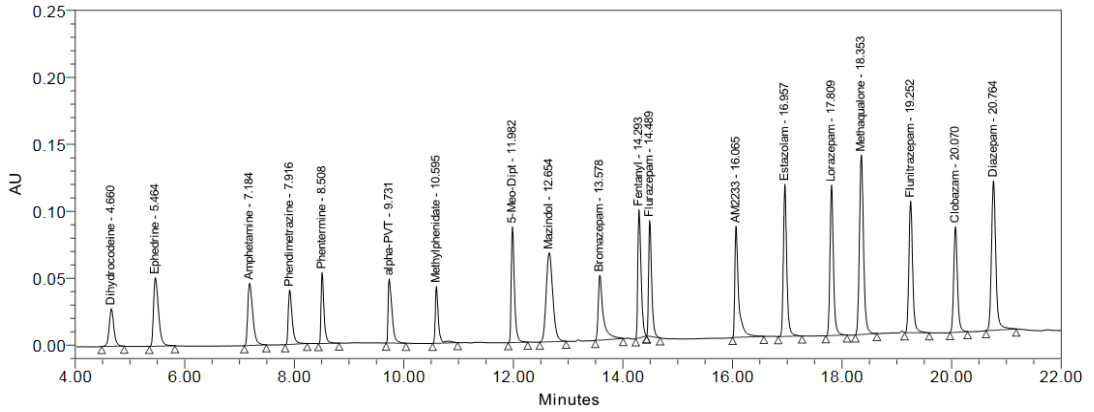
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 150 mm, 1.8 µm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 5 mM NaH <sub>2</sub> PO <sub>4</sub> in Water (pH 2.3, H <sub>3</sub> PO <sub>4</sub> )		
	(B) 90% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	85	15
	1.5	85	15
	3.5	75	25
	7.0	65	35
	12.0	50	50
	18.0	30	70
	20.0	30	70
	20.5	85	15
	25.0	85	15
• Flow Rate	0.13 mL/min		
• Inj. Volume	1 µL		
• UV Detection	200 nm		
• PDA Range	190~400 nm		

○ Analytical condition of HPLC (표준액 3)

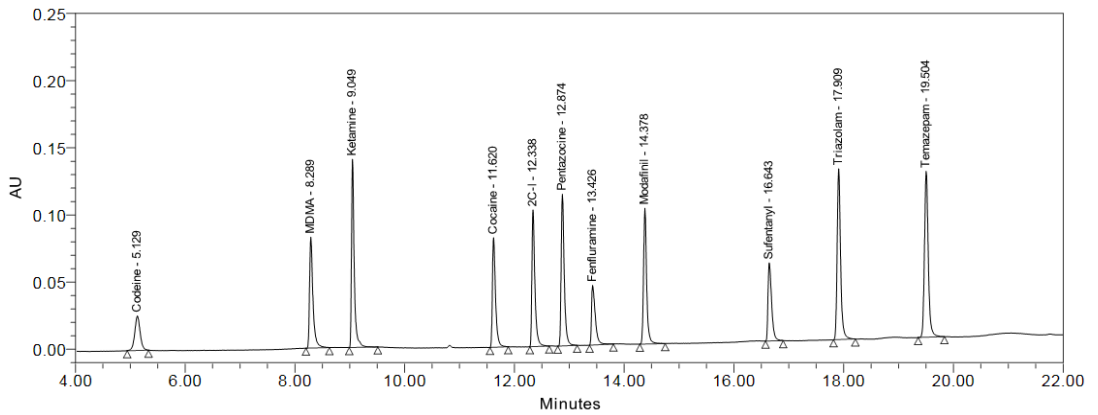
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 150 mm, 1.8 μm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 25 mM NaH <sub>2</sub> PO <sub>4</sub> + 0.01% Sodium hexane sulfonate (pH 3, H <sub>3</sub> PO <sub>4</sub> ) (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	40	60
	4.0	20	80
	9.0	0	100
	11.0	0	100
	11.1	40	60
	15.0	40	60
• Flow Rate	0.18 mL/min		
• Inj. Volume	1 μL		
• UV Detection	210 nm		
• PDA Range	190~400 nm		



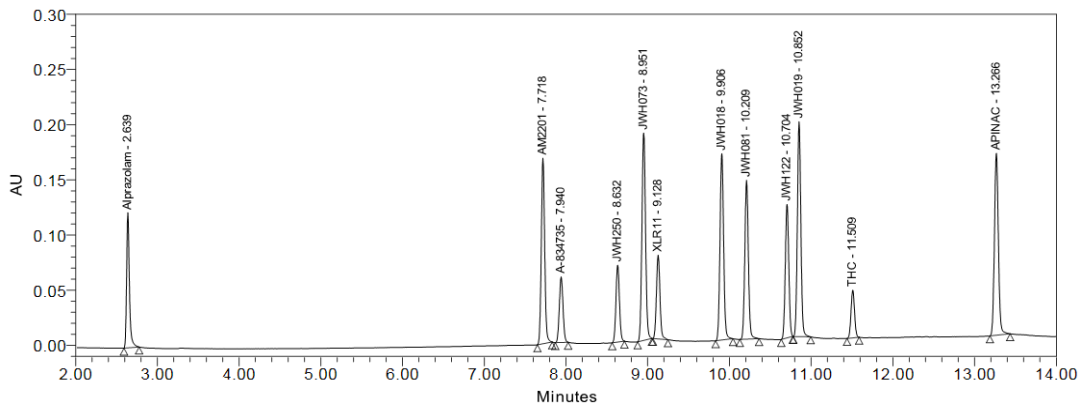
○ Chromatogram



[표준액 1]

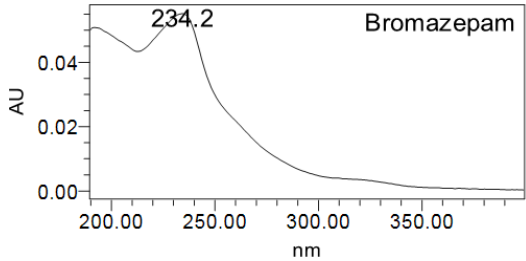
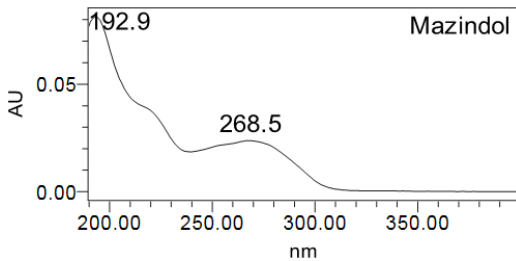
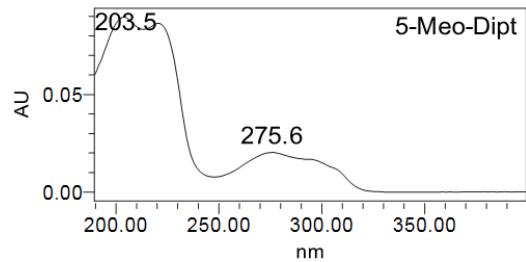
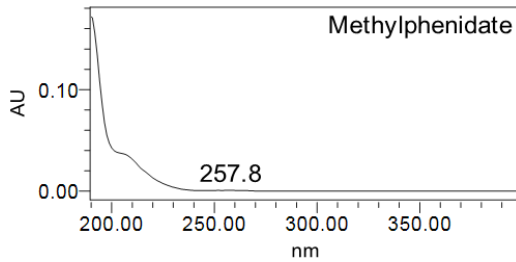
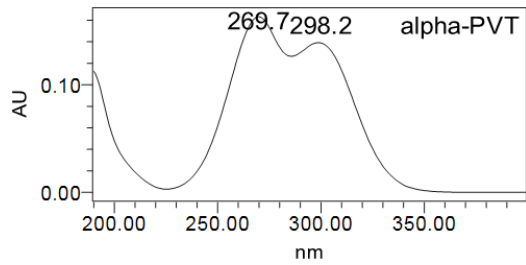
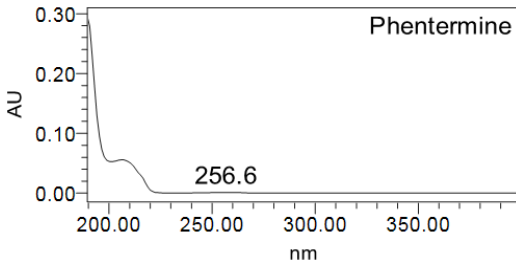
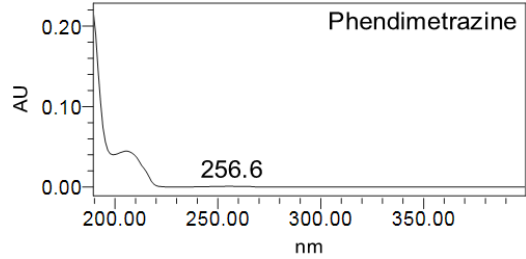
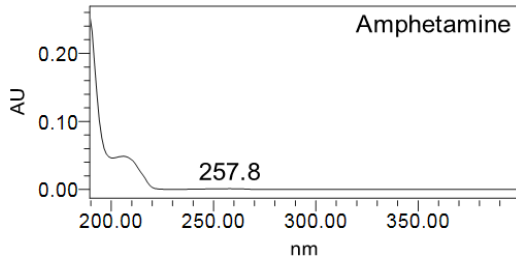
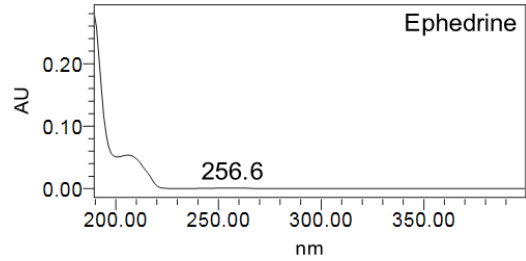
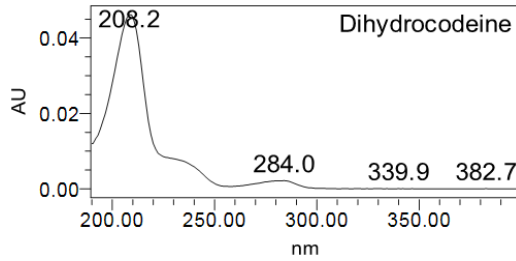


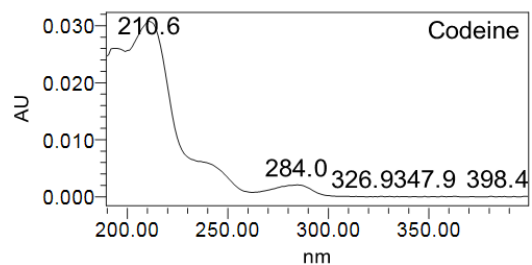
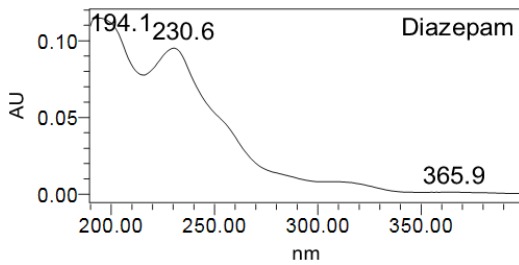
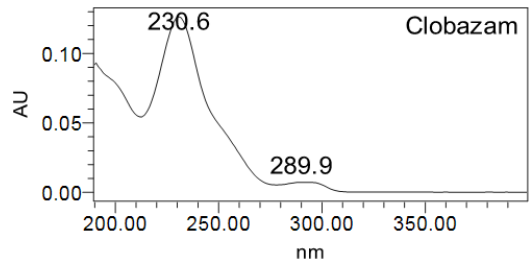
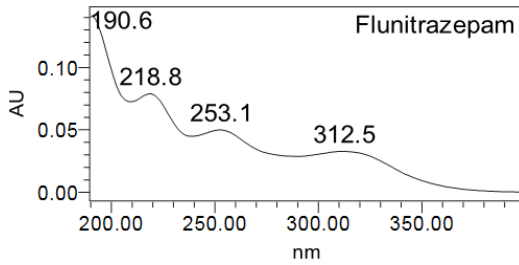
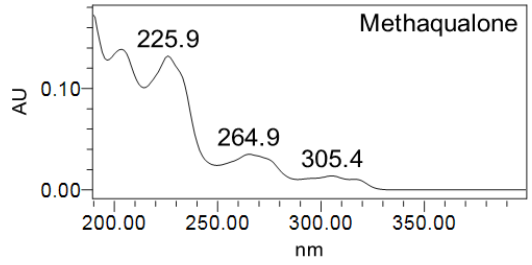
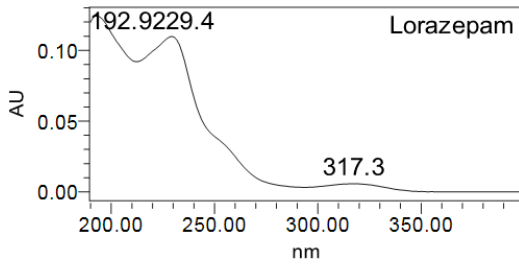
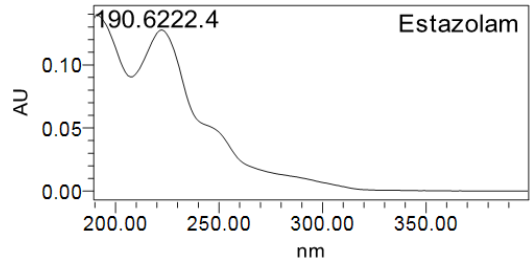
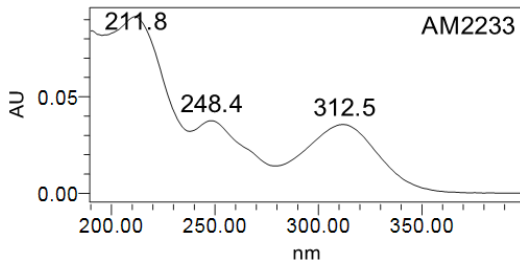
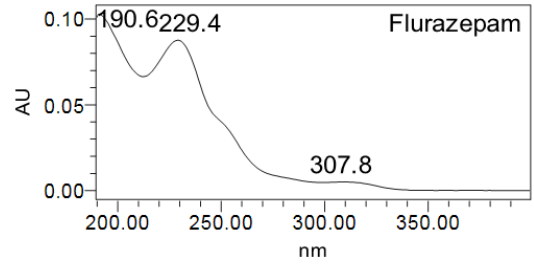
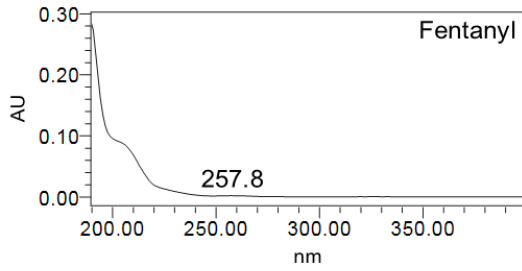
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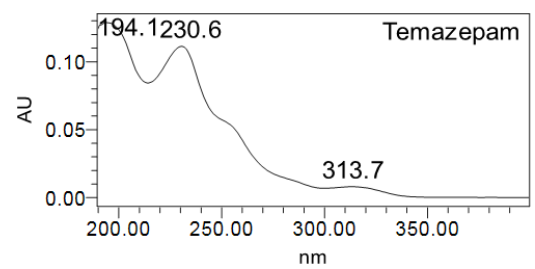
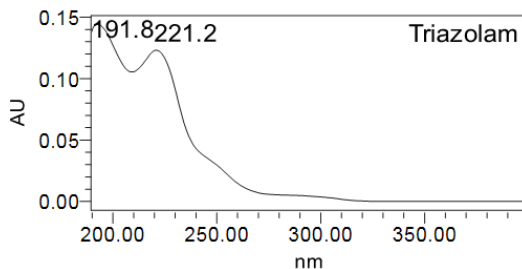
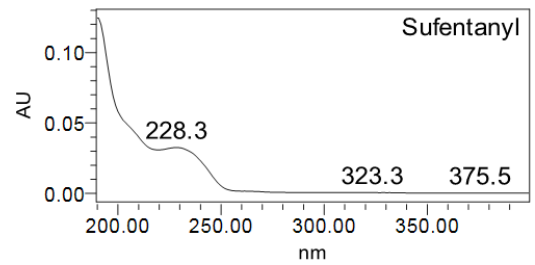
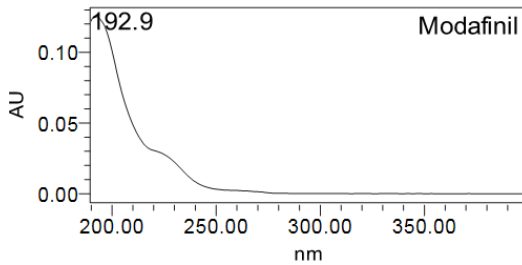
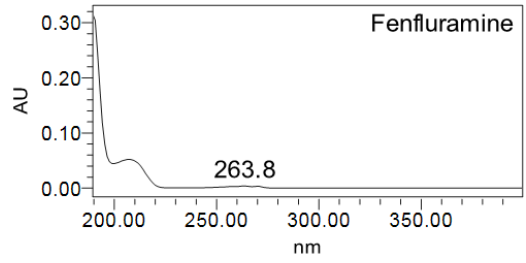
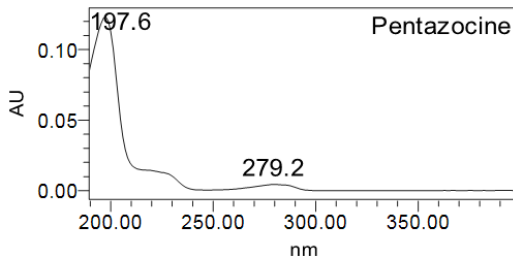
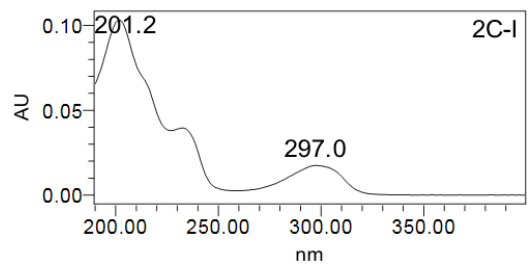
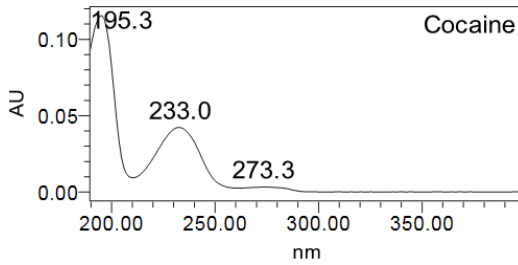
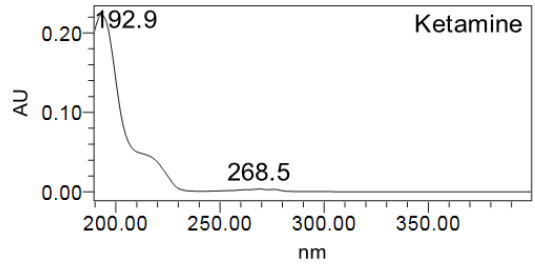
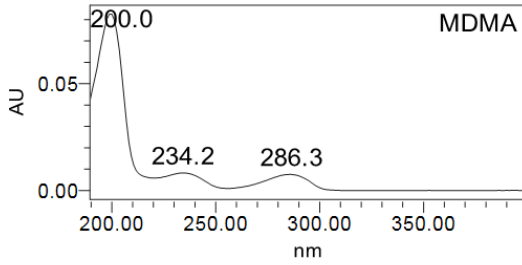


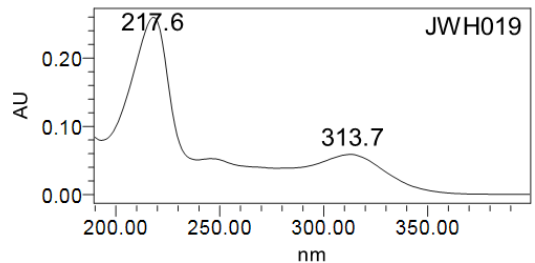
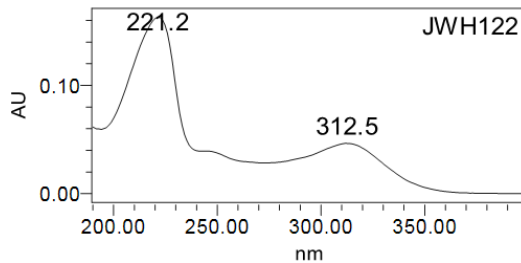
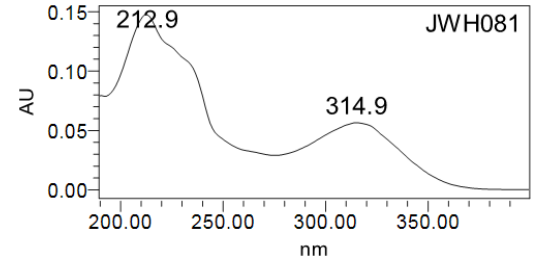
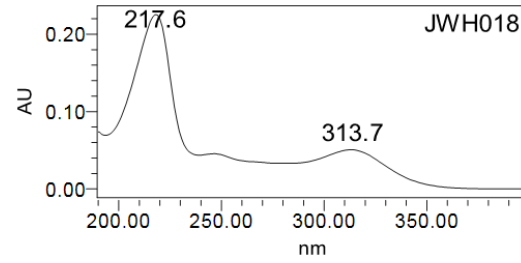
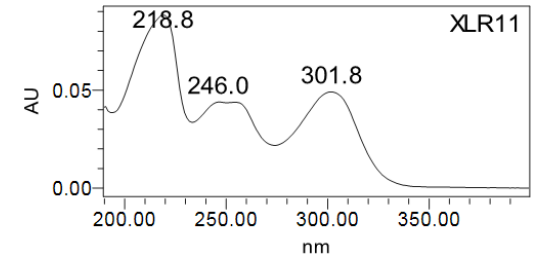
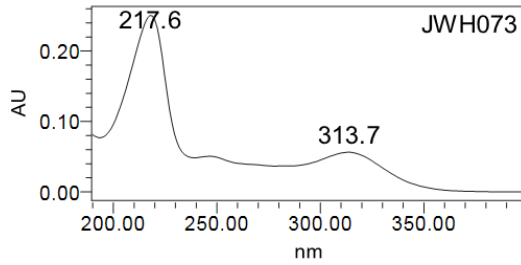
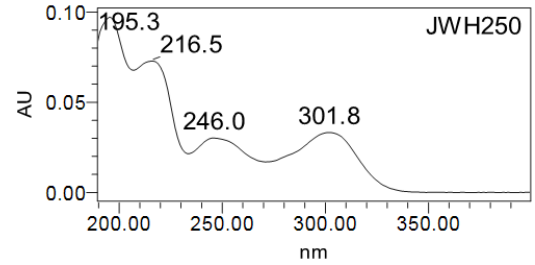
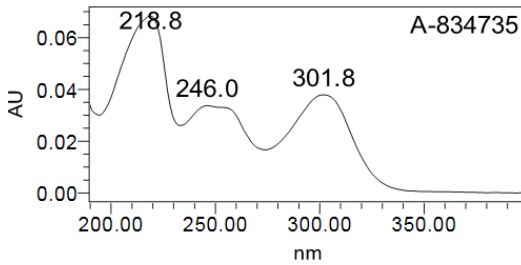
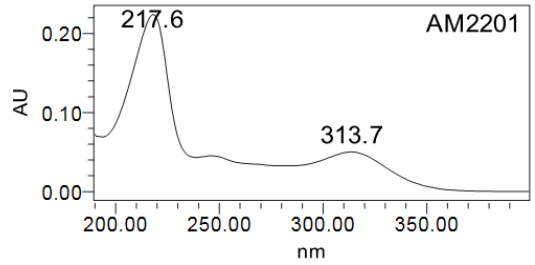
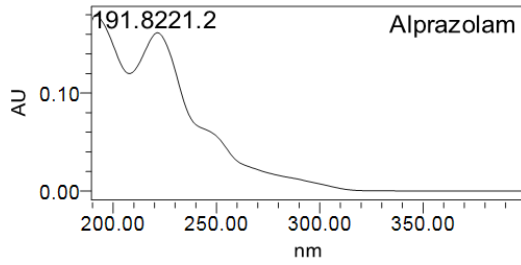
[표준액 3]

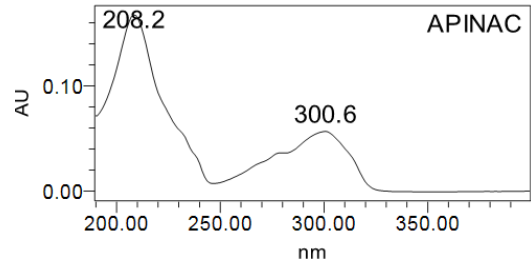
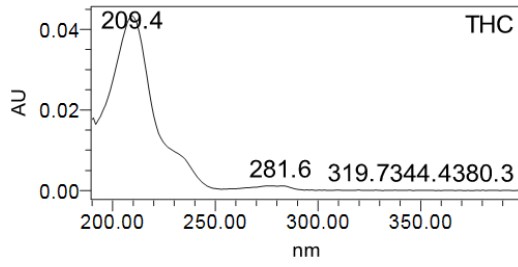
○ PDA Spectrum











## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• <b>Instrument</b>	Waters ACQUITY UPLC		
• <b>Column</b>	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• <b>Column Temp.</b>	30°C		
• <b>Mobile Phase</b>	(A) 0.1% Formic acid in Water		
	(B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	3.0	95	5
	7.0	20	80
	10.0	20	80
	10.1	0	100
	13.0	0	100
	13.1	95	5
	15.0	95	5
• <b>Flow Rate</b>	0.25 mL/min		
• <b>Inj. Volume</b>	2 μL		

### ○ Analytical conditions of LC-MS/MS

• <b>Instrument</b>	Waters Xevo TQ
• <b>Ionization Mode</b>	ESI (+)
• <b>Capillary Voltage</b>	2.7 kV
• <b>Desolvation Temp.</b>	400°C
• <b>Desolvation Gas Flow</b>	600 L/Hr (N <sub>2</sub> )
• <b>Cone Gas Flow</b>	off

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Dihydrocodeine	+	304.65	10	122.20	30
				115.15	25
Ephedrine	+	166.60	20	117.18	20
				148.25	10
				91.17	15
Amphetamine	+	136.60	15	119.20	10
				132.90	25
Phendimetrazine	+	191.85	10	147.95	20
				91.00	18
Phentermine	+	150.14	16	133.04	10
				97.13	25
				111.12	35
Alpha-PVT	+	238.60	20	126.25	20
				84.20	20
Methylphenidate	+	234.63	25	102.23	15
				114.25	15
				159.20	35
5-Meo-Dipt	+	275.68	20	174.23	20
				44.00	25
				130.10	35
Mazindol	+	285.09	35	182.20	30
				209.28	25
Bromazepam	+	316.48	35	105.10	35
				188.20	25
				216.20	20
Fentanyl	+	337.35	35	315.25	25
				319.30	20
				97.85	30
Flurazepam	+	387.90	25	111.85	25
				230.80	35
				295.55	35
AM2233	+	458.80	7	267.25	25
				177.30	45
Estazolam	+	295.55	35	229.25	30
				229.25	30
Lorazepam	+	321.60	30		

표  
1

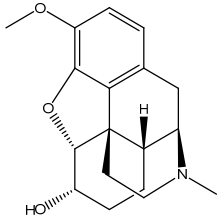


	Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
표준액 1	Lorazepam	+	321.60	30	275.30	20
	Methaqualone	+	251.60	25	91.17	40
					132.20	25
					238.25	35
	Flunitrazepam	+	314.60	25	268.30	25
					Clobazam	+
	Diazepam	+	285.53	35	154.18	25
					193.23	30
					222.25	25
	표준액 2	Codeine	+	302.65	10	115.15
165.20						45
243.30						25
MDMA		+	194.60	15	105.18	25
					133.20	25
					135.10	25
Ketamine		+	238.63	10	163.15	20
					125.15	25
					179.20	20
Cocaine		+	304.65	30	207.20	15
	220.30				15	
	105.15				35	
2C-I	+	308.50	20	154.20	35	
				182.30	30	
Pentazocine	+	286.70	10	218.30	20	
Fenfluramine	+	232.62	25	109.15	40	
				159.18	25	
Modafinil	+	296.08	30	187.22	15	
				128.95	12	
Sulfentanyl	+	386.94	15	110.85	35	
				205.95	30	
Triazolam	+	343.50	30	238.00	20	
				238.20	40	
Temazepam	+	300.77	25	308.30	25	
					254.95	20

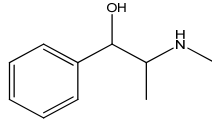
Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Alprazolam	+	309.60	40	274.30	25
				281.28	25
AM2201	+	360.65	35	127.17	45
				155.17	25
				232.25	25
A-834735	+	340.25	30	322.15	20
				307.12	25
				125.00	20
JWH-250	+	336.65	30	91.15	35
				121.15	20
				144.20	30
JWH-073	+	327.90	35	126.85	40
				143.85	35
				154.85	25
XLR11	+	330.68	40	97.20	25
				125.20	25
				144.10	35
JWH-018	+	341.90	40	232.30	25
				126.87	40
				154.90	25
JWH-081	+	371.94	35	184.90	25
				214.00	25
				140.90	40
JWH-122	+	355.92	35	168.90	25
				214.00	25
				126.88	40
JWH-019	+	355.90	25	154.90	25
				192.95	20
THC	+	314.94	30	259.05	20
				135.13	20
APINAC	+	367.23	20	215.11	20

표 3  
의  
3

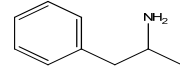
■ 구조식



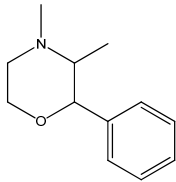
Dihydrocodeine  
[C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>]



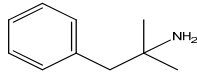
Ephedrine  
[C<sub>10</sub>H<sub>15</sub>NO]



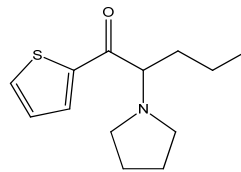
Amphetamine  
[C<sub>9</sub>H<sub>13</sub>N]



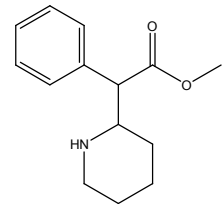
Phendimetrazine  
[C<sub>12</sub>H<sub>17</sub>NO]



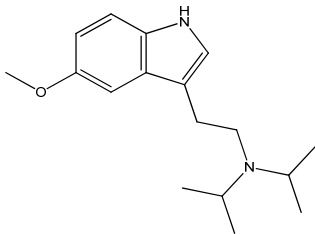
Phentermine  
[C<sub>10</sub>H<sub>15</sub>N]



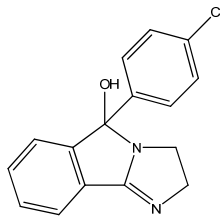
Alpha-PVT  
[C<sub>13</sub>H<sub>19</sub>NOS]



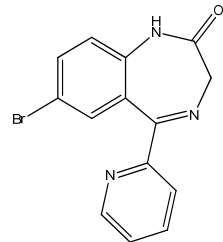
Methylphenidate  
[C<sub>14</sub>H<sub>19</sub>NO<sub>2</sub>]



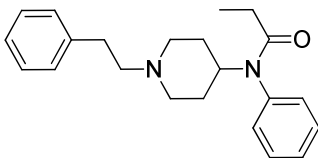
5-Meo-Dipt  
[C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O]



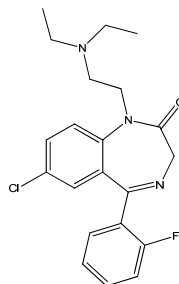
Mazindol  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O]



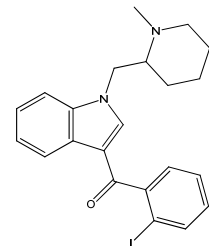
Bromazepam  
[C<sub>14</sub>H<sub>10</sub>BrN<sub>3</sub>O]



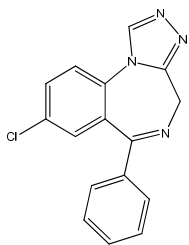
Fentanyl  
[C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O]



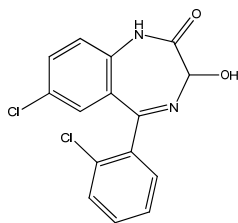
Flurazepam  
[C<sub>21</sub>H<sub>23</sub>ClFN<sub>3</sub>O]



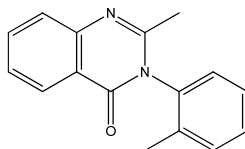
AM2233  
[C<sub>22</sub>H<sub>23</sub>IN<sub>2</sub>O]



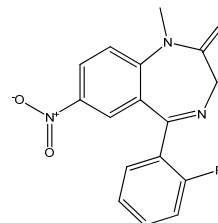
Estazolam  
[C<sub>16</sub>H<sub>11</sub>ClN<sub>4</sub>]



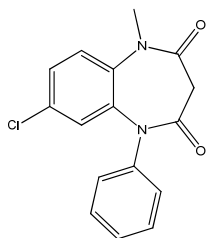
Lorazepam  
[C<sub>15</sub>H<sub>10</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>]



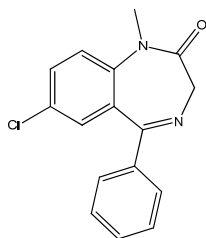
Methaqualone  
[C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O]



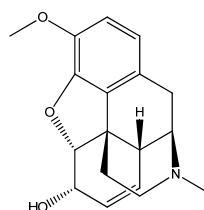
Flunitrazepam  
[C<sub>16</sub>H<sub>12</sub>FN<sub>3</sub>O<sub>3</sub>]



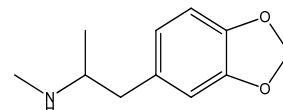
Clobazam  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>2</sub>]



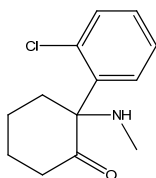
Diazepam  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O]



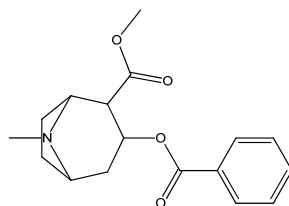
Codeine  
[C<sub>18</sub>H<sub>21</sub>NO<sub>3</sub>]



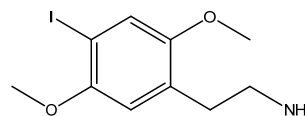
MDMA  
[C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>]



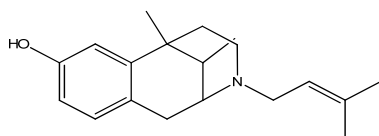
Ketamine  
[C<sub>13</sub>H<sub>16</sub>ClNO]



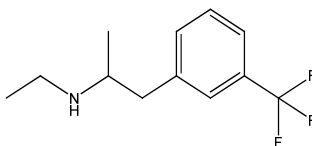
Cocaine  
[C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>]



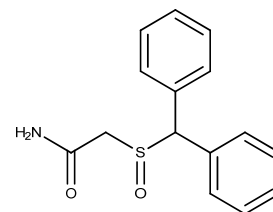
2C-I  
[C<sub>10</sub>H<sub>14</sub>INO<sub>2</sub>]



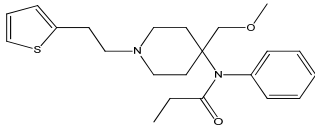
Pentazocine  
[C<sub>19</sub>H<sub>27</sub>NO]



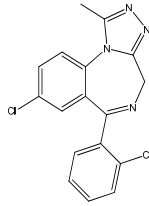
Fenfluramine  
[C<sub>12</sub>H<sub>16</sub>F<sub>3</sub>N]



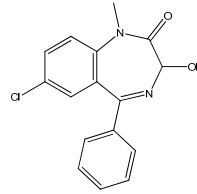
Modafinil  
[C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub>S]



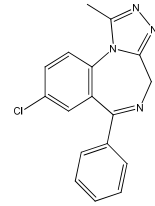
Sufentanyl  
[C<sub>22</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub>S]



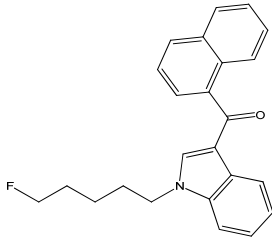
Triazolam  
[C<sub>17</sub>H<sub>12</sub>Cl<sub>2</sub>N<sub>4</sub>]



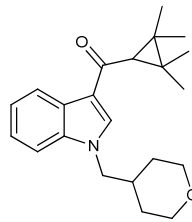
Temazepam  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>2</sub>]



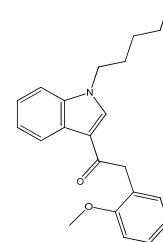
Alprazolam  
[C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>]



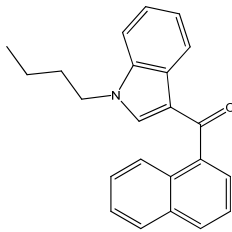
AM2201  
[C<sub>24</sub>H<sub>22</sub>FNO]



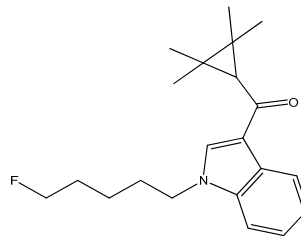
A-834735  
[C<sub>22</sub>H<sub>29</sub>NO<sub>2</sub>]



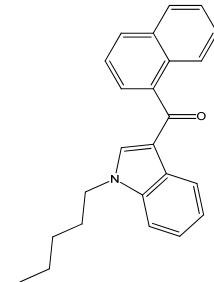
JWH-250  
[C<sub>22</sub>H<sub>25</sub>NO<sub>2</sub>]



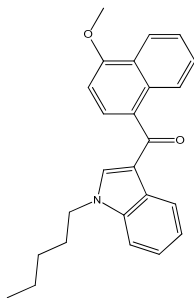
JWH-073  
[C<sub>23</sub>H<sub>21</sub>NO]



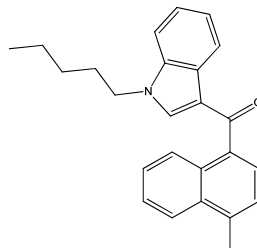
XLR11  
[C<sub>21</sub>H<sub>28</sub>FNO]



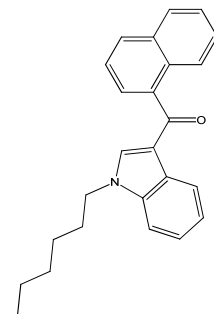
JWH-018  
[C<sub>24</sub>H<sub>23</sub>NO]



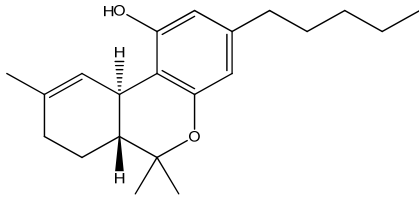
JWH-081  
[C<sub>25</sub>H<sub>25</sub>NO<sub>2</sub>]



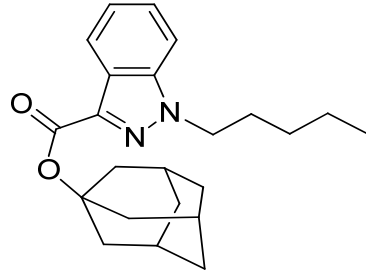
JWH-122  
[C<sub>25</sub>H<sub>25</sub>NO]



JWH-019  
[C<sub>25</sub>H<sub>25</sub>NO]



THC  
[C<sub>21</sub>H<sub>30</sub>O<sub>2</sub>]



APINAC  
[C<sub>22</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub>]

## ■ 참고문헌

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5. Choe, S. G., Woo, S. H., Kim, D. W., Park, Y. H., Choi, H. K., Hwang, B. Y., Lee, D., Kim, S. Development of a target component extraction method from GC-MS data with an in-house program for metabolite profiling. *Anal Biochem* 426(2); 94-102 (2012)
6. Bononii, M., Belgi, P., Tateo, F. Analytical data for identification of the canabimimetic phenylacetylindole JWH-203, *J Anal Toxicol* 35(6); 360-363 (2011)

## II-4 발기부전치료제와 그 유사성분(82종) 분석법

### 배 경

- 발기부전치료제 성분 ‘실데나필’, ‘타라라필’과 유사물질 ‘아미노타다라필’이 들어있는 건강기능식품을 제조·판매한 대학교수 구속(‘15. 7.)
- 길거리 홍보 명함을 이용하여 정품과 유사하게 위조된 비아그라, 시알리스, 레비트라 및 성분과 출처를 알 수 없는 최음 효과를 표방하는 무허가 의약품을 판매한 판매자 구속(‘16. 8.)
- 100억원대 중국산 가짜 비아그라 들여온 일당 적발(‘17. 7.)
- 짝퉁 비아그라 등 가짜 의약품 제조·유통업자 구속(‘17. 8.)



### 특 성

- 대표적인 발기부전치료제로는 타다라필, 실데나필로서 FDA에 승인받은 의약품임
- 발기부전치료제 및 유사물질 52종이 식품공전에 고시(2017. 08.)되어 있으며 식품에 첨가되어서는 아니 됨
- 발기부전치료제 및 유사물질은 장기 복용 시 심장마비, 뇌졸중, 흉통, 고혈압 등의 부작용을 나타낼 수 있음

### 분석 사례

- 이엑스티 파워플러스: 하이드록시호모 실데나필 0.140mg/캡슐 검출  
 디메틸실데나필 0.118mg/캡슐 검출  
 하이드록시티오호모 실데나필 16.2mg/캡슐 검출  
 디메틸티오 실데나필 1.47mg/캡슐

## ■ 분석법

### 1. HPLC

#### ○ 전처리 방법

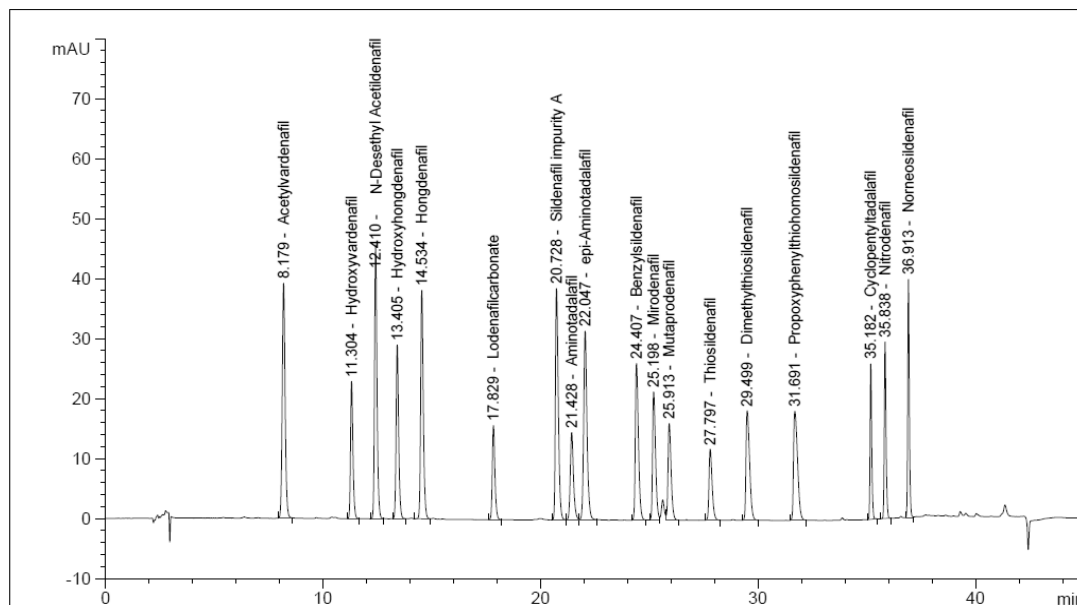
- |          |   |
|----------|---|
| • 표준액 조제 | : 표준액 1* Acetylwardenafil 등 18종                 |
|          | 표준액 2* Vardenafil 등 16종                         |
|          | 표준액 3* Thioquinapiperifil 등 15종                 |
|          | 표준액 4* Yohimbine 등 18종                          |
|          | 표준액 5* Desmethylpiperazinylsildenafil 등 15종     |
|          | → 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 5~60 µg/mL) |
| • 검액 조제  | : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용     |
- \* 표준액 1 : Acetylwardenafil, Hydroxywardenafil, N-Desethylacetildenafil, Hydroxyhongdenafil (Hydroxyacetildenafil), Hongdenafil(Acetildenafil), Lodenafilcarbonate, Sildenafil Impurity A(Isobutylsildenafil, Despropylisobutylsildenafil), Aminotadalafil, epi-Aminotadalafil, Benzylsildenafil, Mutaprodenafil(Nitroprodenafil), Mirodenafil, Thiosildenafil(Sulfosildenafil, Sildenafil thione), Dimethylthiosildenafil, Propoxyphenylthiohomosildenafil, cis-Cyclopentyltadalafil, Nitrodenafil, Norneosildenafil(Piperidinosildenafil)
  - \* 표준액 2 : Vardenafil hydrochloride, Carbodenafil(Fondenafil), Dimethylacetildenafil, Avanafil, Sildenafil citrate salt, Homosildenafil, Dimethylsildenafil(Aildenafil, Methisosildenafil), Udenafil, Cyclopentynafil, Dioxohongdenafil(Dioxoacetildenafil), Tadalafil(Tildenafil), Xanthoanthrafil(Benzamidafil), Pseudovardenafil(Piperadinovardenafil, Piperidenafil), Propoxyphenylthiohydroxyhomosildenafil(Propoxyphenylhydroxythiosildenafil, Sildenafil analogue 1), Gendenafil, Chloropretadalafil
  - \* 표준액 3 : Thioquinapiperifil, Desmethylcarbodenafil(Norcarbodenafil), Norneovardenafil, Piperidinhongdenafil(Piperiacetildenafil, Piperidinoacetildenafil), Methylhydroxyhomosildenafil(Propoxyphenylhydroxyhomosildenafil, Propoxyphenylhomohydroxysildenafil), Hydroxythiovardenafil, Desulfovardenafil, Cinnamylidenafil, *trans*-Tadalafil, Hydroxythiohomosildenafil(Hydroxyhomosildenafil thione, Sulfohydroxyhomosildenafil, Thiohydroxyhomosildenafil), Dithiodesmethylcarbodenafil, Propoxyphenylthioaildenafil (Propoxyphenylthiomethisosildenafil), Dithiopropylcarbodenafil, Chlorodenafil, Octylnortadalafil
  - \* 표준액 4 : Yohimbine, Pyrazole N-desmethylsildenafil, Demethylhongdenafil(Noracetildenafil), Oxohongdenafil, Icariin, Hydroxyhomosildenafil, Acetaminotadalafil, Demethyltadalafil(Nortadalafil), Diethylaminopretadalafil, 2-Hydroxypropylnortadalafil, Acetil acid, Thiohomosildenafil(Sulfohomosildenafil, Homosildenafil thione), Propoxyphenylthiosildenafil, Hydroxychlorodenafil, N-butyltadalafil, *trans*-Cyclopentyltadalafil, Imidazosagatriazinone, Dichlorodenafil(Des-N-ethyl 3,5-dimethylacetildenafil)
  - \* 표준액 5 : Desmethylpiperazinylsildenafil(Sildenafil desmethylpiperaziny), N-Desethylwardenafil(Vardenafil m1), Papaverine hydrochloride, Tadalafil impurity A, Descarbonsildenafil, N-Desmethylsildenafil(Desmethylsildenafil, N-Demethylsildenafil), Apixaban, Propoxyphenylsildenafil(O-Desethyl O-propylsildenafil), Sildenafil coupled, Dapoxetine hydrochloride(Dapoxetina, Dapoxetinum), Tadalafil impurity C(Tadalafil), (6S, 12αR)-, Homotadalafil(N-Ethyl tadalafil), Isopropylnortadalafil, Bisprenortadalafil, Desulfonylchlorosildenafil(5-chloroimidazosagatriazinone)



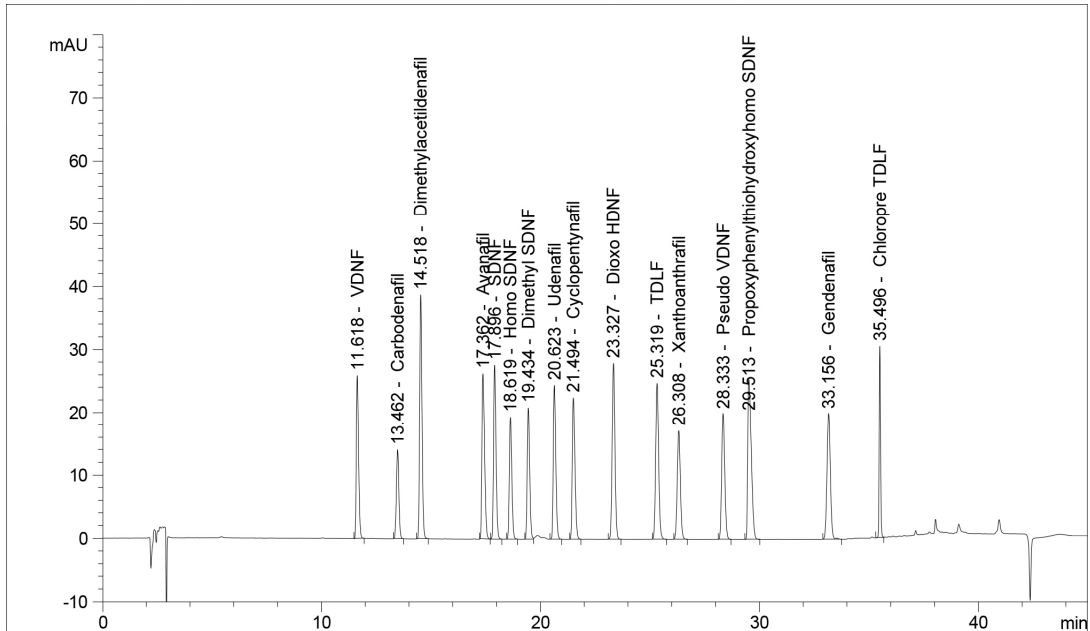
○ Analytical conditions of HPLC

• Instrument	Agilent DE/1200 HPLC (DAD)																								
• Column	Agilent Eclipse XDB C <sub>18</sub> (4.6 mm × 250 mm, 5 μm)																								
• Column Temp.	40°C																								
• Mobile Phase	(A) 0.5 mM Sodium-1-hexane sulfonate in Water (0.1% H <sub>3</sub> PO <sub>4</sub> ) (B) 95% Acetonitrile																								
	<table border="1"> <thead> <tr> <th>Time (min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0.0</td> <td>80</td> <td>20</td> </tr> <tr> <td>2.0</td> <td>80</td> <td>20</td> </tr> <tr> <td>30.0</td> <td>50</td> <td>50</td> </tr> <tr> <td>35.0</td> <td>0</td> <td>100</td> </tr> <tr> <td>39.0</td> <td>0</td> <td>100</td> </tr> <tr> <td>40.0</td> <td>80</td> <td>20</td> </tr> <tr> <td>45.0</td> <td>80</td> <td>20</td> </tr> </tbody> </table>	Time (min)	A (%)	B (%)	0.0	80	20	2.0	80	20	30.0	50	50	35.0	0	100	39.0	0	100	40.0	80	20	45.0	80	20
Time (min)	A (%)	B (%)																							
0.0	80	20																							
2.0	80	20																							
30.0	50	50																							
35.0	0	100																							
39.0	0	100																							
40.0	80	20																							
45.0	80	20																							
• Flow Rate	1.0 mL/min																								
• Inj. Volume	10 μL																								
• UV Detection	291 nm																								
• PDA Range	190~400 nm																								

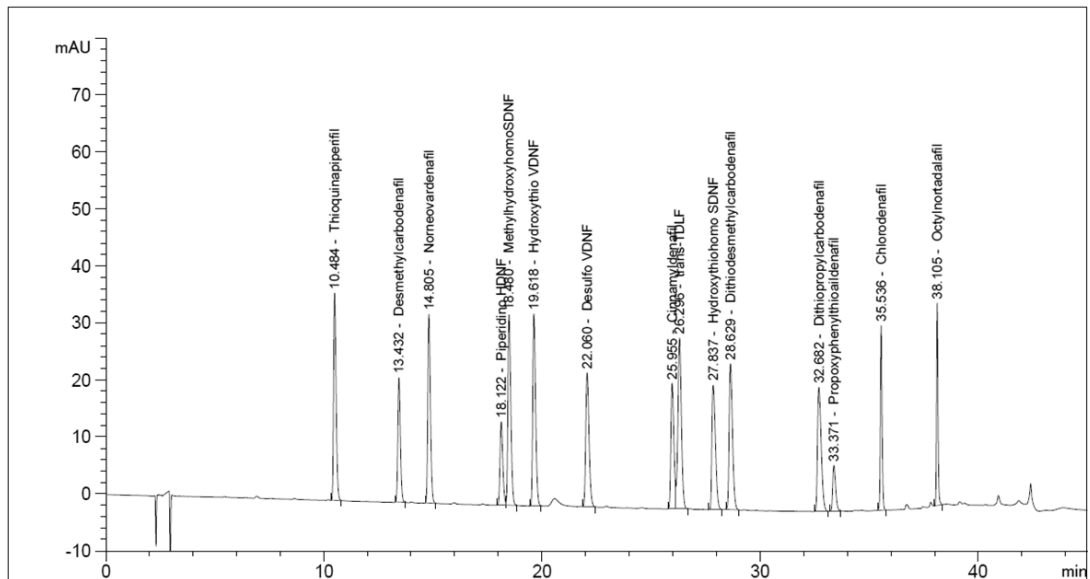
○ Chromatogram



[표준액 1]

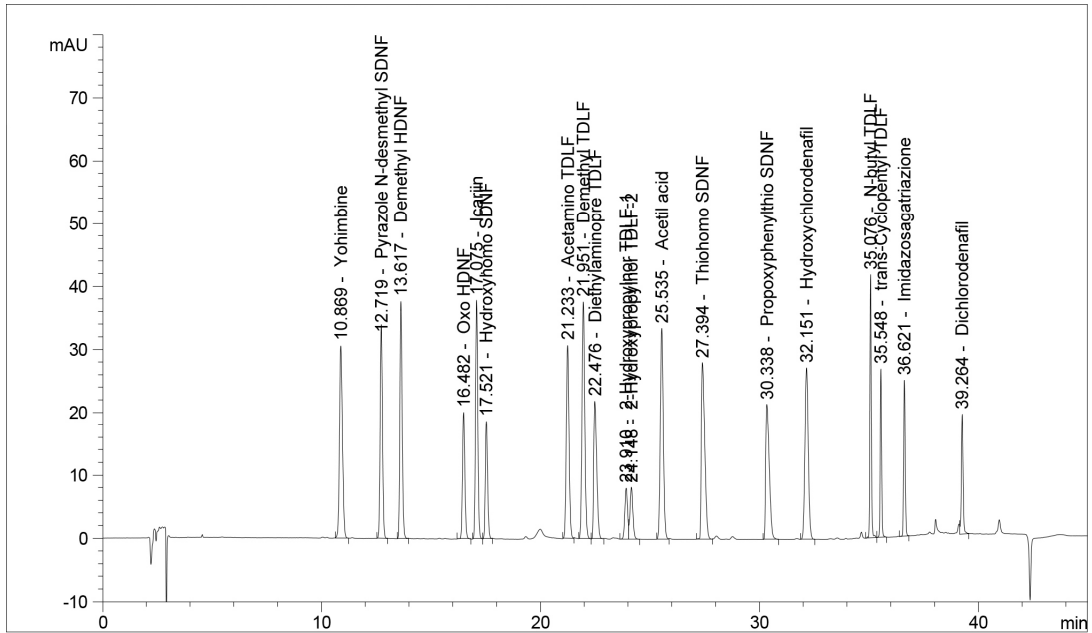


[표준액 2]

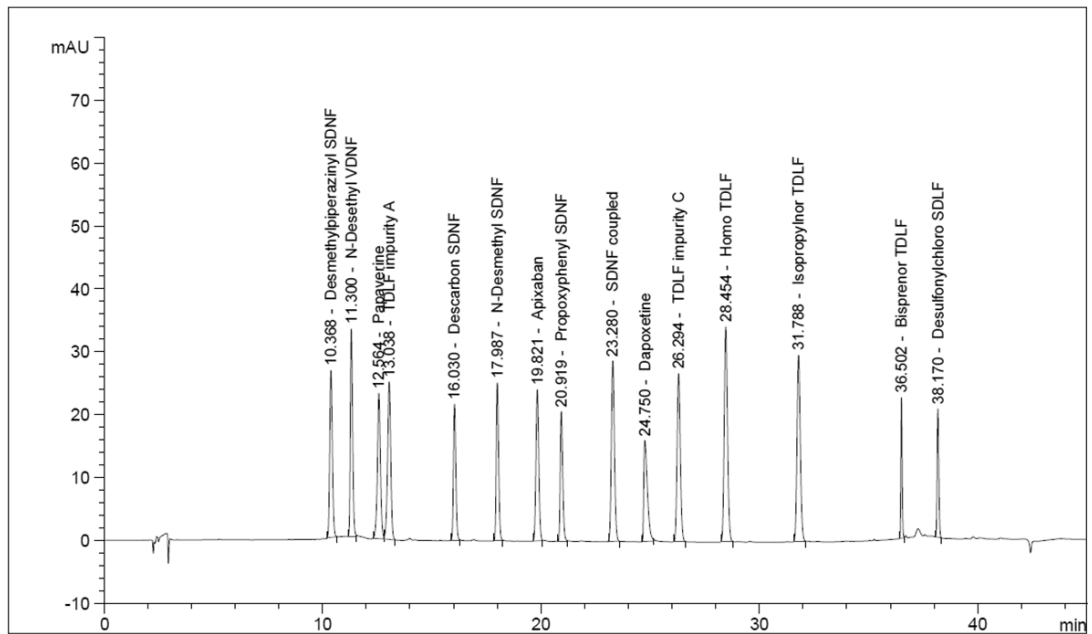


[표준액 3]

II - 4. 발기부전치료제와 그 유사성분(82종) 분석법

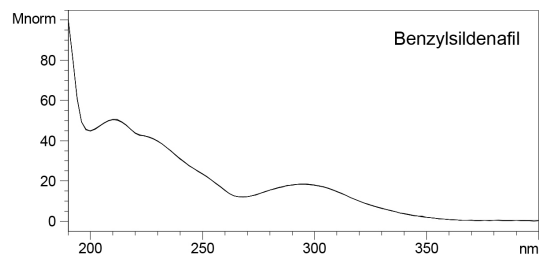
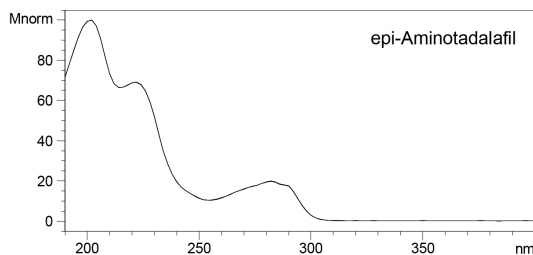
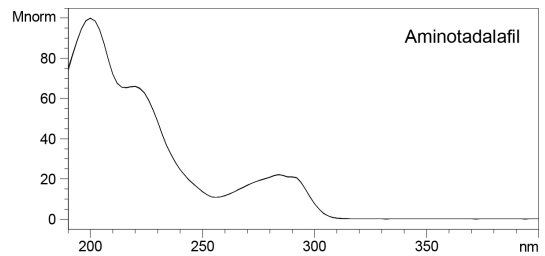
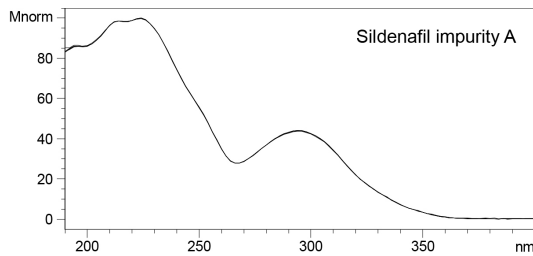
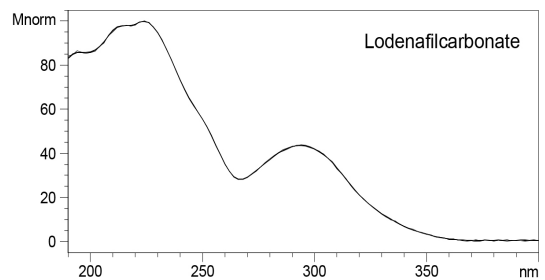
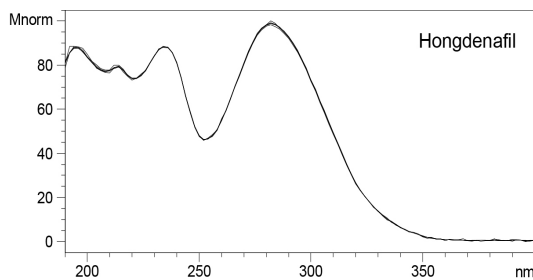
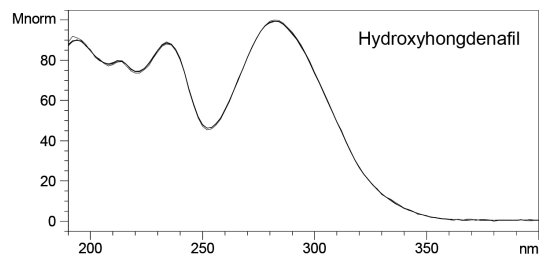
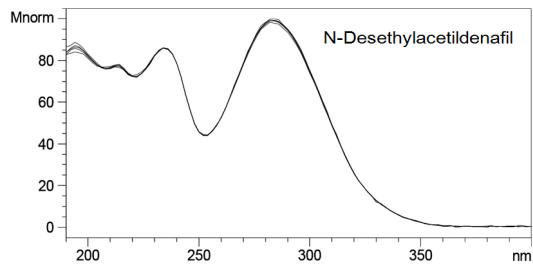
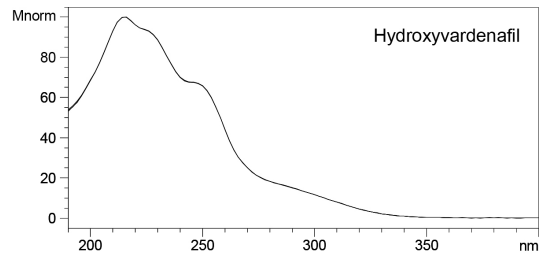
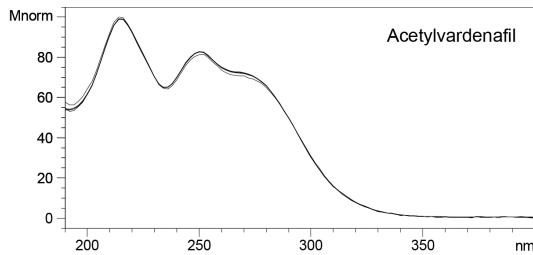


[표준액 4]

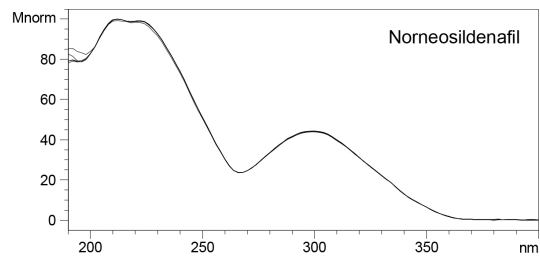
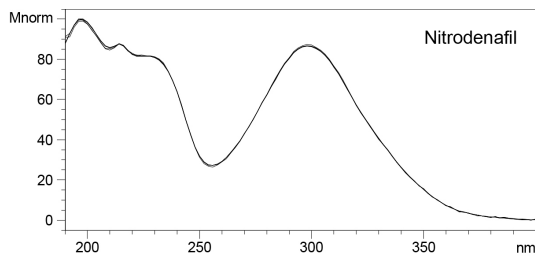
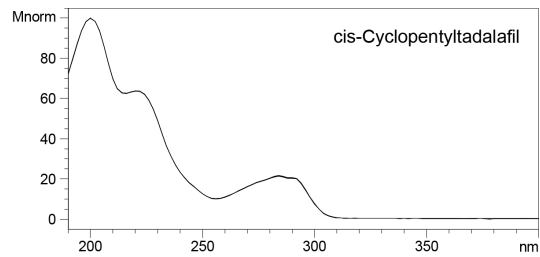
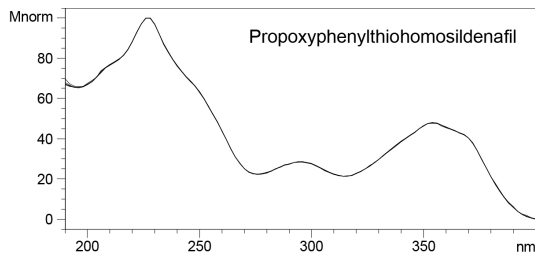
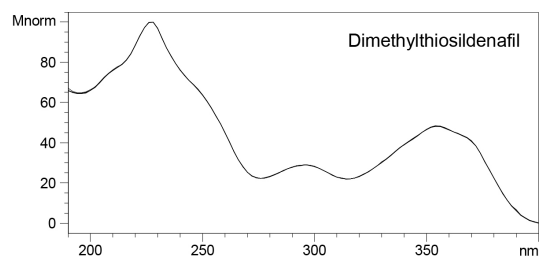
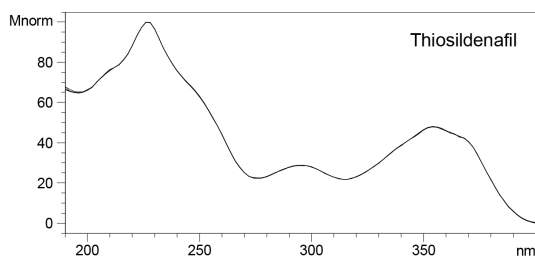
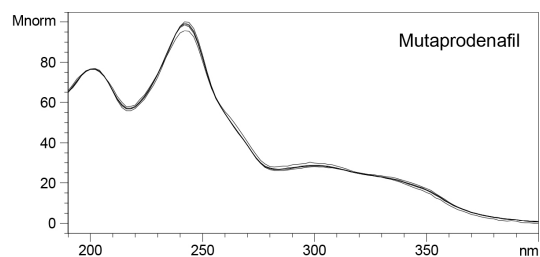
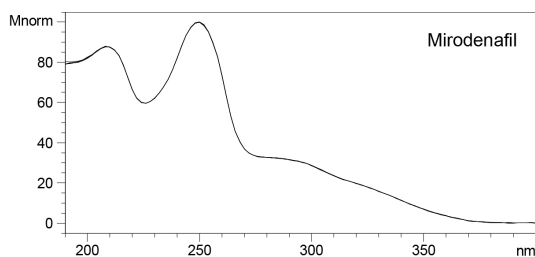


[표준액 5]

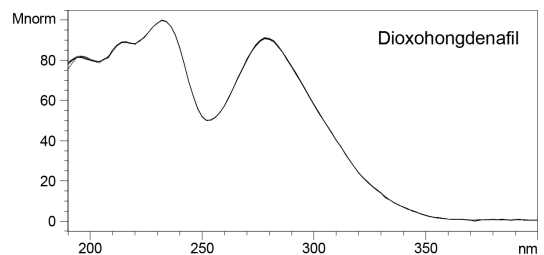
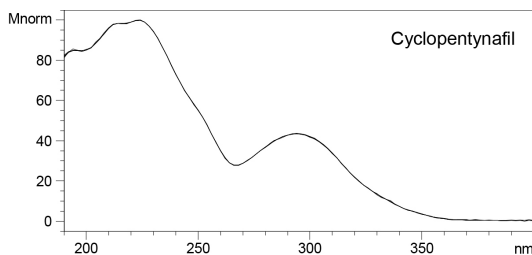
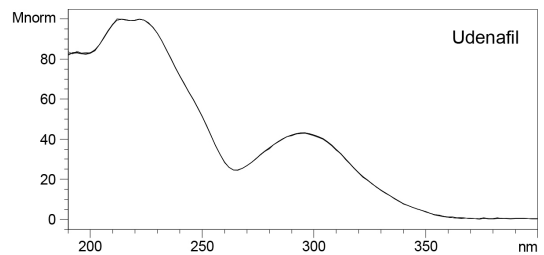
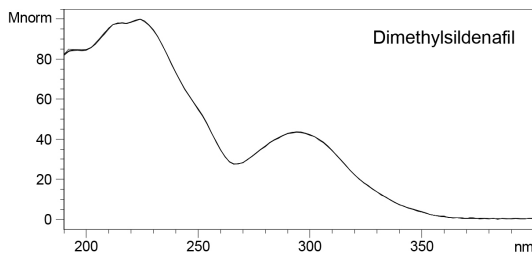
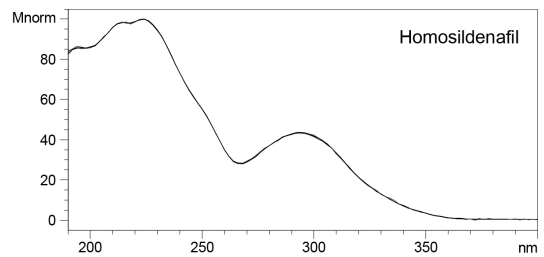
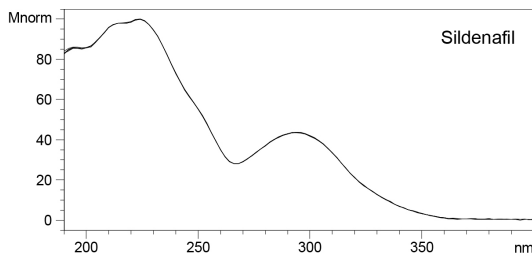
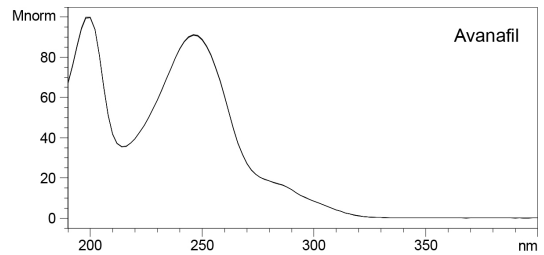
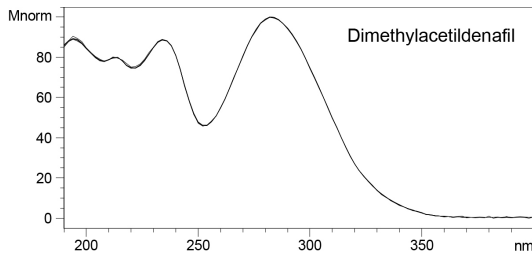
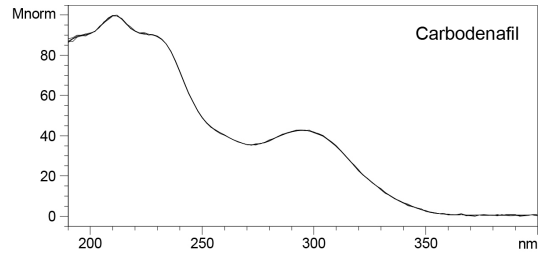
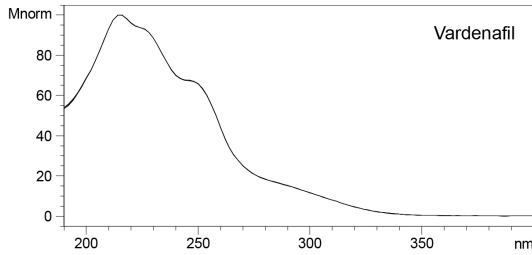
○ PDA Spectrum \* 표준액 1

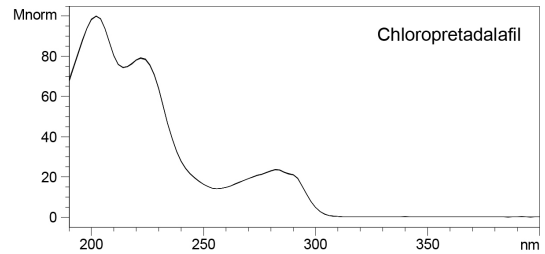
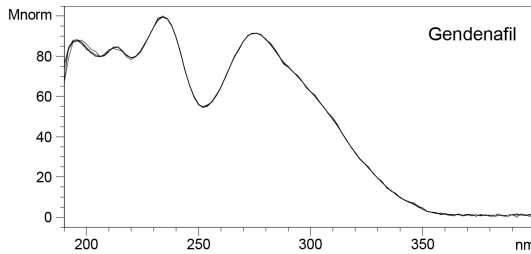
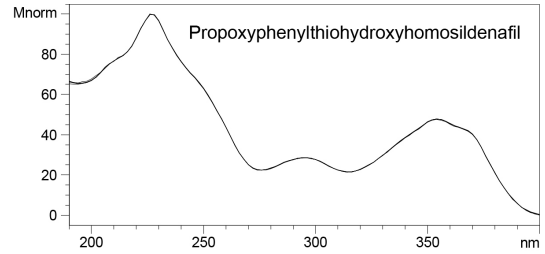
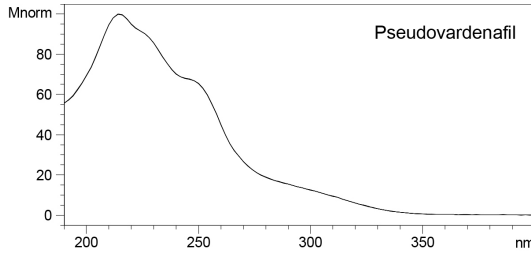
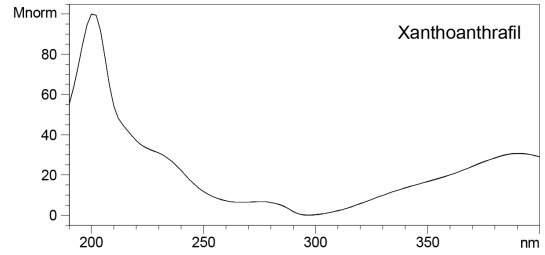
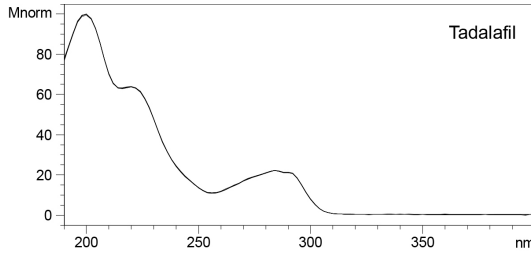


## II-4. 발기부전치료제와 그 유사성분(82종) 분석법

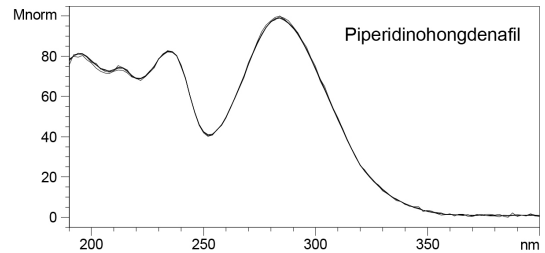
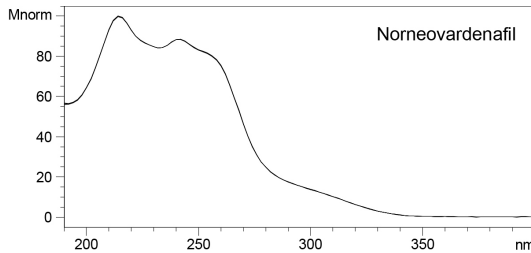
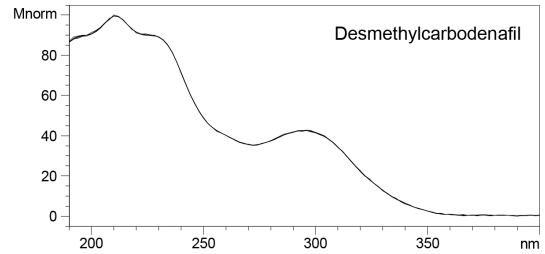
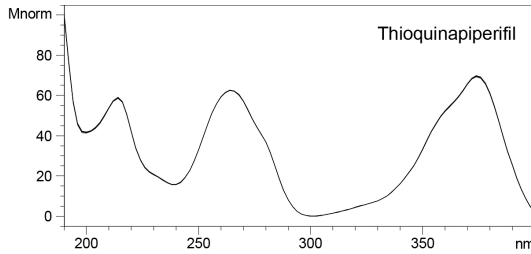


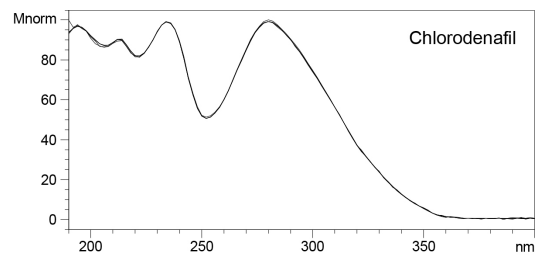
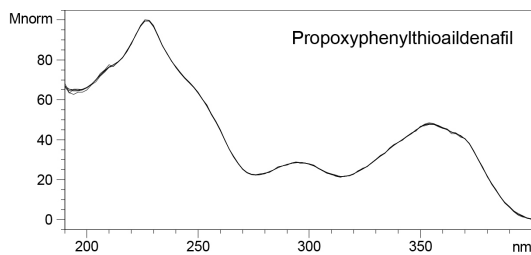
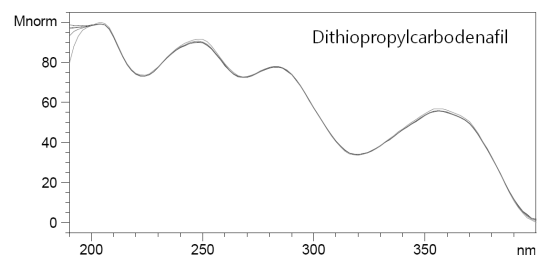
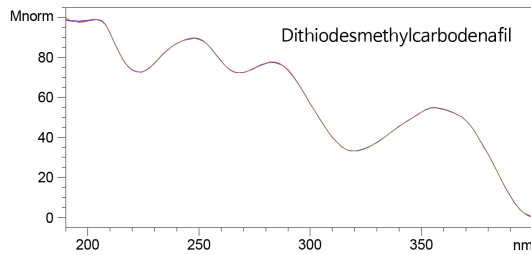
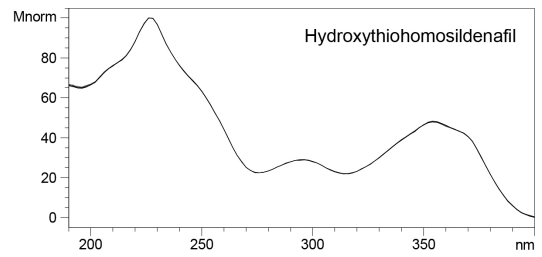
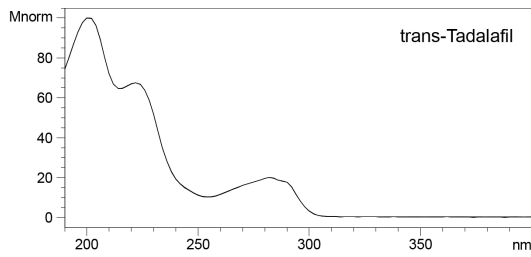
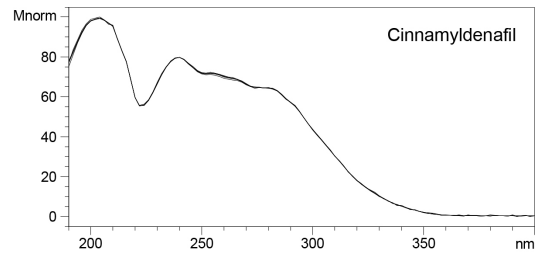
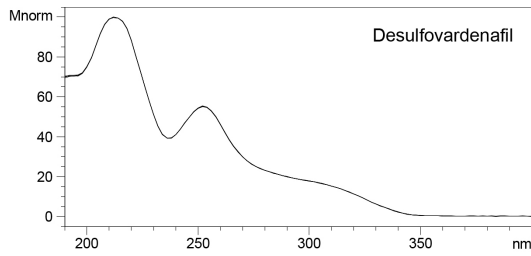
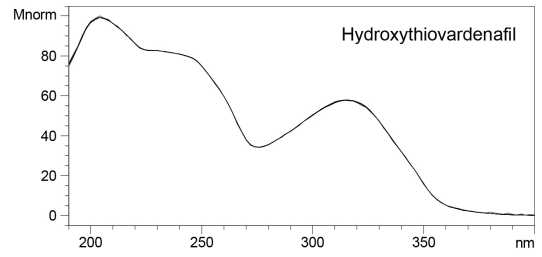
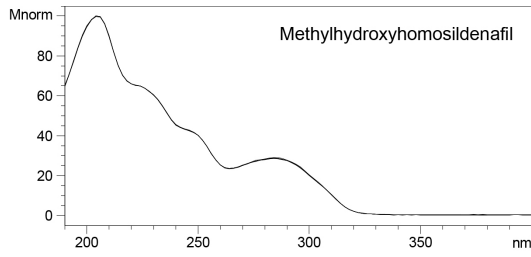
\* 표준액 2



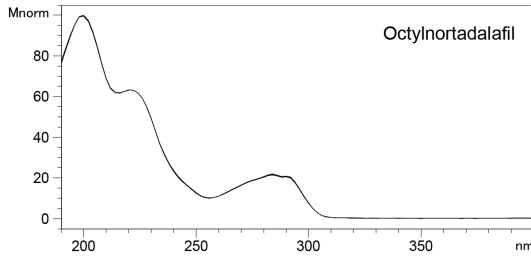


**\* 표준액 3**

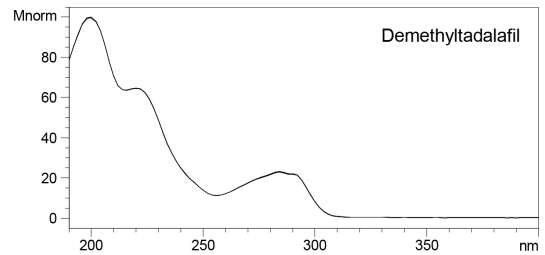
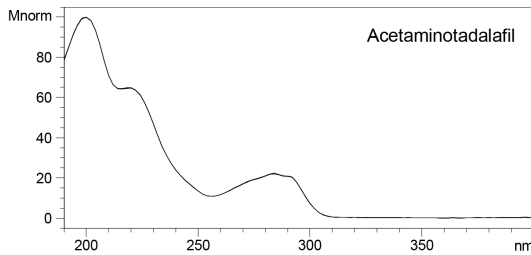
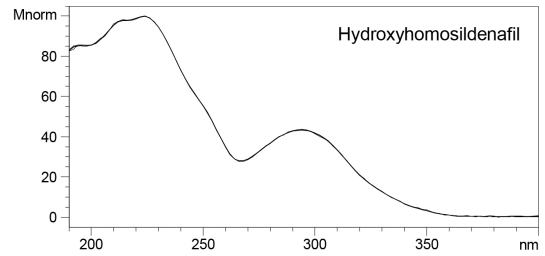
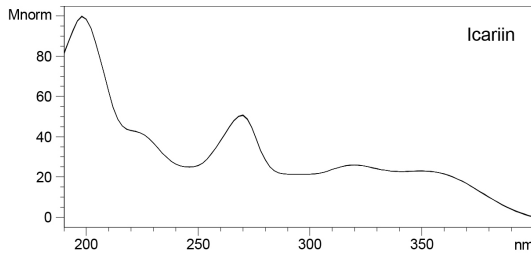
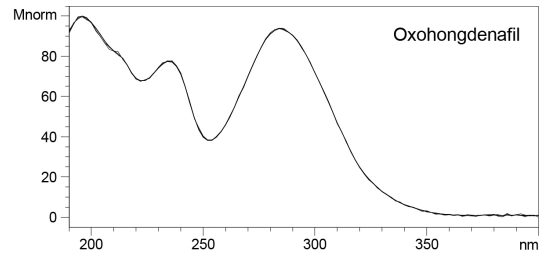
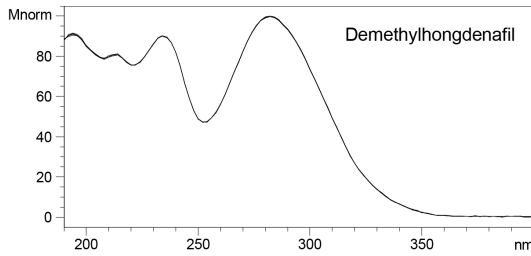
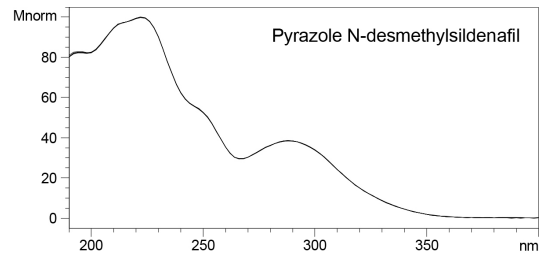
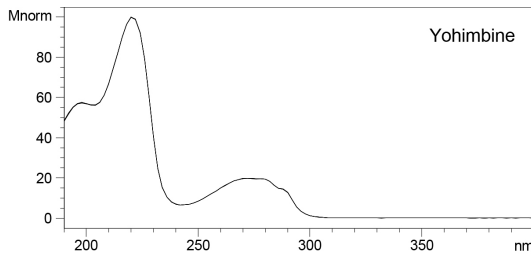


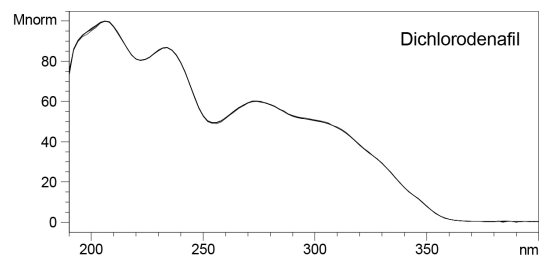
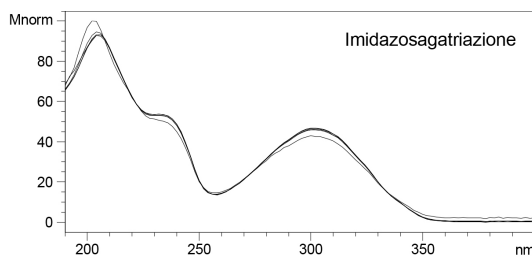
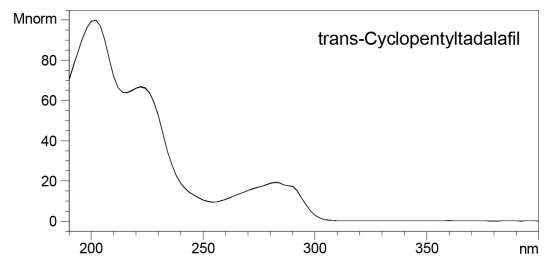
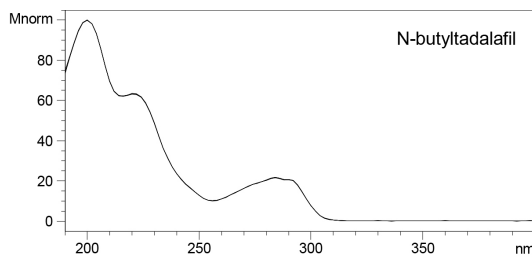
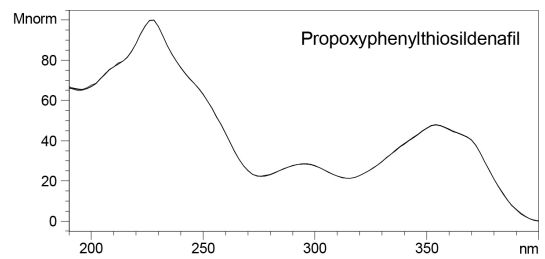
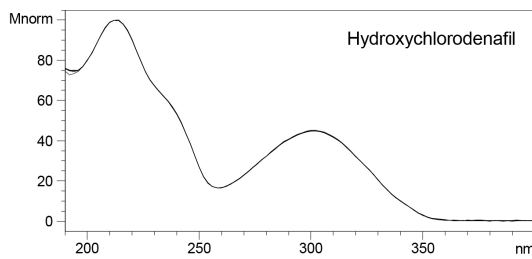
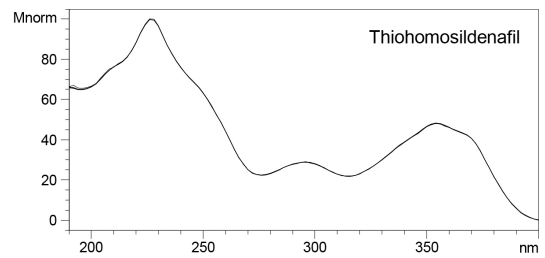
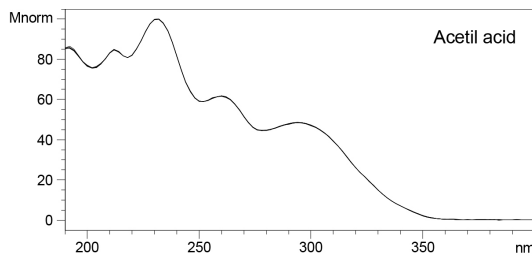
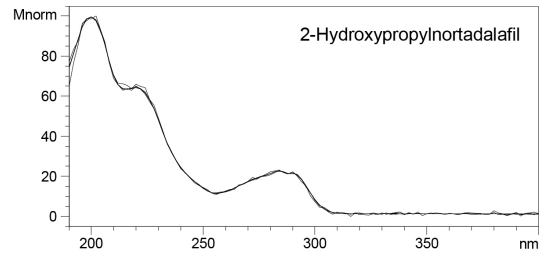
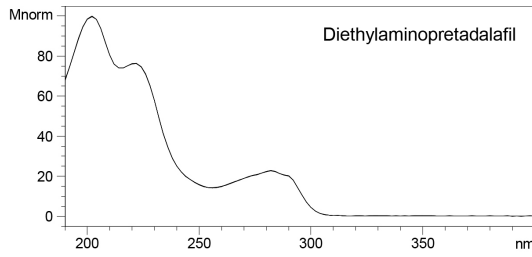




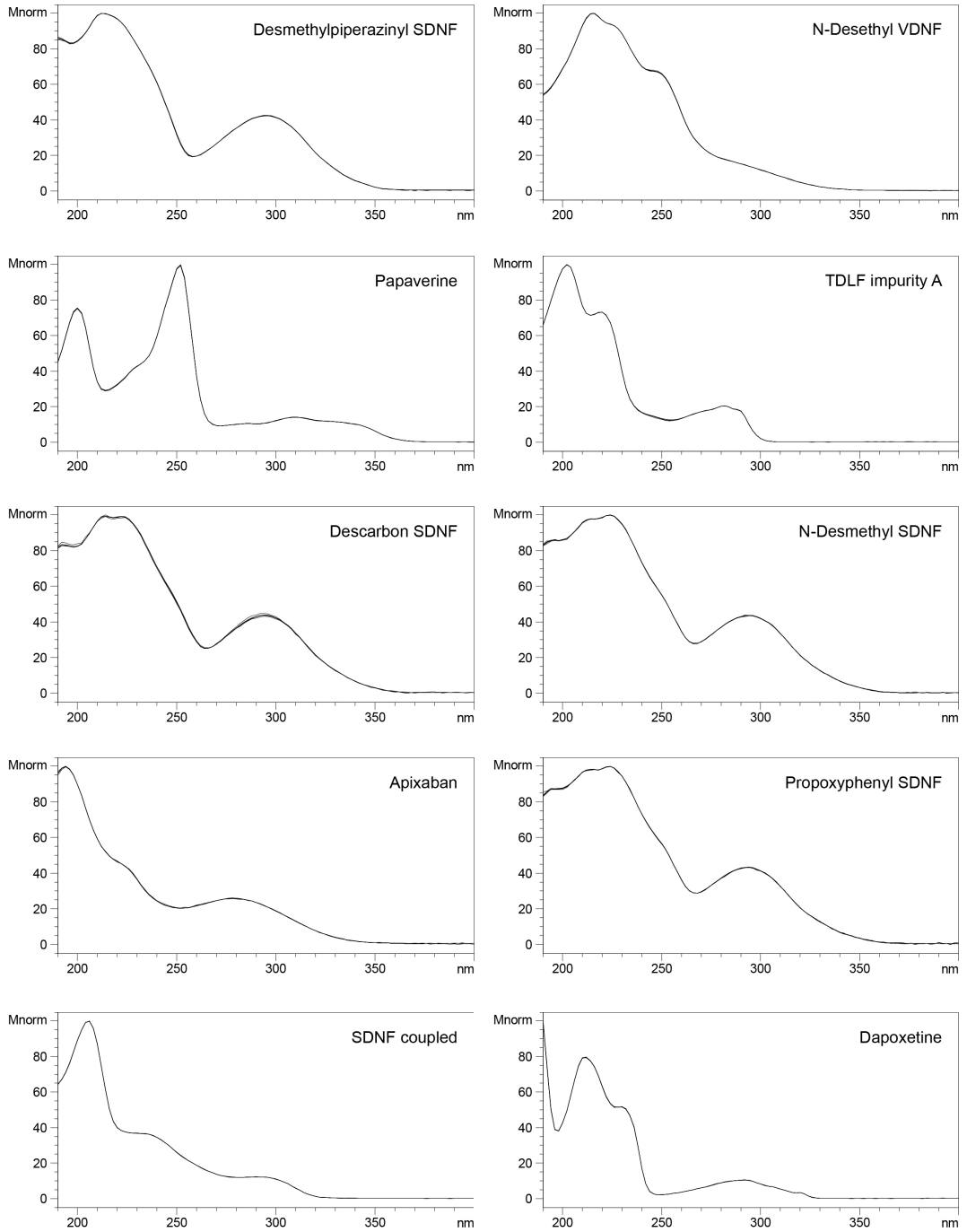


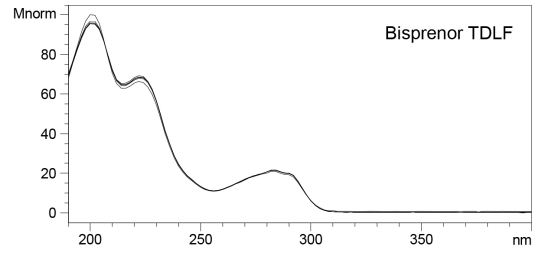
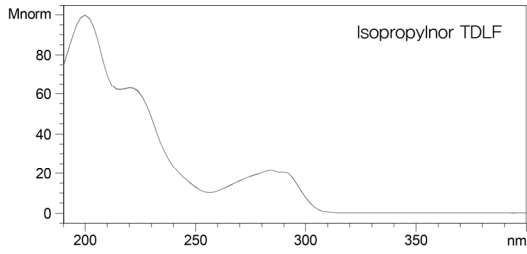
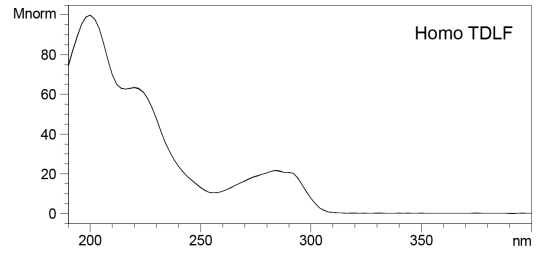
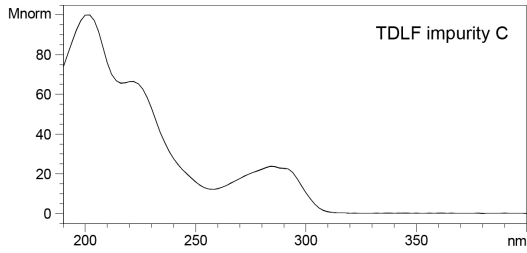
**\* 표준액 4**





\* 표준액 5





## 2. LC-MS/MS

### ○ Analytical conditions of HPLC

• Instrument	Shiseido SP3133		
• Column	CAPCELL PAK C <sub>18</sub> UG120 (2.0 mm × 150 mm, 3.0 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.1% Formic acid in Water		
	(B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	2.0	90	10
	2.5	80	20
	5.0	80	20
	15.0	50	50
	23.0	10	90
	26.0	10	90
	26.5	90	10
	30.0	90	10
• Flow Rate	0.2 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500	
• Ionization Mode	ESI (+)	ESI (-)
• Curtain Gas	30 psi	30 psi
• Collision Gas	9 psi	9 psi
• Ion Voltage	5000 V	4500 V
• Ion Source Gas 1	50 psi	55 psi
• Ion Source Gas 2	50 psi	50 psi
• Source Temp.	450°C	500°C

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion (m/z)	DP (V)	Product Ion (m/z)	CE (V)	CXP (V)
Acetylvardenafil	+	467.2	146	151.1	63	12
				341.2	45	12
				127.0	41	14
Hydroxyvardenafil	+	505.2	176	151.0	57	12
				312.1	57	24
				299.0	57	12
N-Desethyl acetildenafil	+	439.2	146	99.1	39	8
				297.2	53	18
				166.0	65	10
Hydroxyhongdenafil	+	483.2	76	127.0	41	10
				297.2	55	14
				143.1	43	14
Hongdenafil	+	467.2	146	111.0	39	12
				127.1	41	8
				297.1	55	12
Lodenafilcarbonate	+	505.2	76	487.3	33	16
				283.1	57	10
				129.1	39	8
Sildenafil Impurity A	+	489.1	201	297.2	53	10
				325.1	43	10
				136.1	85	12
Aminotadalafil	+	391.1	86	269.0	29	16
				169.3	47	14
				262.1	47	11
epi-Aminotadalafil	+	391.1	80	269.1	19	15
				262.1	47	11
				169.0	42	14
Benzylsildenafil	+	551.2	91	377.2	39	16
				134.1	61	20
Mirodenafil	+	532.2	216	296.0	55	12
				312.0	59	16
Mutaprodenafil	+	630.2	156	141.9	35	14
				377.1	31	10
				312.0	47	32

표준액 1

Compound	Ion Mode	Precursor Ion (m/z)	DP (V)	Product Ion (m/z)	CE (V)	CXP (V)
Thiosildenafil	+	491.1	86	299.0	53	14
				341.2	41	10
				327.0	41	12
Dimethylthiosildenafil	+	505.2	26	299.0	51	22
				327.0	43	22
				113.0	39	10
Propoxyphenylthio homosildenafil	+	519.2	130	299.1	50	10
				327.1	40	13
				113.2	47	11
cis-Cyclopentyl tadalafil	+	444.3	79	322.1	25	28
				169.1	60	11
				134.9	30	11
Nitrodenafil	+	358.2	71	284.2	43	16
				136.1	63	12
Norneosildenafil	+	460.2	71	166.1	69	12
				136.0	81	12
Vardenafil	+	489.2	186	151.1	75	14
				312.0	57	16
Carbodenafil	+	453.2	101	339.2	33	10
				311.1	47	12
				166.0	59	22
Dimethylacetildenafil	+	467.2	81	325.1	51	16
				127.0	41	14
				297.2	57	8
Avanafil	+	484.2	95	375.1	36	23
				155.1	53	12
				221.1	37	13
Sildenafil	+	475.1	176	100.0	37	14
				283.0	51	12
				311.1	41	12
Homosildenafil	+	489.2	116	112.9	39	12
				283.0	53	16
				311.0	43	16
Dimethylsildenafil	+	489.2	131	113.1	39	10
				283.1	55	18
				311.2	43	10

표준액 1

표준액 2

Compound	Ion Mode	Precursor Ion (m/z)	DP (V)	Product Ion (m/z)	CE (V)	CXP (V)
Homosildenafil	+	489.2	116	112.9	39	12
				283.0	53	16
				311.0	43	16
Dimethylsildenafil	+	489.2	131	113.1	39	10
				283.1	55	18
				311.2	43	10
Udenafil	+	517.2	71	283.2	61	14
				325.3	51	12
Cyclopentynafil	+	529.2	216	461.2	41	14
				283.1	61	20
Dioxohongdenafil	+	495.3	176	127.1	47	10
				311.2	55	14
				268.1	19	10
Tadalafil	+	390.1	61	168.9	47	14
				134.9	31	12
				151.1	33	18
Xanthoanthrafil	+	390.1	71	107.2	83	12
				151.1	63	12
Pseudovardenafil	+	460.2	96	110.1	97	14
				299.1	53	18
Propoxyphenylthiohydroxy homosildenafil	+	535.2	51	128.9	41	16
				315.0	55	16
				285.0	43	24
Gendenafil	+	355.1	46	326.9	35	18
				135.1	27	14
Chloropretadalafil	+	427.1	136	274.2	43	14
				204.1	35	8
Thioquinapiperifil	+	449.2	126	186.1	55	8
				118.0	71	16
				339.1	35	10
Desmethylcarbodenafil	+	439.3	130	166.1	60	20
				147.1	55	15
Norneovardenafil	+	357.1	121	151.0	43	12
				300.1	43	16
Piperidinohongdenafil	+	438.2	211	98.2	41	10
				166.1	67	20

표준액 2

표준액 3



Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	DP (V)	Product Ion ( <i>m/z</i> )	CE (V)	CXP (V)
Methylhydroxyhomo sildenafil	+	519.2	126	129.1	43	16
				297.2	53	10
				267.2	75	10
				328.0	57	10
Hydroxythiovarденаafil	+	521.2	176	167.0	73	22
				314.9	61	24
Desulfovardenafil	+	313.1	196	151.1	37	10
				256.1	41	8
Cinnamylденafil	+	555.2	81	116.9	59	16
				437.2	31	12
				355.2	41	18
<i>trans</i> -Tadalafil	+	390.1	81	268.1	19	12
				169.1	57	14
				135.1	29	12
Hydroxythiohomo sildenafil	+	521.2	191	99.1	41	10
				299.1	55	12
Dithiodesmethyl carbodenafil	+	471.1	146	371.0	33	22
				343.0	47	20
				178.8	63	16
Propoxyphenylthio aildenafil	+	519.1	151	299.1	49	10
				113.0	41	14
				315.1	51	12
Chlorodenafil	+	389.1	136	361.1	37	12
				285.0	43	12
Octylnortadalafil	+	488.3	86	366.3	25	12
				204.2	109	14
				343.1	49	10
Dithiopropylcarbodenafil	+	499.1	96	371.1	35	16
				178.9	67	16
Yohimbine	+	355.2	156	144.2	43	10
				212.1	33	12
Pyrazole <i>N</i> -Desmethylsildenafil	+	461.2	101	100.1	35	10
				269.1	53	10
				297.1	43	8
Demethylhongdenafil	+	453.2	130	113.2	41	12
				297.2	47	11

표준액 3

Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	DP (V)	Product Ion ( <i>m/z</i> )	CE (V)	CXP (V)
Oxohongdenafil	+	481.2	141	410.1	43	24
				297.1	57	10
				165.0	47	14
Icariin	-	675.1	95	513.2	16	15
				367.1	44	11
Hydroxyhomo sildenafil	+	505.1	86	487.2	37	18
				283.1	55	12
				112.0	39	8
Acetaminotadalafil	+	434.1	136	262.2	45	8
				134.9	27	10
				311.0	25	12
Demethyltadalafil	+	377.1	81	255.0	19	16
				204.9	56	14
Diethylaminopretadalafil	+	464.2	1	86.1	43	14
				274.1	57	8
				134.9	37	18
2-Hydroxypropyl nortadalafil	+	434.2	91	312.1	21	8
				135.0	37	10
				262.1	49	24
Acetil acid	+	357.2	84	329.2	42	11
				300.1	52	22
				256.2	53	9
Thiohomosildenafil	+	505.1	16	299.0	53	20
				327.1	45	16
				355.1	43	14
Propoxyphenylthio sildenafil	+	505.2	176	299.1	51	10
				315.0	57	12
				271.1	59	12
Hydroxychlorodenafil	+	391.1	130	313.1	47	11
				285.1	47	11
N-Butyltadalafil	+	432.3	41	310.0	23	20
				134.9	35	16
				322.2	23	14
<i>trans</i> -Cyclopentyl tadalafil	+	444.2	1	169.2	57	12
				204.0	87	22

표준액 4

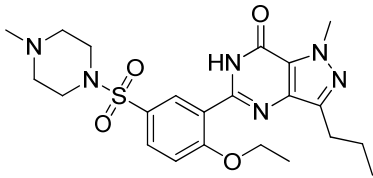
	Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	DP (V)	Product Ion ( <i>m/z</i> )	CE (V)	CXP (V)
표준액 4	Imidazosagatriazione	+	313.1	61	285.0	35	26
					256.0	43	20
	Dichlorodenafil	+	407.1	71	378.9	39	24
					349.9	45	12
N-Desmethylpiperazinyl sildenafil sulfonic acid	+	393.1	100	364.9	37	22	
				256.1	49	12	
N-Desethylvardenafil	+	461.1	96	151.1	51	14	
				312.2	51	12	
Papaverine	+	340.1	101	284.1	51	14	
				324.1	43	12	
Tadalafil Impurity A	+	350.1	71	202.0	37	10	
				171.0	51	14	
Descarbonsildenafil	+	463.2	131	264.1	25	16	
				333.0	19	10	
N-Desmethylsildenafil	+	461.2	61	206.0	47	22	
				418.2	43	10	
Apixaban	+	460.2	126	311.2	53	10	
				283.1	37	14	
Propoxyphenyl sildenafil	+	489.2	136	283.1	51	18	
				164.8	61	14	
Sildenafil coupled	+	331.1	55	121.1	39	15	
				149.0	30	12	
Dapoxetine	+	306.1	70	314.1	26	14	
				261.2	20	10	
Dapoxetine	+	306.1	70	183.2	27	11	
				157.0	40	15	

Compound	Ion Mode	Precursor Ion (m/z)	DP (V)	Product Ion (m/z)	CE (V)	CXP (V)
Tadalafil Impurity C	+	426.1	121	135.1	37	10
				395.0	17	20
				276.0	27	12
Homotadalafil	+	404.2	11	282.0	19	10
				204.0	83	18
				169.1	47	11
Isopropyl nortadalafil	+	418.1	105	296.2	30	10
				135.2	37	9
				360.2	45	11
Bisprenortadalafil	+	766.2	130	334.0	45	11
				262.0	60	20
				319.1	38	13
Desulfonylchlorosildenafil	+	347.2	130	289.6	51	10

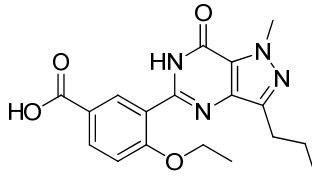
표준액 5

■ 구조식

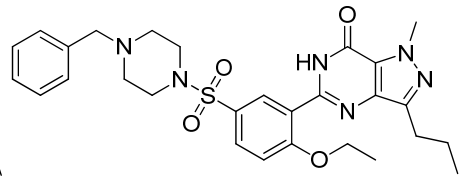
○ Sildenafil analogue(38종)



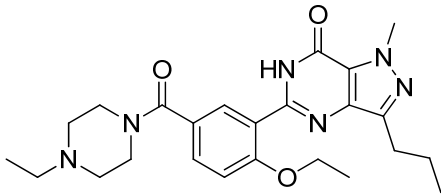
Sildenafil  
[C<sub>22</sub>H<sub>30</sub>N<sub>6</sub>O<sub>4</sub>S]



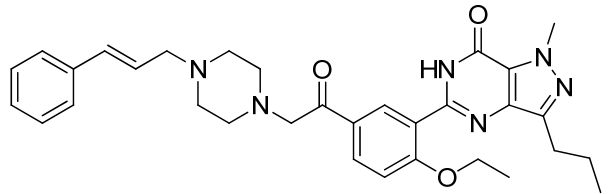
Acetil acid  
[C<sub>18</sub>H<sub>20</sub>N<sub>4</sub>O<sub>4</sub>]



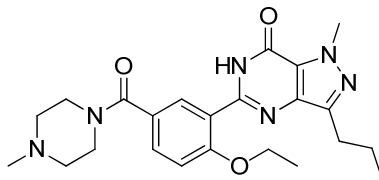
Benzylsildenafil  
[C<sub>28</sub>H<sub>34</sub>N<sub>6</sub>O<sub>4</sub>S]



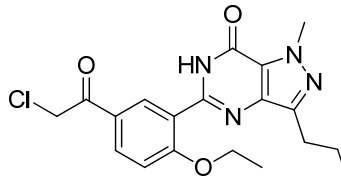
Carbodenafil  
[C<sub>24</sub>H<sub>32</sub>N<sub>6</sub>O<sub>3</sub>]



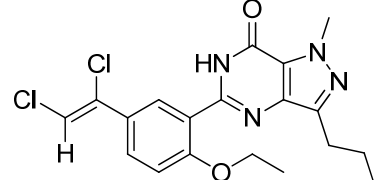
Cinnamyldenafil  
[C<sub>32</sub>H<sub>38</sub>N<sub>6</sub>O<sub>3</sub>]



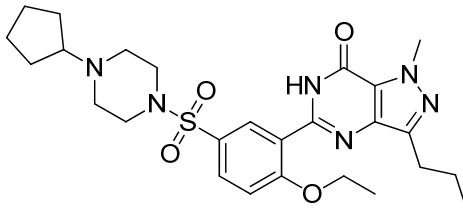
Desmethylcarbodenafil  
[C<sub>23</sub>H<sub>30</sub>N<sub>6</sub>O<sub>3</sub>]



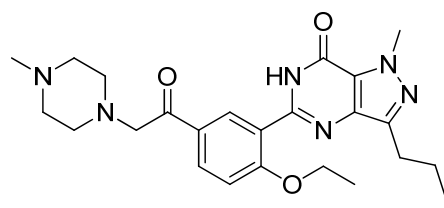
Chlorodenafil  
[C<sub>19</sub>H<sub>21</sub>ClN<sub>4</sub>O<sub>3</sub>]



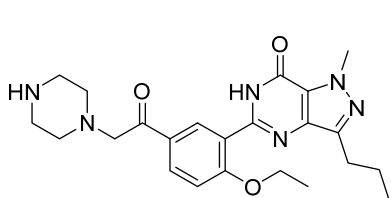
Dichlorodenafil  
[C<sub>19</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>]



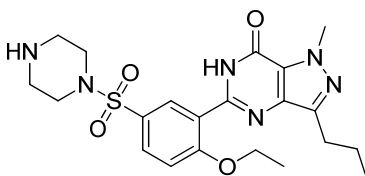
Cyclopentynafil  
[C<sub>26</sub>H<sub>36</sub>N<sub>6</sub>O<sub>4</sub>S]



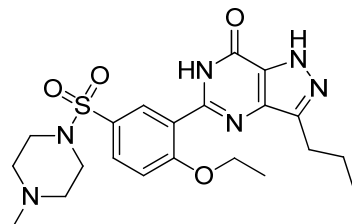
Demethylhongdenafil  
[C<sub>24</sub>H<sub>32</sub>N<sub>6</sub>O<sub>3</sub>]



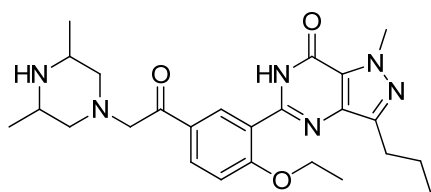
*N*-Desethylacetildenafil  
[C<sub>23</sub>H<sub>30</sub>N<sub>6</sub>O<sub>3</sub>]



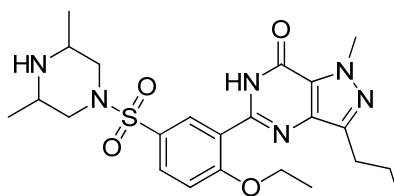
*N*-Desmethylsildenafil  
[C<sub>21</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>S]



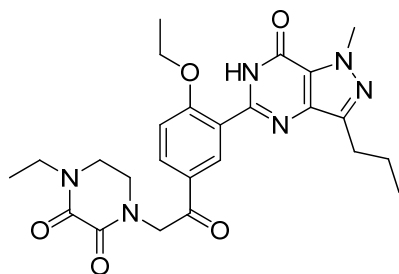
Pyrazole *N*-Desmethylsildenafil  
[C<sub>21</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>S]



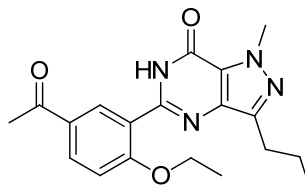
Dimethylacetildenafil  
[C<sub>25</sub>H<sub>34</sub>N<sub>6</sub>O<sub>3</sub>]



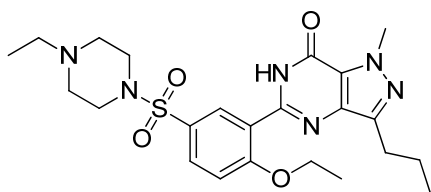
Dimethylsildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S]



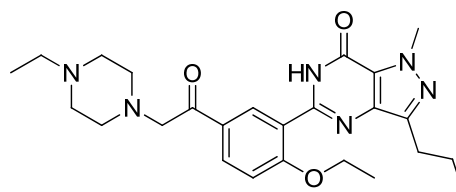
Dioxohongdenafil  
[C<sub>25</sub>H<sub>30</sub>N<sub>6</sub>O<sub>5</sub>]



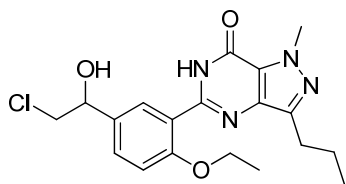
Gendenafil  
[C<sub>19</sub>H<sub>22</sub>N<sub>4</sub>O<sub>3</sub>]



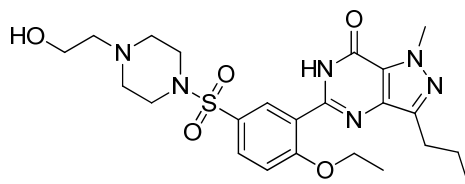
Homosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S]



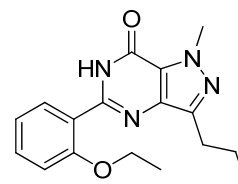
Hongdenafil  
[C<sub>28</sub>H<sub>34</sub>N<sub>6</sub>O<sub>3</sub>]



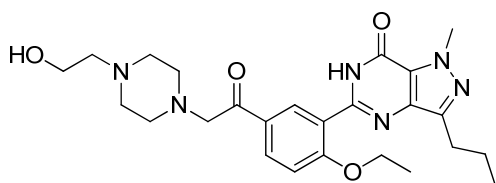
Hydroxychlorodenafil  
[C<sub>19</sub>H<sub>23</sub>ClN<sub>4</sub>O<sub>3</sub>]



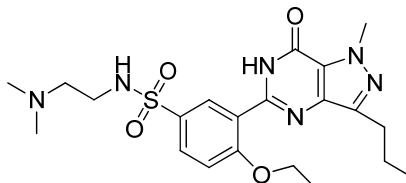
Hydroxyhomosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>5</sub>S]



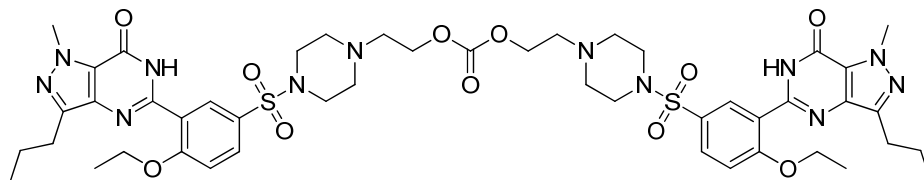
Imidazosagatriazinone  
[C<sub>17</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>]



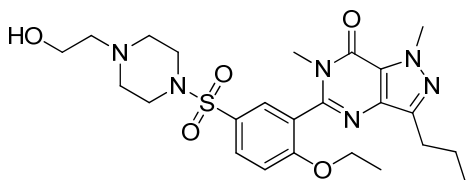
Hydroxyhongdenafil  
[C<sub>25</sub>H<sub>34</sub>N<sub>6</sub>O<sub>4</sub>]



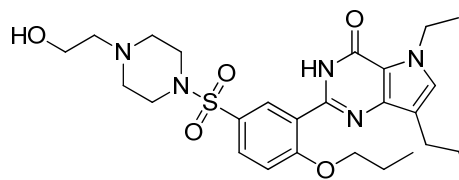
Descarbonsildenafil  
[C<sub>21</sub>H<sub>30</sub>N<sub>6</sub>O<sub>4</sub>S]



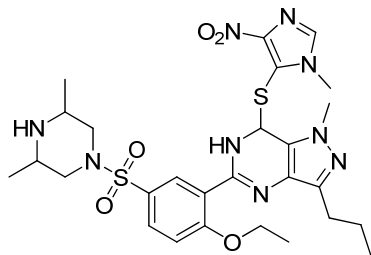
Lodenafilcarbonate  
[C<sub>47</sub>H<sub>62</sub>N<sub>12</sub>O<sub>11</sub>S<sub>2</sub>]



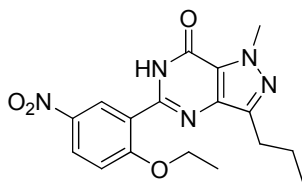
Methylhydroxyhomosildenafil  
[C<sub>24</sub>H<sub>34</sub>N<sub>6</sub>O<sub>5</sub>S]



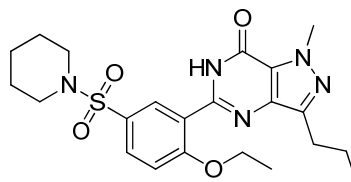
Mirodenafil  
[C<sub>26</sub>H<sub>37</sub>N<sub>5</sub>O<sub>5</sub>S]



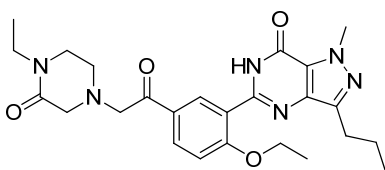
Mutaprodenafil  
[C<sub>27</sub>H<sub>35</sub>N<sub>9</sub>O<sub>5</sub>S<sub>2</sub>]



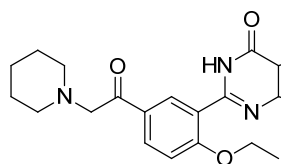
Nitrodenafil  
[C<sub>17</sub>H<sub>19</sub>N<sub>5</sub>O<sub>4</sub>]



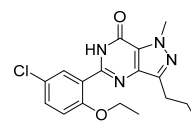
Norneosildenafil  
[C<sub>22</sub>H<sub>29</sub>N<sub>5</sub>O<sub>4</sub>S]



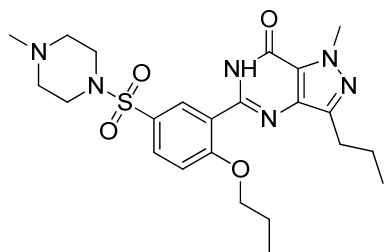
Oxohongdenafil  
[C<sub>25</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>]



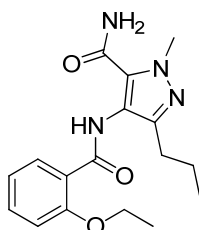
Piperidinohongdenafil  
[C<sub>24</sub>H<sub>31</sub>N<sub>5</sub>O<sub>3</sub>]



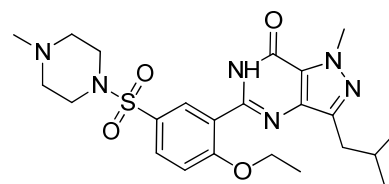
Desulfonylchlorosildenafil  
[C<sub>17</sub>H<sub>19</sub>ClN<sub>4</sub>O<sub>2</sub>]



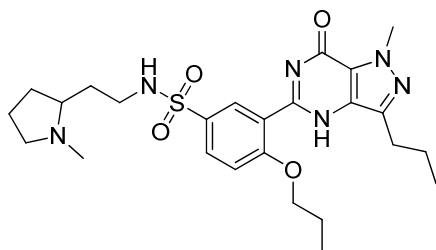
Propoxyphenylsildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S]



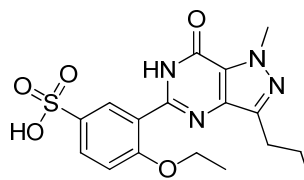
Sildenafil coupled  
[C<sub>17</sub>H<sub>22</sub>N<sub>4</sub>O<sub>3</sub>]



Sildenafil Impurity A  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S]



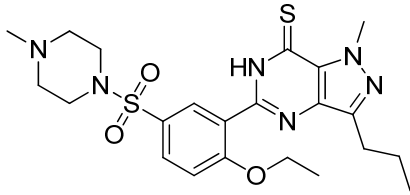
Udenafil  
[C<sub>25</sub>H<sub>36</sub>N<sub>6</sub>O<sub>4</sub>S]



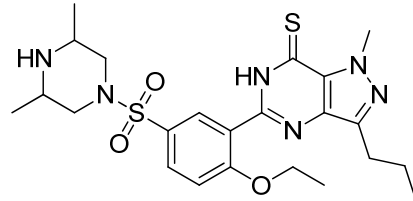
N-Desmethylpiperazinyl sildenafil sulfonic acid  
[C<sub>17</sub>H<sub>20</sub>N<sub>4</sub>O<sub>5</sub>S]



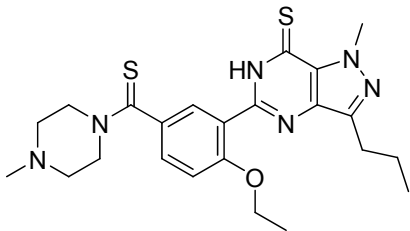
○ Thiosildenafil analogue(10종)



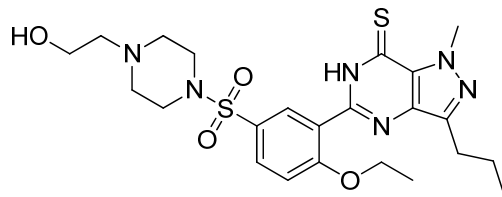
Thiosildenafil  
[C<sub>22</sub>H<sub>30</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]



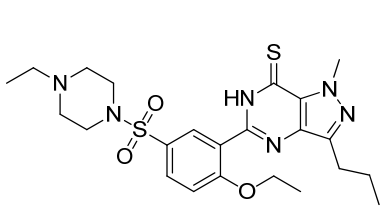
Dimethylthiosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]



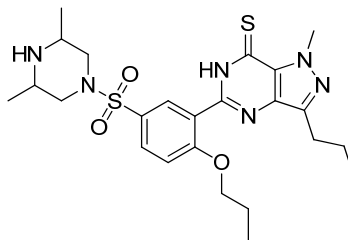
Dithiodesmethylcarbodenafil  
[C<sub>23</sub>H<sub>30</sub>N<sub>6</sub>OS<sub>2</sub>]



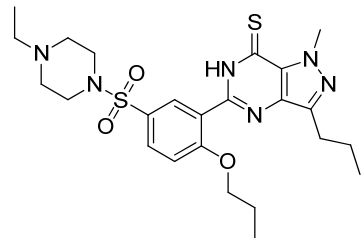
Hydroxythiohomosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S<sub>2</sub>]



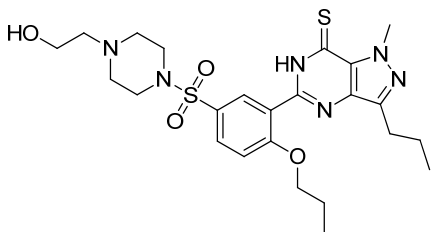
Thiohomosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]



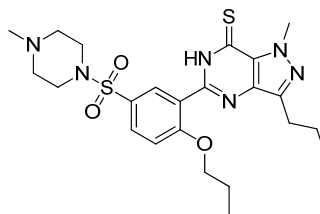
Propoxyphenylthioaidenafil  
[C<sub>24</sub>H<sub>34</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]



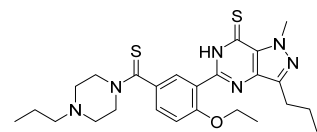
Propoxyphenylthiohomosildenafil  
1  
[C<sub>24</sub>H<sub>34</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]



Propoxyphenylthiohydroxyhomosildenafil  
[C<sub>24</sub>H<sub>34</sub>N<sub>6</sub>O<sub>4</sub>S<sub>2</sub>]

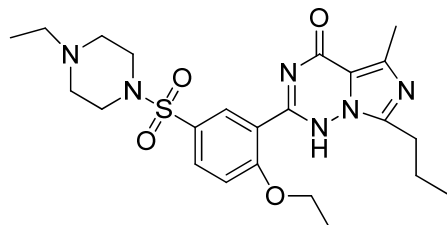


Propoxyphenylthiosildenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>3</sub>S<sub>2</sub>]

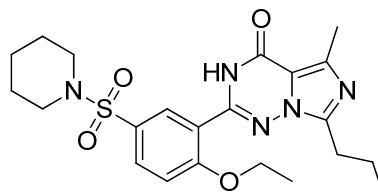


Dithiopropylcarbodenafil  
[C<sub>25</sub>H<sub>34</sub>N<sub>6</sub>OS<sub>2</sub>]

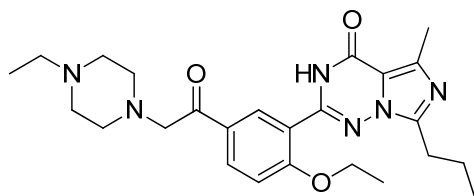
○ Vardenafil analogue(8종)



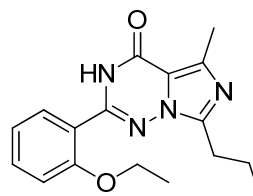
Vardenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S]



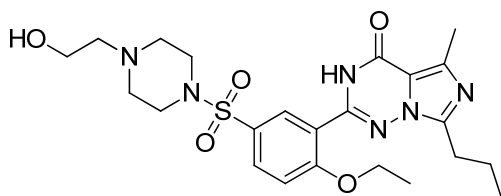
Pseudovardenafil  
[C<sub>22</sub>H<sub>29</sub>N<sub>5</sub>O<sub>4</sub>S]



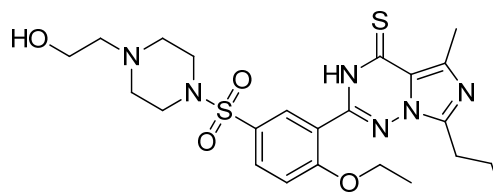
Acetylvardenafil  
[C<sub>25</sub>H<sub>34</sub>N<sub>6</sub>O<sub>3</sub>]



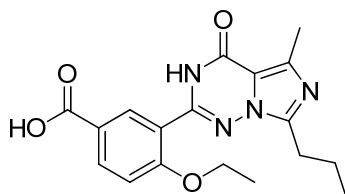
Desulfovardenafil  
[C<sub>17</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>]



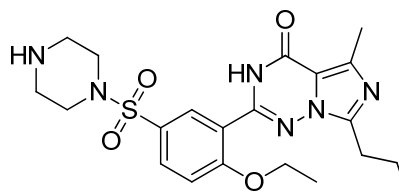
Hydroxyvardenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>5</sub>S]



Hydroxythiovardenafil  
[C<sub>23</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>S<sub>2</sub>]

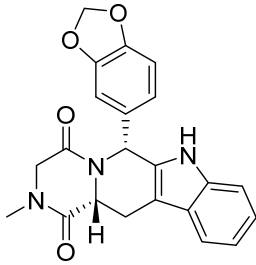


Norneovardenafil  
[C<sub>18</sub>H<sub>20</sub>N<sub>4</sub>O<sub>4</sub>]

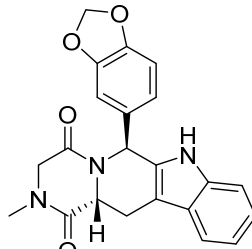


N-Desethylvardenafil  
[C<sub>21</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>S]

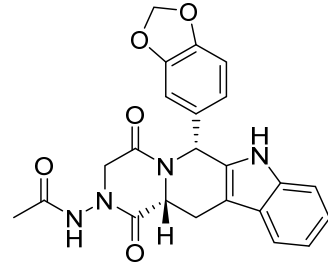
○ Tadalafil analogue(18종)



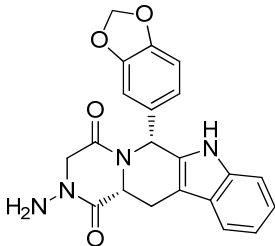
Tadalafil  
[C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>]



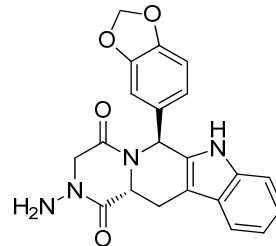
*trans*-Tadalafil  
[C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>]



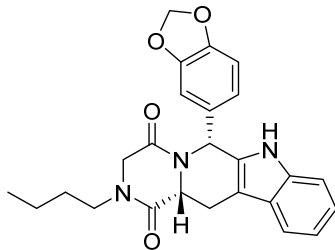
Acetaminotadalafil  
[C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O<sub>5</sub>]



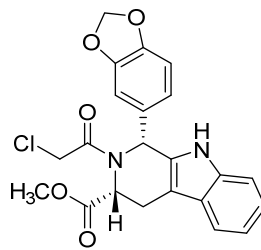
Aminotadalafil  
[C<sub>21</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>]



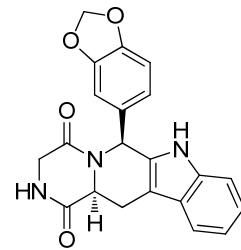
*epi*-Aminotadalafil  
[C<sub>21</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>]



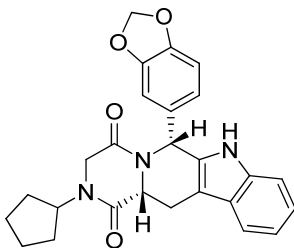
*N*-Butyltadalafil  
[C<sub>25</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>]



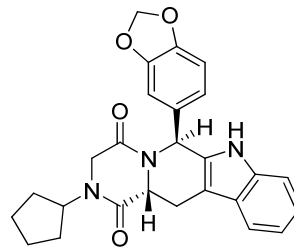
Chloropretadalafil  
[C<sub>22</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>5</sub>]



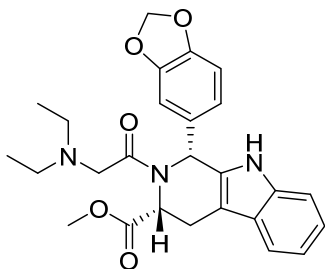
Demethyltadalafil  
[C<sub>21</sub>H<sub>17</sub>N<sub>3</sub>O<sub>4</sub>]



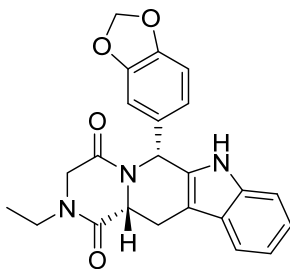
Cyclopentyltadalafil  
[C<sub>26</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>]



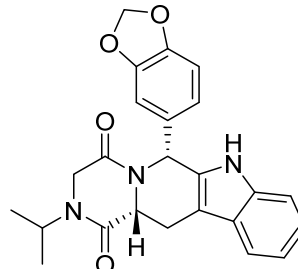
*trans*-Cyclopentyltadalafil  
[C<sub>26</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>]



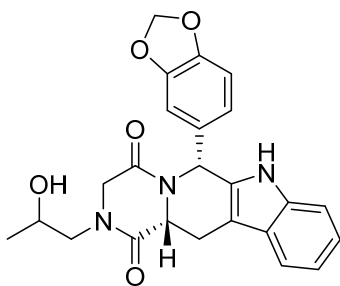
Diethylaminopretadalafil  
[C<sub>26</sub>H<sub>29</sub>N<sub>3</sub>O<sub>5</sub>]



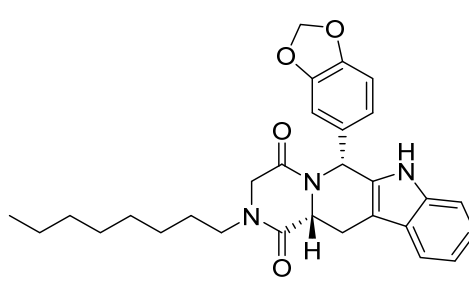
Homotadalafil  
[C<sub>23</sub>H<sub>21</sub>N<sub>3</sub>O<sub>4</sub>]



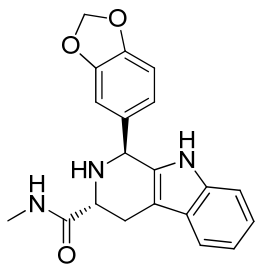
Isopropylpretadalafil  
[C<sub>24</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub>]



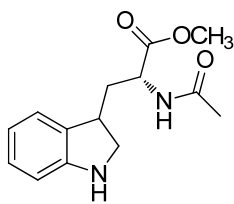
2-Hydroxypropylpretadalafil  
[C<sub>24</sub>H<sub>23</sub>N<sub>3</sub>O<sub>5</sub>]



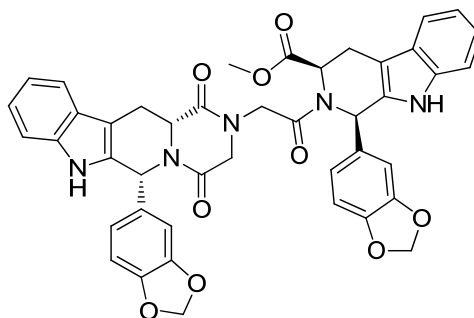
N-Octylpretadalafil  
[C<sub>29</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>]



Tadalafil Impurity A  
[C<sub>20</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>]

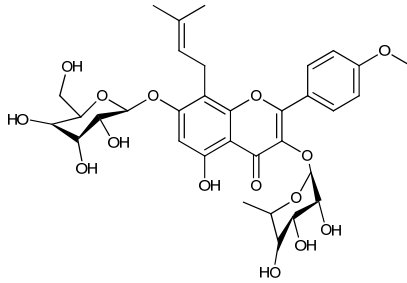


Tadalafil Impurity C  
[C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>]

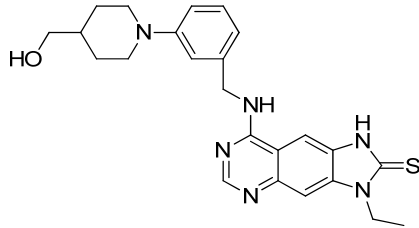


Bispretadalafil  
[C<sub>43</sub>H<sub>35</sub>N<sub>5</sub>O<sub>9</sub>]

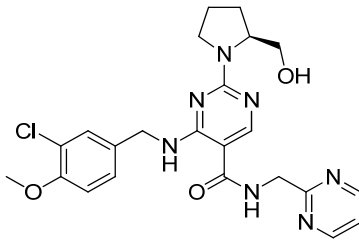
○ Etc.(8종)



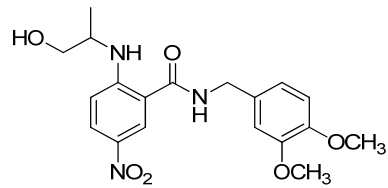
Icaritin  
[C<sub>33</sub>H<sub>40</sub>O<sub>15</sub>]



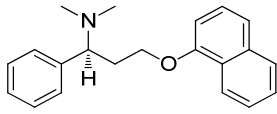
Thioquinapiperifil  
[C<sub>24</sub>H<sub>28</sub>N<sub>6</sub>OS]



Avanafil  
[C<sub>23</sub>H<sub>26</sub>ClN<sub>7</sub>O<sub>3</sub>]

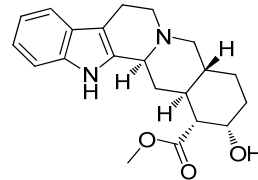


Xanthoanthrafil  
[C<sub>19</sub>H<sub>23</sub>N<sub>3</sub>O<sub>6</sub>]

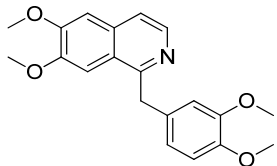


• HCl

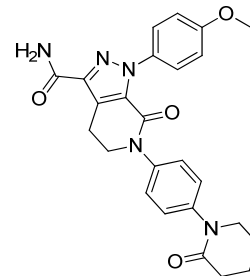
Dapoxetine HCl  
[C<sub>21</sub>H<sub>23</sub>NO·HCl]



Yohimbine  
[C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>]



Papaverine  
[C<sub>20</sub>H<sub>21</sub>NO<sub>4</sub>]



Apixaban  
[C<sub>25</sub>H<sub>25</sub>N<sub>5</sub>O<sub>4</sub>]

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5. Sooyeun Lee, Dajeong Ji, Meejung Park, Kyu Hyuck Chung, Development of a comprehensive spectral library of sildenafil and related active analogues using LC - QTOF - MS and its application for screening counterfeit pharmaceuticals, *Forensic Science International*, 257, 182-188 (2015)
6. Sara E. Kern, Lisa M. Lorenz, Adam Lanzarotta, Elisa A. Nickum, Jonathan J. Litzau, Isolation and structural characterization of a new tadalafil analog (chloropropanoylpretadalafil) found in a dietary supplement, *Journal of Pharmaceutical and Biomedical Analysis*, 128, 360 - 366 (2016)

## II-5 체중감량성분\_비만치료관련성분(35종) 분석법

### 배 경

- 식품 제조·가공업체에서 제조한 ‘벨런스 F-190’ 제품에서 비만치료제 유사물질인 ‘클로로시부트라민’이 검출되어 식품 회수 조치('14.11.)
- 식품으로 사용할 수 없는 의약품 성분인 ‘시부트라민’, ‘데스메칠시부트라민’ 함유된 밀수입 중국산 다이어트 제품 적발('16. 6.)
- 해외 직구 다이어트 제품에서 ‘센노사이드’ 등 유해물질 검출('16. 7)



### 특 성

- 시부트라민: 가장 흔히 사용되던 비만치료제였으나 두통, 불면증, 우울증 등의 부작용으로 인해 2010년 국내시장에서 퇴출됨
- 오르리스타트: 지방흡수 억제 의약품으로 섭취한 지방을 흡수시키지 않고 배설시키며 FDA 승인받은 의약품
- 펜디메트라진, 펜플루라민: 항정신성 의약품 중 대표적인 비만치료제로 4주만 복용해도 중독 우려가 있고 3개월 이상 복용시 폐동맥 고혈압 등 부작용을 나타냄
- 에페드린: 대사 촉진 물질로 안전성이 확립되지 않아 FDA 승인을 받지 못하였음. 어지러움, 불면증, 흥분, 빈맥, 등 부작용 우려가 있음

### 분석사례

- 다빠 1호 : Phenolphthalein 24.7 mg/g 검출
- 벨런스 F-190 : Chlorosibutramine 672 ug/g 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

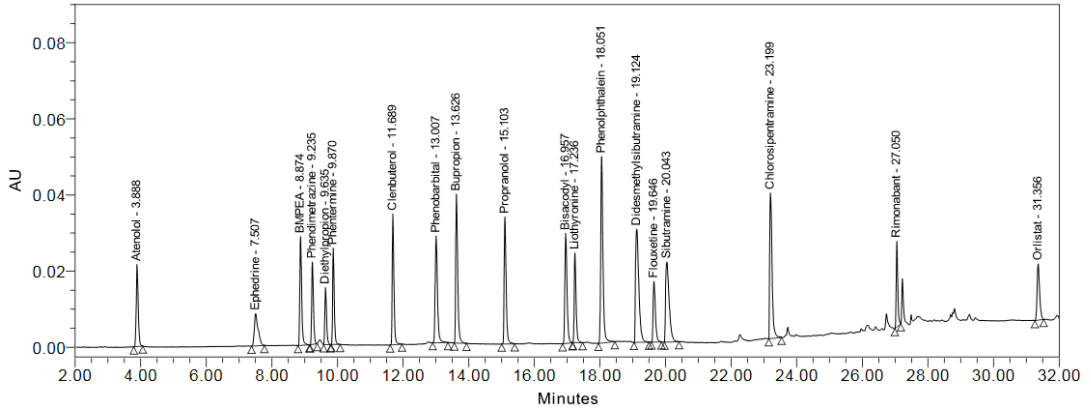
- 표준액 조제 : 표준액 1\* Atenolol 등 19종  
 표준액 2\* 2-Phenethylamine hydrochloride 등 16종  
 → 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10~200 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용
- \* 표준액 1 : Atenolol, Ephedrine hydrochloride, β-Methylphenethylamine, Phendimetrazine tartrate, Diethylpropion hydrochloride, Phentermine hydrochloride, Clenbuterol, Phenobarbital, Bupropion hydrochloride, Propranolol hydrochloride, Bisacodyl, Liothyronine, Phenolphthalein, Didesmethylsibutramine, Fluoxetine hydrochloride, Sibutramine hydrochloride, Chlorosipentramine, Rimonabant, Orlistat
- \* 표준액 2 : 2-Phenethylamine hydrochloride, Pseudoephedrine hydrochloride, Captopril, Sennoside B, Sennoside A, Lorcaserine hydrochloride, Mazindol, Fenfluramine hydrochloride, Modafinil, Phenytoin sodium, Paroxetine hydrochloride, Levothyroxine, Desmethylsibutramine hydrochloride salt, Sertraline hydrochloride, Benzylsibutramine hydrochloride, Chlorosibutramine

#### ○ Analytical conditions of HPLC

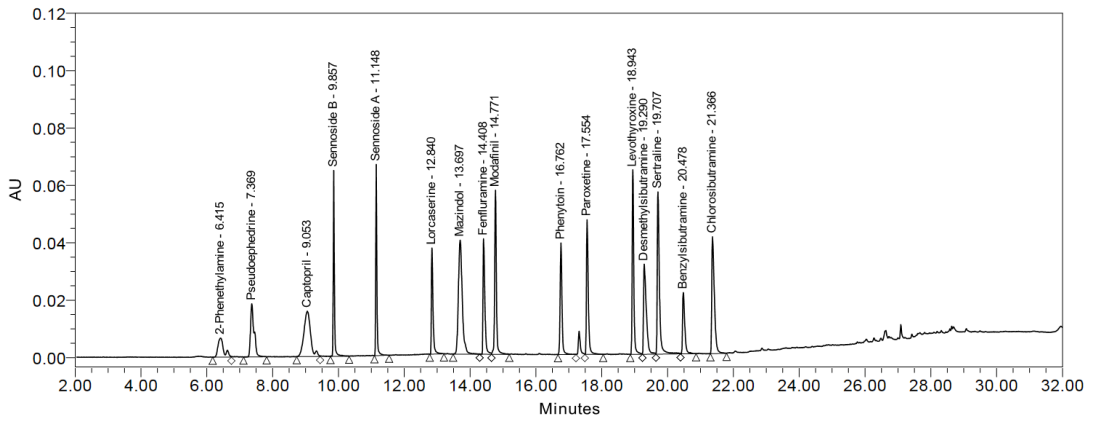
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 150 mm, 1.8 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.5 mM Sodium 1-hexane sulfonate in Water (0.1% H <sub>3</sub> PO <sub>4</sub> ) (B) 95% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	3.0	90	10
	20.0	50	50
	25.5	10	90
	25.6	0	100
	30.0	0	100
	31.0	90	10
	35.0	90	10
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 µL		
• UV Detection	210 nm		
• PDA Range	190~400 nm		



○ Chromatogram

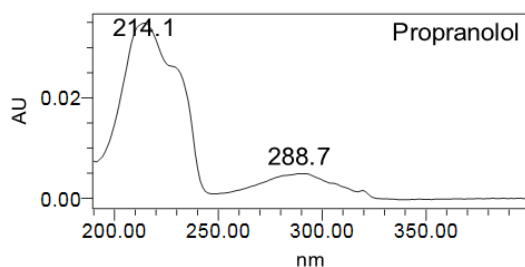
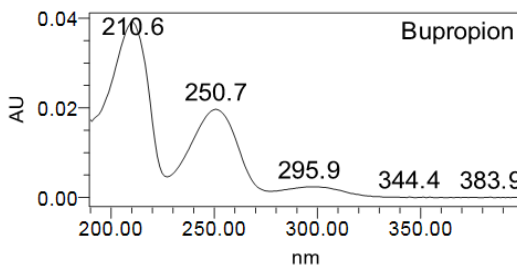
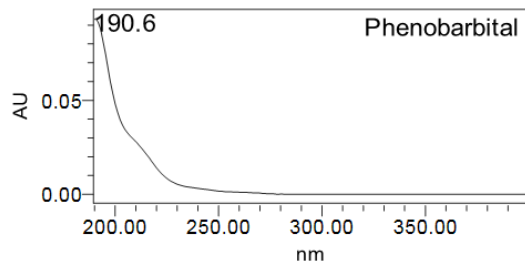
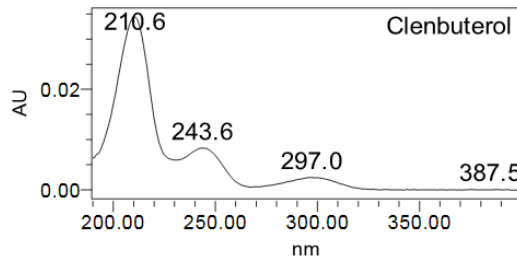
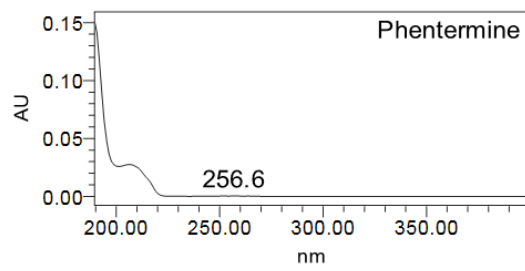
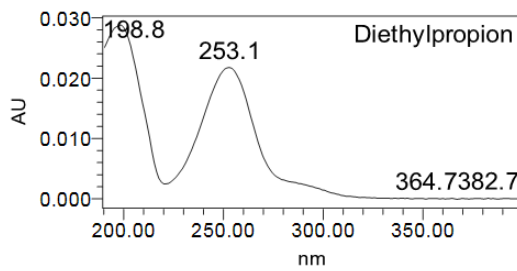
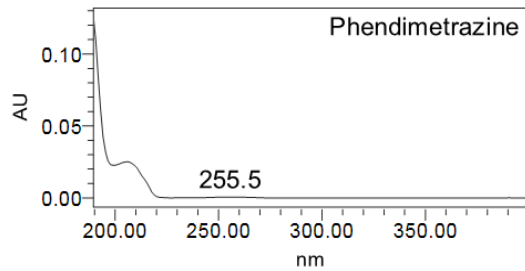
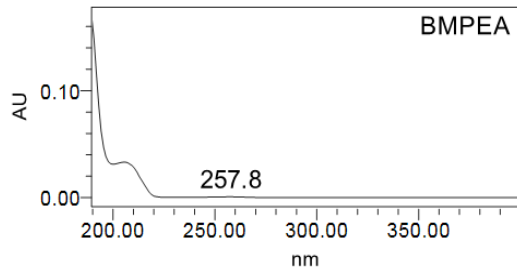
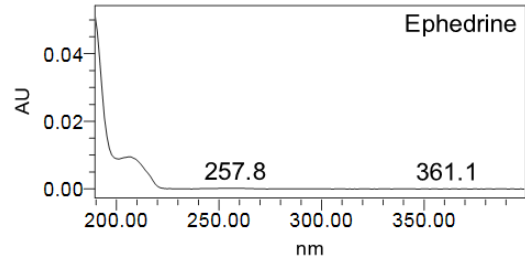
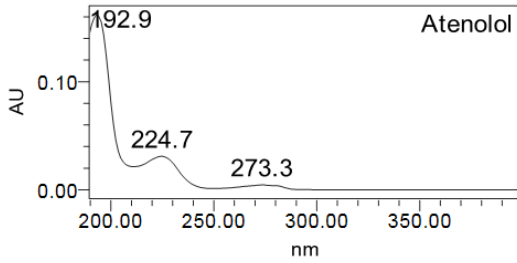


[표준액 1]

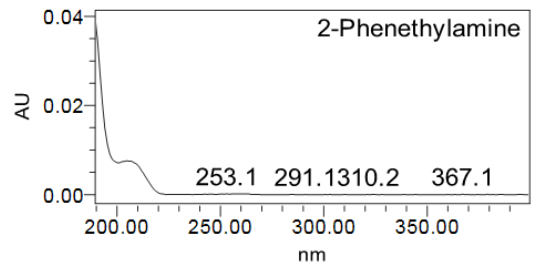
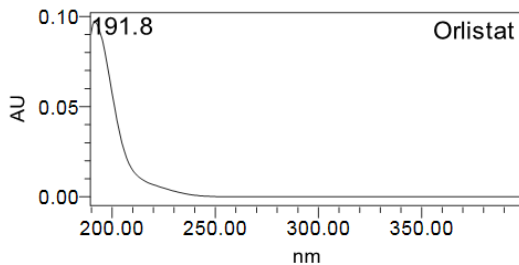
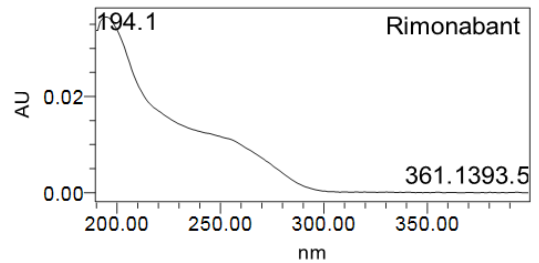
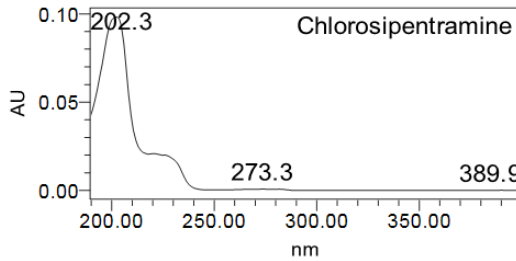
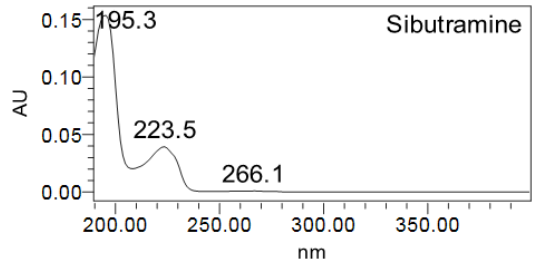
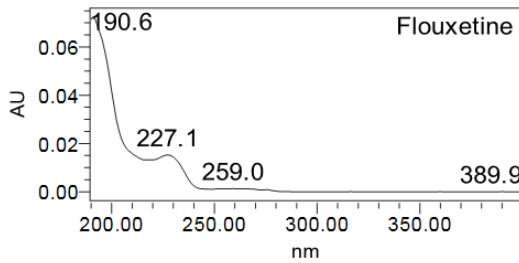
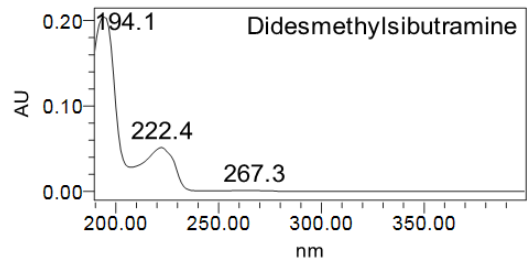
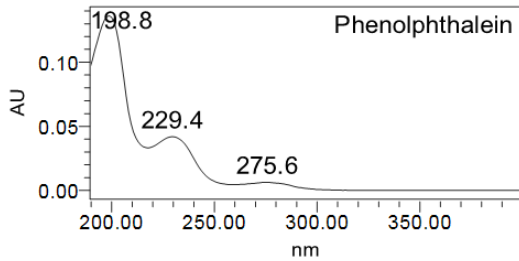
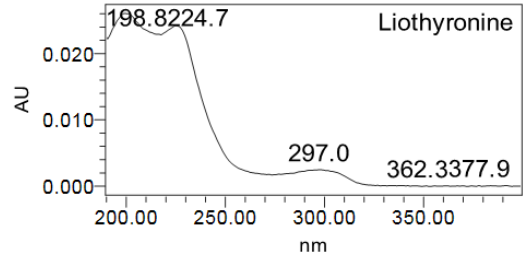
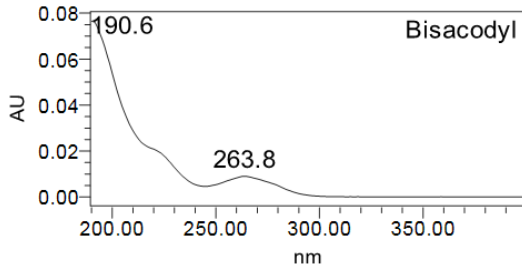


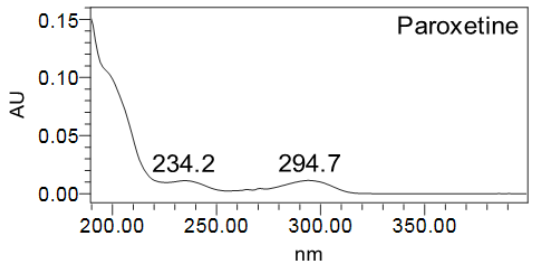
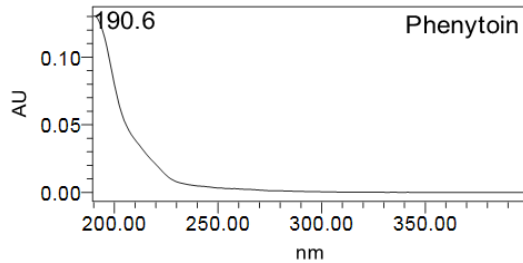
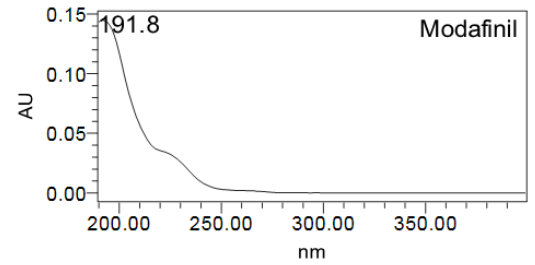
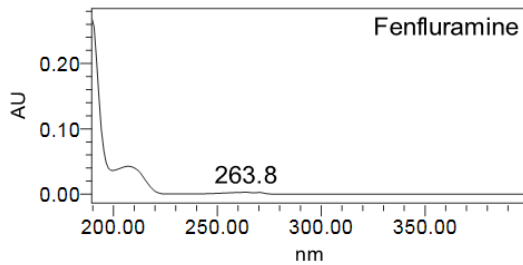
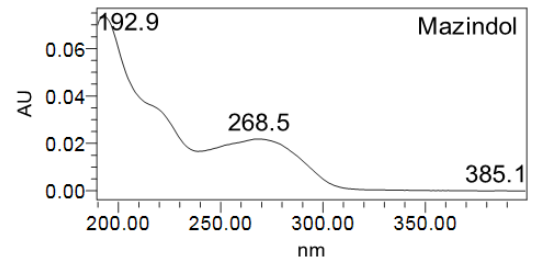
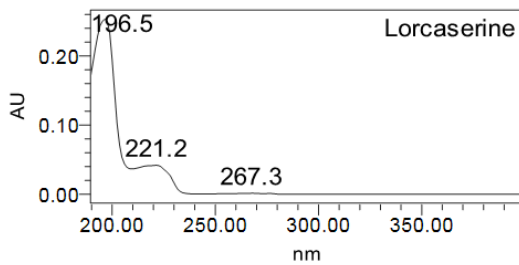
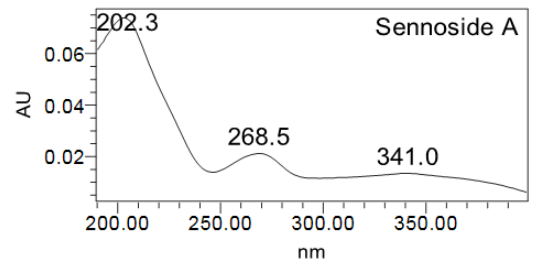
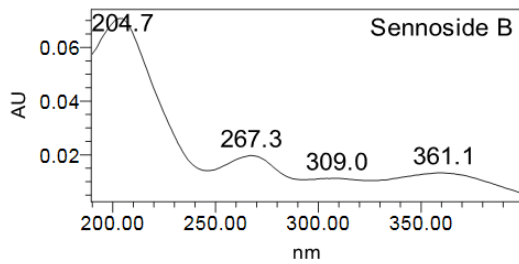
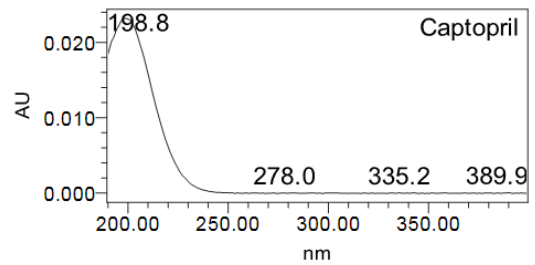
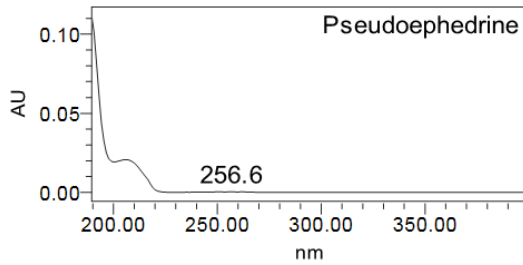
[표준액 2]

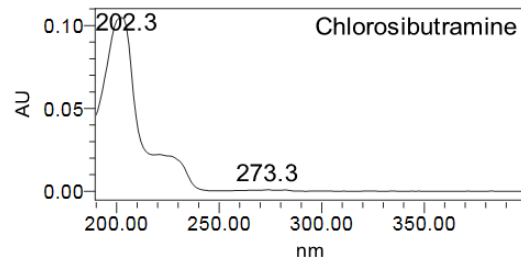
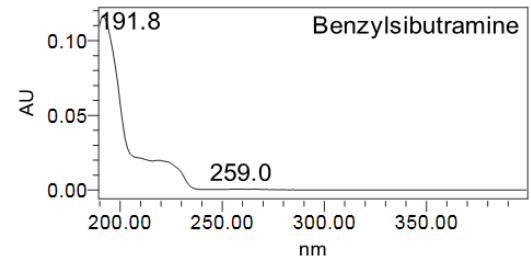
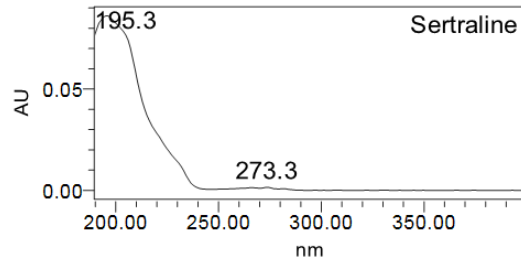
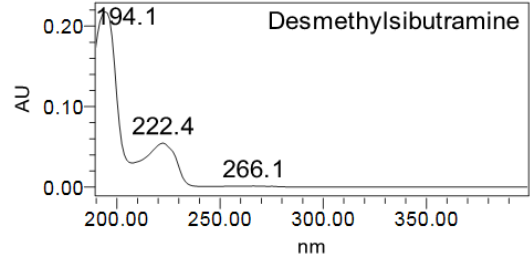
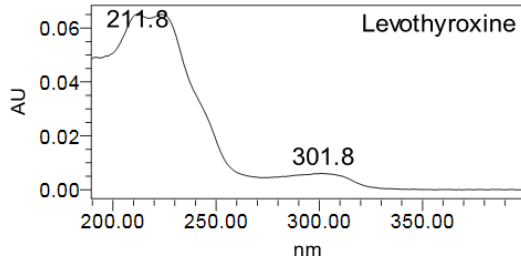
○ PDA Spectrum



II-5. 체중감량성분\_비만치료관련성분(35종) 분석법







## 2. LC-MSMS

### ○ Analytical conditions of HPLC

• Instrument	UPLC Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	30℃		
• Mobile Phase	(A) 0.1% Formic acid in Water:Acetonitrile (95:5) (B) 0.1% Formic acid in Water:Acetonitrile (5:95)		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	1.0	95	5
	3.0	0	100
	8.0	0	100
	8.1	95	5
	10.0	95	5
• Flow Rate	0.25 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ	
• Ionization Mode	ESI (+)	ESI (-)
• Capillary Voltage	2.7 kV	2.8 kV
• Desolvation Temp.	400℃	300℃
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )	550 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )	off

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Atenolol	+	267.30	30	144.85	25
				189.95	20
Ephedrine	+	166.15	20	148.00	10
				116.85	20
				114.90	25
β-Methylphenethylamine	+	136.10	10	118.95	10
				90.85	15
				64.80	30
Phendimetrazine	+	192.19	35	148.00	20
				114.85	28
Diethylpropion	+	206.25	35	104.85	20
				132.90	10
Phentermine	+	150.14	15	132.90	10
				90.80	15
				132.10	25
Clenbuterol	+	277.17	20	203.05	17
				259.15	10
Phenobarbital	-	230.85	25	84.80	10
				187.8	10
Bupropion	+	240.25	20	183.90	15
				165.9	15
Propranolol	+	260.35	25	73.82	20
				115.90	20
Bisacodyl	+	362.16	30	226.00	20
				183.90	30
Liothyronine	+	652.12	30	606.06	20
				478.10	40
Phenolphthalein	+	319.25	25	196.90	35
				224.85	20
				138.85	10
Didesmethylsibutramine	+	252.20	15	152.90	10
				178.95	10
Fluoxetine	+	310.35	15	43.80	10
				148.00	10

표준액 1

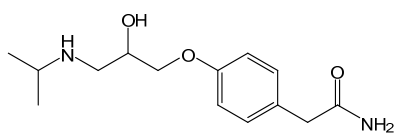
	Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
표준액 1	Sibutramine	+	280.40	20	124.80	20
					138.80	15
					159.00	25
	Chlorosipentramine	+	328.25	25	173.00	20
					185.00	25
					199.05	20
					265.02	50
	Rimonabant	+	463.10	42	299.10	52
					362.99	32
					319.25	13
Orlistat	+	496.36	25	160.05	13	
				105.00	20	
2-Phenethylamine	+	122.10	20	76.80	15	
				147.95	10	
				116.85	20	
Pseudoephedrine	+	166.15	15	114.85	25	
				69.80	20	
				74.80	20	
Captopril	+	218.10	15	116.00	12	
				386.20	40	
표준액 2	Sennoside B	-	861.69	60	224.02	50
					386.20	60
	Sennoside A	-	861.65	40	224.02	35
					144.10	20
	Lorcaserine	+	196.15	35	151.05	25
					179.10	15
	Mazindol	+	285.25	35	49.82	20
					129.82	35
					108.88	35
	Fenfluramine	+	232.25	25	158.90	20
186.90					15	
Modafinil	+	296.20	20	128.80	15	
Phenytoin sodium	+	253.06	29	77.01	43	
				182.08	15	



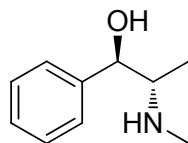
Compound	Ion Mode	Precursor ion ( $m/z$ )	CV (V)	Product ion ( $m/z$ )	CE (eV)
Paroxetine	+	330.30	25	150.90	20
				177.95	20
				192.00	20
Levothyroxine	+	778.09	28	732.02	20
				324.07	50
Desmethyisibutramine	+	266.30	20	138.85	15
				152.90	15
				178.90	15
Sertraline	+	306.25	15	158.80	25
				274.95	15
				124.92	20
Benzylsibutramine	+	314.35	20	156.95	15
				176.90	15
				158.93	30
Chlorosibutramine	+	314.16	20	172.97	16
				187.02	16

표준액 2

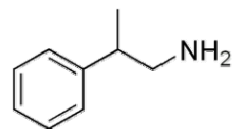
### 구조식



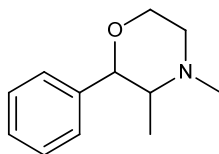
Atenolol  
[C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>]



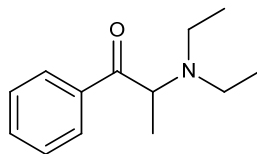
Ephedrine  
[C<sub>10</sub>H<sub>15</sub>NO]



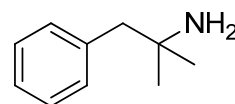
beta-Methylphenethylamine  
[C<sub>9</sub>H<sub>13</sub>N]



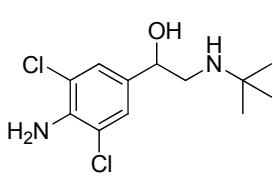
Phendimetrazine  
[C<sub>12</sub>H<sub>17</sub>NO]



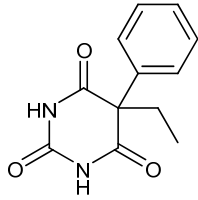
Diethylpropion  
[C<sub>13</sub>H<sub>19</sub>NO]



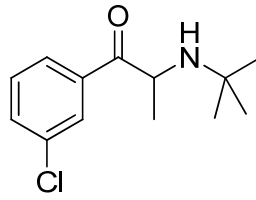
Phentermine  
[C<sub>10</sub>H<sub>15</sub>N]



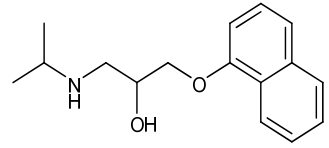
Clenbuterol  
[C<sub>12</sub>H<sub>18</sub>Cl<sub>2</sub>N<sub>2</sub>O]



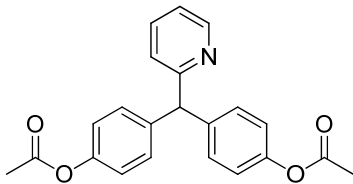
Phenobarbital  
[C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>]



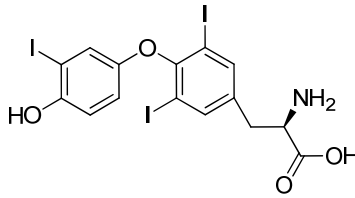
Bupropion  
[C<sub>13</sub>H<sub>18</sub>ClNO]



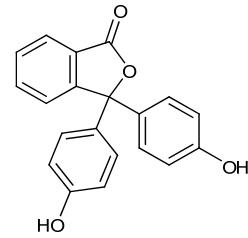
Propranolol  
[C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub>]



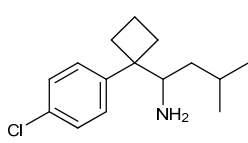
Bisacodyl  
[C<sub>22</sub>H<sub>19</sub>NO<sub>4</sub>]



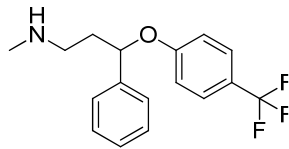
Liothyronine  
[C<sub>15</sub>H<sub>12</sub>I<sub>3</sub>NO<sub>4</sub>]



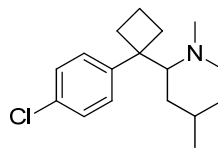
Phenolphthalein  
[C<sub>20</sub>H<sub>14</sub>O<sub>4</sub>]



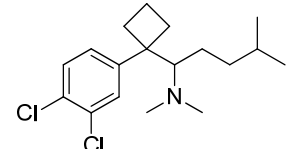
Didesmethylsibutramine  
[C<sub>15</sub>H<sub>22</sub>ClN]



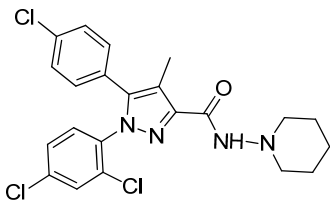
Fluoxetine  
[C<sub>17</sub>H<sub>18</sub>F<sub>3</sub>NO]



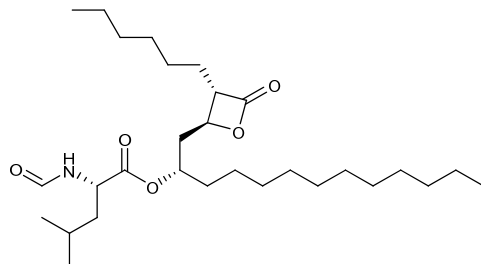
Sibutramine  
[C<sub>17</sub>H<sub>26</sub>ClN]



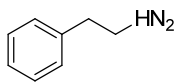
Chlorosipentramine  
[C<sub>18</sub>H<sub>27</sub>Cl<sub>2</sub>N]



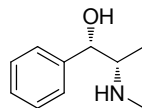
Rimonabant  
[C<sub>22</sub>H<sub>21</sub>Cl<sub>3</sub>N<sub>4</sub>O]



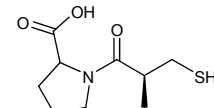
Orlistat  
[C<sub>29</sub>H<sub>53</sub>NO<sub>5</sub>]



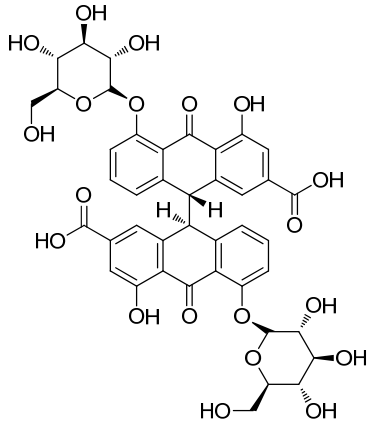
2-phenethylamine  
[C<sub>8</sub>H<sub>11</sub>N]



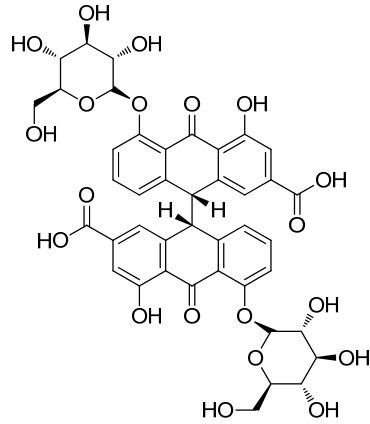
Pseudoephedrine  
[C<sub>10</sub>H<sub>15</sub>NO]



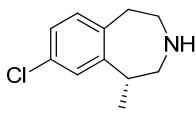
Captopril  
[C<sub>9</sub>H<sub>15</sub>NO<sub>3</sub>S]



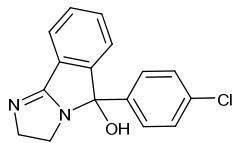
Sennoside B  
[C<sub>42</sub>H<sub>38</sub>O<sub>20</sub>]



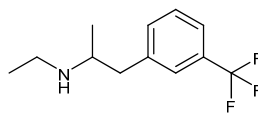
Sennoside A  
[C<sub>42</sub>H<sub>38</sub>O<sub>20</sub>]



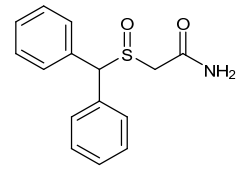
Lorcaserin  
[C<sub>11</sub>H<sub>14</sub>ClN]



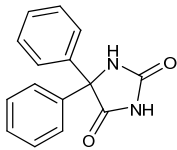
Mazindol  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O]



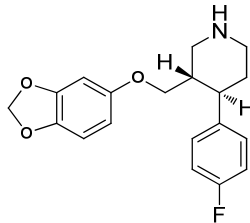
Fenfluramine  
[C<sub>12</sub>H<sub>16</sub>F<sub>3</sub>N]



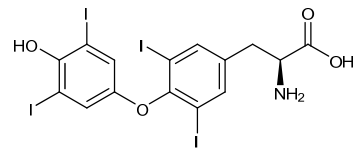
Modafinil  
[C<sub>15</sub>H<sub>13</sub>NO<sub>2</sub>S]



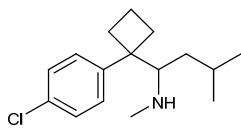
Phenytoin  
[C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>]



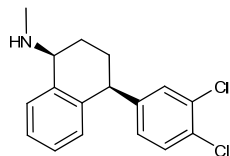
Paroxetine  
[C<sub>19</sub>H<sub>20</sub>FNO<sub>3</sub>]



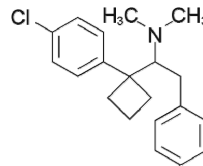
Levothyroxine  
[C<sub>15</sub>H<sub>11</sub>I<sub>4</sub>NO<sub>4</sub>]



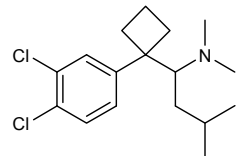
Desmethylsibutramine  
[C<sub>16</sub>H<sub>24</sub>ClN]



Sertraline  
[C<sub>17</sub>H<sub>17</sub>Cl<sub>2</sub>N]



Benzylsibutramine  
[C<sub>20</sub>H<sub>24</sub>ClN]



Chlorosibutramine  
[C<sub>17</sub>H<sub>25</sub>Cl<sub>2</sub>N]

## ■ 참고문헌

1. Hyung Joo Kim, Ji Hyun Lee, Hyoung Joon Park, So-Hyun Cho, SooYeul Cho, Woo Seoug Kim. Monitoring of 29 weight loss compounds in food and dietary supplements by LC-MS/MS. *Food Additives and Contaminants*. 31(5), 777-783 (2014)
2. P. Ravi Kumar Reddy, V. Krishna Reddy, E. Sasikiran Goud. Development and validation of UPLC method for determination of atenolol in tablets form. *World J Pharm Pharmaceu Sci*. 3(9), 808-816 (2014)
3. Ji Won Kim, Soon Jae Kweon, Seon Kyung Park, Jung Yeon Kim, Ji Hyun Lee, Kyoung Moon Han, Sooyeul Cho, Jinho Kim, Soon Young Han, Hyoung Ja Kim and Woo Seong Kim. Isolation and identification of a sibutramine analogue adulterated in slimming dietary supplements. *Food Additives and Contaminants, Part A*. 30(4) 621-626 (2013)
4. Kim, S. H., Lee, J., Yoon, T., Choi, J., Choi, D., Kim, D. & Kwon, S. W. Simultaneous determination of anti-diabetes/anti-obesity drugs by LC/PDA, and targeted analysis of Sibutramine analog in dietary supplements by LC/MS/MS. *Biomed Chromatogr*. 23, 1259-1265 (2009)
5. Sherma, J. High-performance liquid chromatography/mass spectrometry analysis of botanical medicines and dietary supplements : A Review. *Journal of AOAC International*. 86, 873-881, (2003)

## II-6 수면유도제(15종) 분석법

### 배 경

- 수면유도제 몰래 투약하던 간호조무사 사망('16. 8.)
- 마약성 수면유도제 ‘졸피뎀’ 관련 범죄 기승('15. 11.)
- 금은방 주인에게 수면유도제 먹이고 귀금속 털어('13. 6.)
- 수면유도제를 식품에 혼입해 범죄에 이용하는 사례가 증가하고 있음
- 향정신성의약품 빼들린 목포 한국병원 간호사 입건('17. 7.)



### 특 성

- 수면유도제 종류로 크게 벤조디아제핀계 약물, 바비튜레이트(바비탈)계 약물, 비 벤조디아제핀계 약물, 항히스타민제 등이 있음
  - 벤조디아제핀계 약물 : 뇌신경계에서 전반적으로 진정, 이완작용을 하는 가바(GABA)라는 물질의 수용체를 활성화시킴  
(ex) Midazolam, Flurazepam 등
  - 바비튜레이트(바비탈)계 약물 : 전반적인 중추신경계의 작용, 특히 호흡을 억제하는 역할  
(ex) Hexobarbital, Pentobarbital, Phenobarbital 등
  - 비벤조디아제핀계 약물 : 특정 가바 수용체에만 작용하여 벤조디아제핀계 약물에 비해 안전하다고 여겨짐 (ex) Zolpidem 등
  - 항히스타민제 : 신경을 진정시키는 성분이 들어있어 수면유도제로 쓰임  
(ex) Diphenhydramine hydrochloride 등

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

• 표준액 조제 : Diphenhydramine 등 15종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 5~20 µg/mL)

• 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Zolpidem, Phenobarbital, Midazolam, Flurazepam, Diphenhydramine hydrochloride, Pentobarbital, Hexobarbital, Estazolam, Flunitrazepam, Lorazepam, Triazolam, Temazepam Alprazolam, Clonazepam, Clemastine

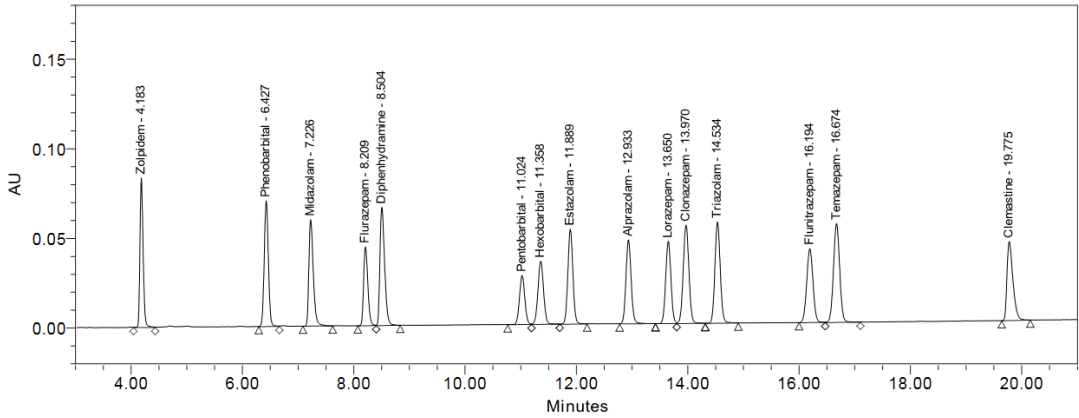
#### ○ Analytical condition of HPLC

- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC HSS T3 (2.1 mm × 150 mm, 1.8 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.5 mM Sodium-1-hexane sulfonate in Water (0.1% H<sub>3</sub>PO<sub>4</sub>)  
(B) 95% Acetonitrile

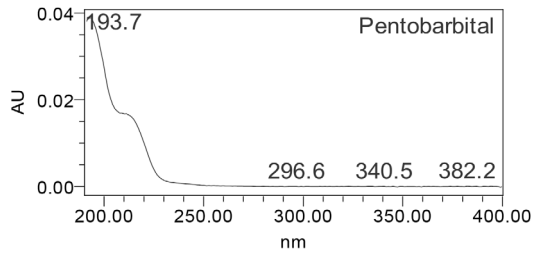
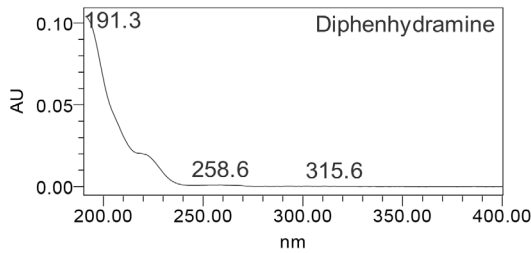
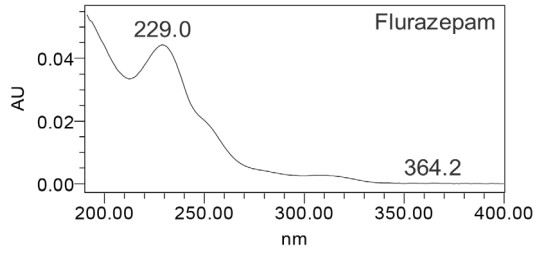
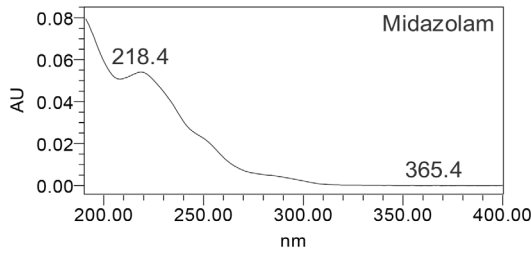
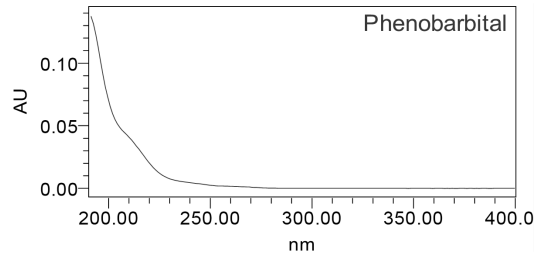
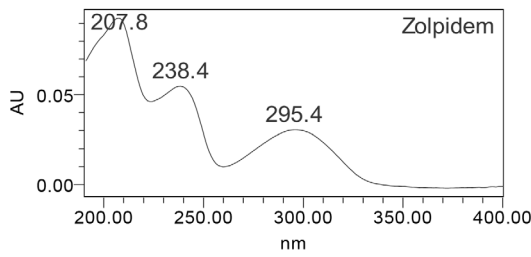
Time (min)	A (%)	B (%)
0.0	68	32
2.0	68	32
19.0	50	50
19.1	10	90
22.0	10	90
22.1	68	32
28.0	68	32

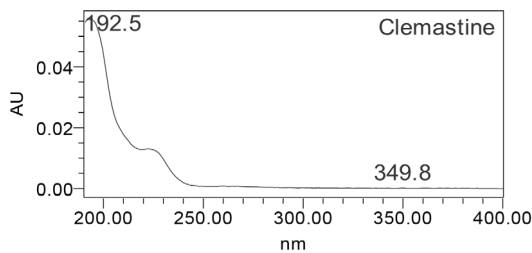
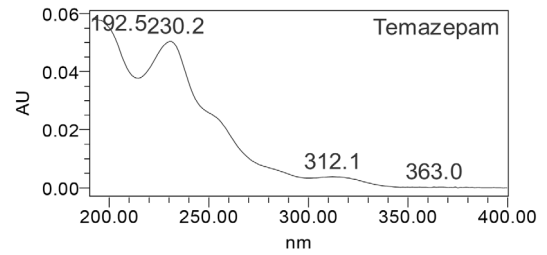
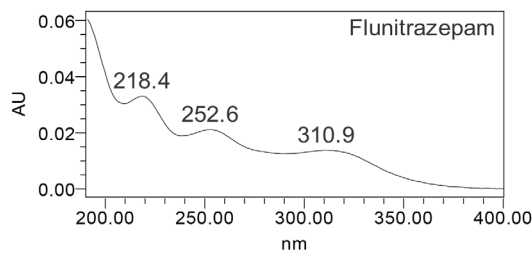
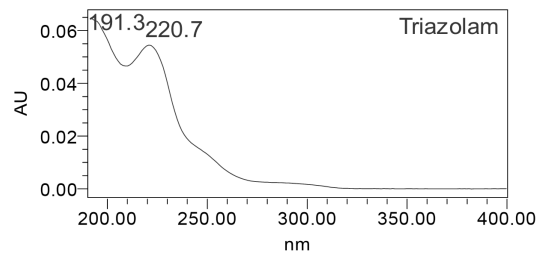
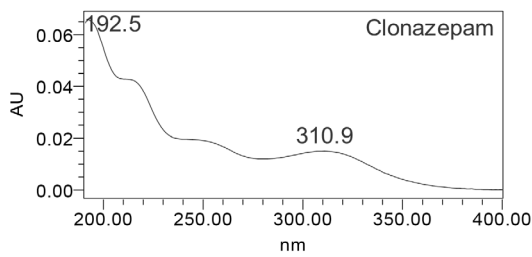
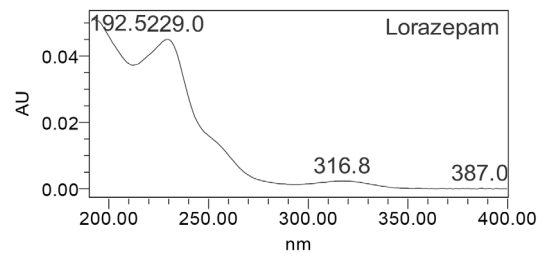
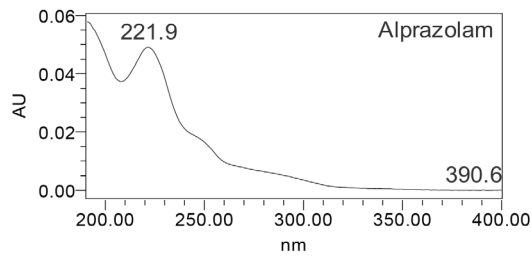
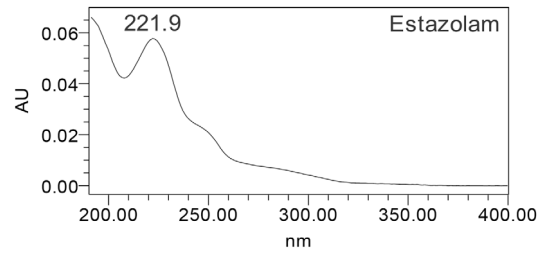
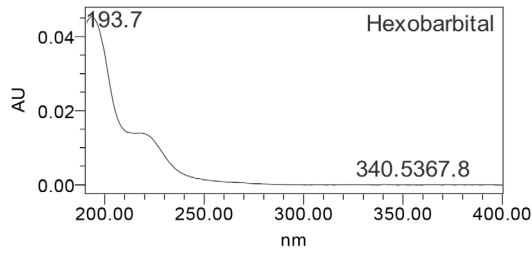
- Flow Rate 0.18 mL/min
- Inj. Volume 1 µL
- UV Detection 200 nm
- PDA Range 190~400 nm

○ Chromatogram



○ PDA Spectrum







## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	80	20
	2.0	80	20
	7.0	40	60
	8.0	10	90
	10.0	10	90
	10.1	80	20
	12.0	80	20
• Flow Rate	0.25 mL/min		
• Inj. Volume	1 μL		

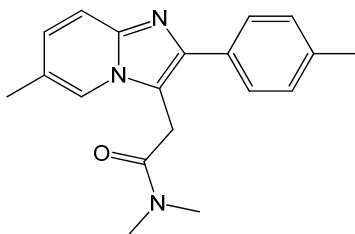
### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ	
• Ionization Mode	ESI (+)	ESI (-)
• Capillary Voltage	2.8 kV	2.6 kV
• Desolvation Temp.	400°C	400°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	off	off

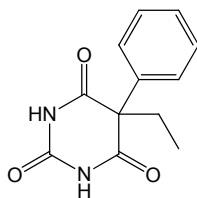
○ Analytical conditions of LC-MS/MS

Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Zolpidem	+	308.10	35	221.05	40
				235.08	30
				263.05	30
Phenobarbital	-	231.05	25	84.80	10
				187.90	10
				209.00	35
Midazolam	+	326.05	35	243.95	25
				291.08	25
				288.05	25
Flurazepam	+	388.10	30	315.03	20
				317.00	20
				151.95	30
Diphenhydramine	+	256.10	15	164.98	35
				167.00	15
				41.90	15
Pentobarbital	-	225.10	25	84.80	15
				182.00	15
				81.00	20
Hexobarbital	+	237.00	20	157.00	15
				205.00	35
				241.00	20
Estazolam	+	295.00	35	266.98	25
				211.00	35
				240.05	25
Flunitrazepam	+	314.00	35	268.05	25
				205.00	35
				274.05	25
Alprazolam	+	309.00	30	281.05	25
				213.95	35
				270.00	25
Clonazepam	+	315.95	25	228.95	30
				274.95	20
				302.95	15
Larazepam	+	320.95	30	238.95	35
				308.00	25
				314.95	25
Triazolam	+	343.00	30	130.00	10
				179.00	30
				215.00	15
Clemestine	+	344.10	20	255.00	25
				283.00	15
Temazepam	+	301.00	30		

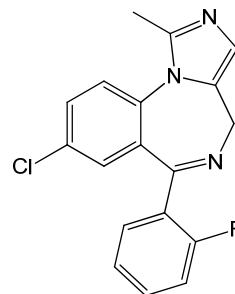
■ 구조식



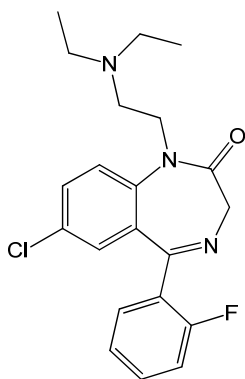
Zolpidem  
[C<sub>19</sub>H<sub>21</sub>N<sub>3</sub>O]



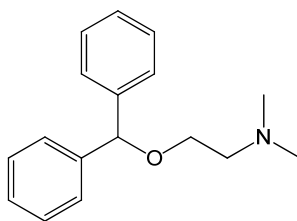
Phenobarbital  
[C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>]



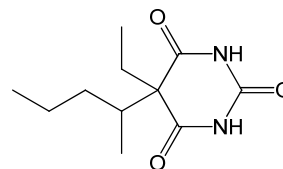
Midazolam  
[C<sub>18</sub>H<sub>13</sub>ClFN<sub>3</sub>]



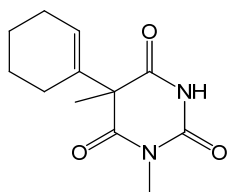
Flurazepam  
[C<sub>21</sub>H<sub>23</sub>ClFN<sub>3</sub>O]



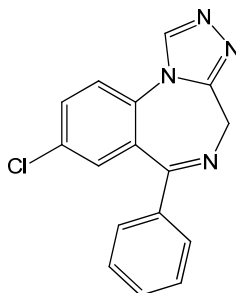
Diphenhydramine  
[C<sub>17</sub>H<sub>21</sub>NO]



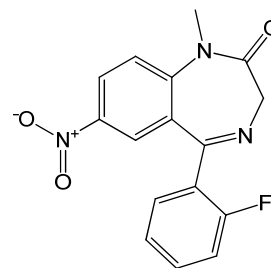
Pentobarbital  
[C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>]



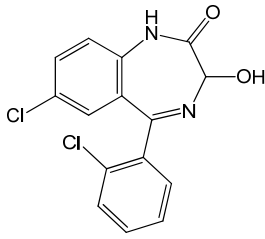
Hexobarbital  
[C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>]



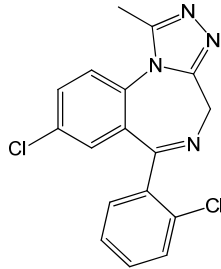
Estazolam  
[C<sub>16</sub>H<sub>11</sub>ClN<sub>4</sub>]



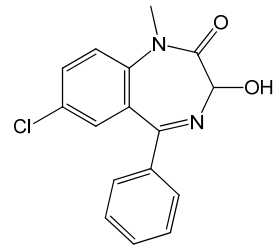
Flunitrazepam  
[C<sub>16</sub>H<sub>12</sub>FN<sub>3</sub>O<sub>3</sub>]



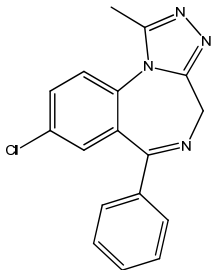
Lorazepam  
[C<sub>15</sub>H<sub>10</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>]



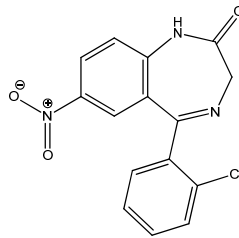
Triazolam  
[C<sub>17</sub>H<sub>12</sub>Cl<sub>2</sub>N<sub>4</sub>]



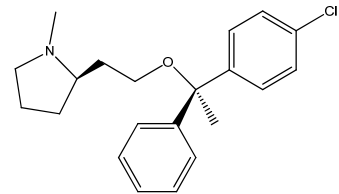
Temazepam  
[C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>2</sub>]



Alprazolam  
[C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>]



Clonazepam  
[C<sub>15</sub>H<sub>10</sub>ClN<sub>3</sub>O<sub>3</sub>]



Clemastine  
[C<sub>21</sub>H<sub>26</sub>ClNO]

## ■ 참고문헌

1. B.E. Smink, J.E. Bramdsma, A.Dijkhuizen, K.J. Luthof, J.J. de Gier, A.C.G Egberts, D.R.A. Uges. Quantitative analysis of 33 benzodiazepines, metabolites and benzodiazepine-like substances in whole blood by liquid chromatography-(tandem) mass spectrometry. *J Chromatogr B.* 811, 13-20 (2004)
2. Hajime Miyabuchi, Kenji Kuwayama, Kenji Tsujikawa, Tatsuyuki Kanamori, Yuko T. Iwata, Hiroyuki Inoue, Tohru Kishi. A method for screening for various sedative-hypnotics in serum by liquid chromatography/single quadrupole mass spectrometry. *J Forensic science international.* 157, 57-70 (2006)
3. E. Kono, A.H. Mohsen Sarrafi, R. Abdolahnejad, M. bahrami-Zonoz. Development and validation of a reversed-phase HPLC method for the estimation of zolpidem in bulk drug and tablets. *J Chemistry.* 357890, 6 (2013)

## II-7 <진통관련성분(22종) 분석법

### ■ 배경

- 소염진통제를 섞어 관절염과 신경통에 특효가 있는 것처럼 판매한 건강기능식품 (알쓰맥스, 알쓰케어) 적발('13. 4.)
- '조인트케어골드(기타가공식품)'에서 식품에 사용할 수 없는 진통제 성분인 '아세트아미노펜'이 검출되어 해당 제품을 판매금지 및 회수 조치 ('13. 9.)
- 진통제 성분인 '피록시캄', '덱사메타손'이 함유된 원료를 사용해 제조된 환제품을 유통한 업자 적발('14. 5)
- 중국에서 밀수입 된 불법 다이어트 제품에서 진통제 성분인 '디피론' 검출('15. 5)



### ■ 특성

- 이부프로펜, 디클로페낙, 피록시캄 등은 근육 관절통에 널리 쓰이는 소염 진통제로 장기간 복용하게 되면 심혈관, 위내 출혈 등 소화기 부작용을 일으킬 수 있어 의사의 처방과 약사의 복약지도에 따라 복용하여야 하는 약물임

### ■ 분석사례

- 알쓰케어 제품: Naproxen 3.28 mg/정, Indomethacin 2.73 mg/정, Ibuprofen 16.3 mg/정, Piroxicam 2.02 mg/정, Diclofenac 2.89 mg/정 검출
- 관절제품: Piroxicam 0.320 mg/g 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

• 표준액 조제 : 표준액 1\* Acetaminophen 등 13종

표준액 2\* Dipyron 등 9종

→ 각각 일정량 취함 → 100% 메탄올 가함

→ 최종 농도(약 5~40 µg/mL)

• 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 1 : Acetaminophen, 4-Aminoantipyrine(Ampyrone),  
4-Dimethylaminoantipyrine(Aminophenazone), Phenacetin, Carbamazepine, Sulindac,  
Piroxicam, Naproxen sodium, Meloxicam, Fenoprofen calcium, Indomethacin, Ibuprofen,  
Meclofenamate sodium

\* 표준액 2 : Dipyron, Aspirin(Aspirin + Salicylic acid), Ketorolac, 4-Isopropylantipyrine, Ketoprofen,  
Diclofenac sodium, Celecoxib, Mefenamic acid, Flurbiprofen

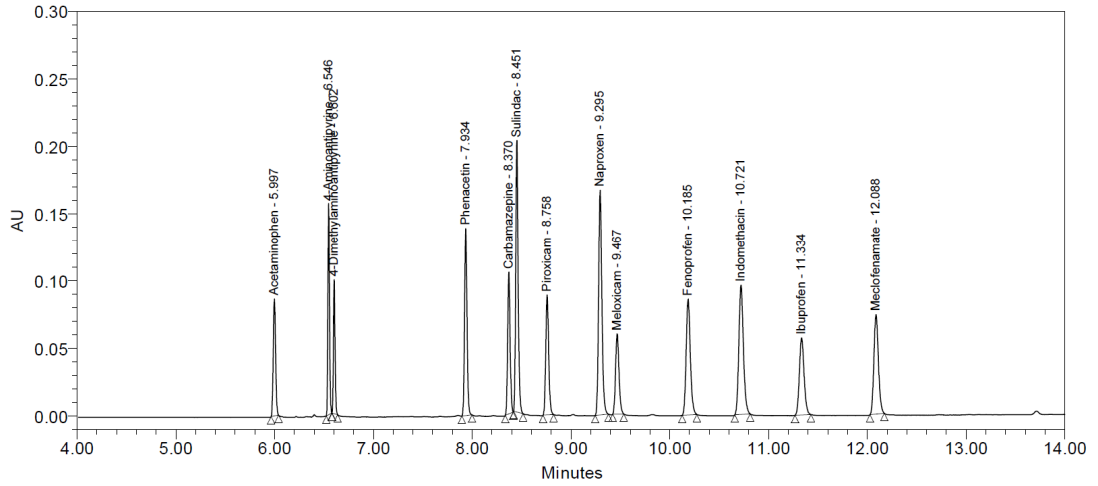
#### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 150 mm, 1.8 µm)
• Column Temp.	40°C
• Mobile Phase	(A) 0.5 mM Sodium 1-hexane sulfonate in Water (0.1% H <sub>3</sub> PO <sub>4</sub> ) (B) 95% Acetonitrile

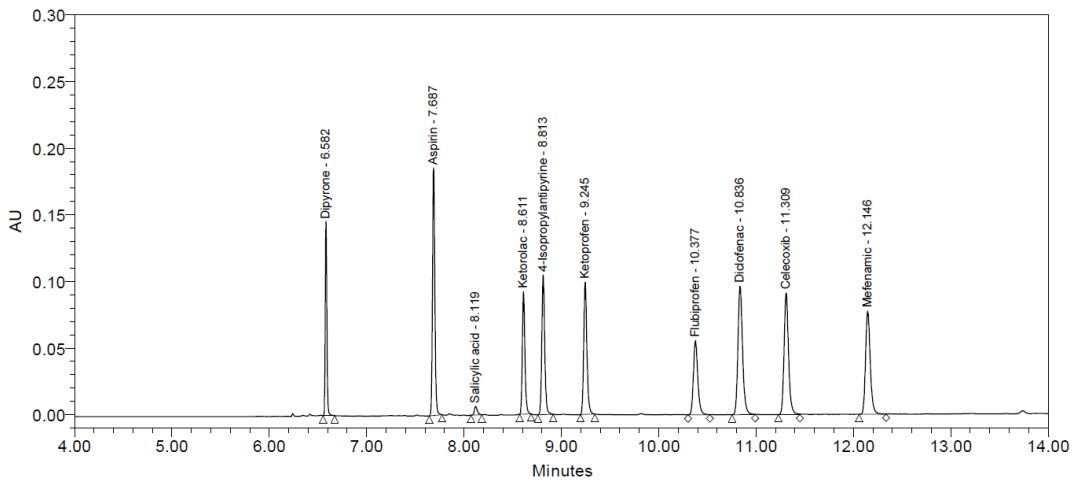
Time (min)	A (%)	B (%)
0.0	95	5
2.0	95	5
6.0	30	70
8.0	30	70
12.0	5	95
16.0	5	95
16.1	95	5
20.0	95	5

• Flow Rate	0.2 mL/min
• Inj. Volume	1 µL
• UV Detection	230 nm
• PDA Range	190~400 nm

○ Chromatogram

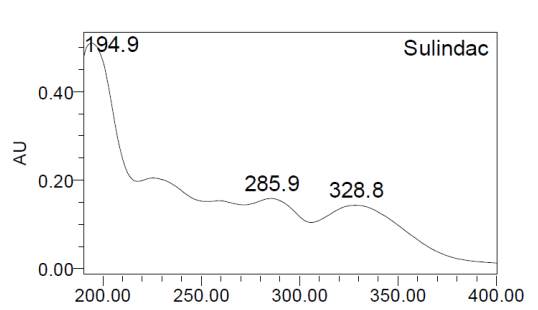
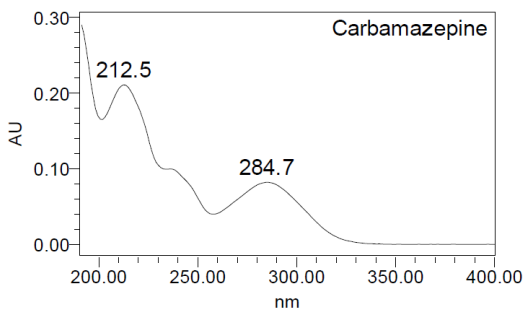
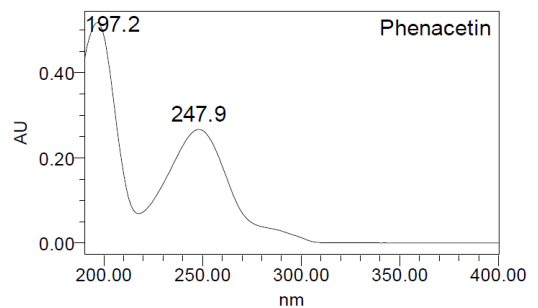
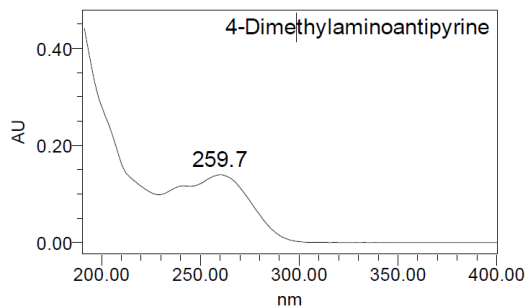
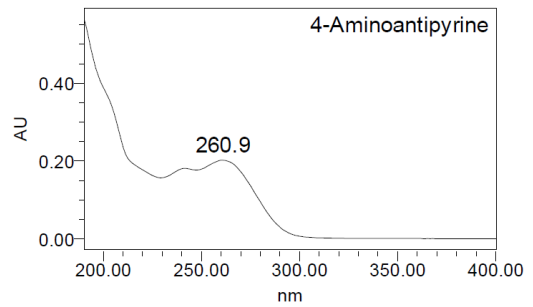
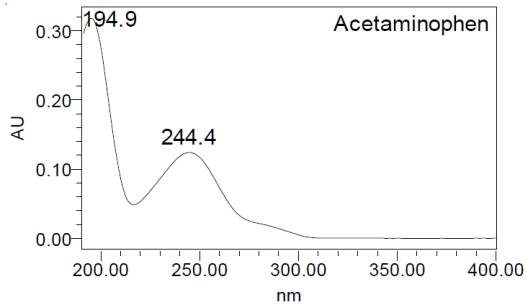


[표준액 1]

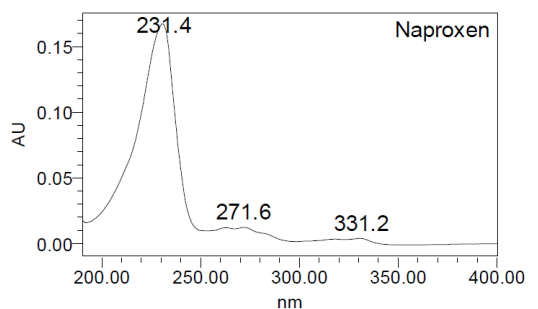
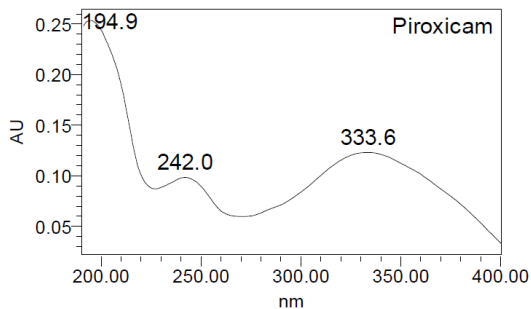


[표준액 2]

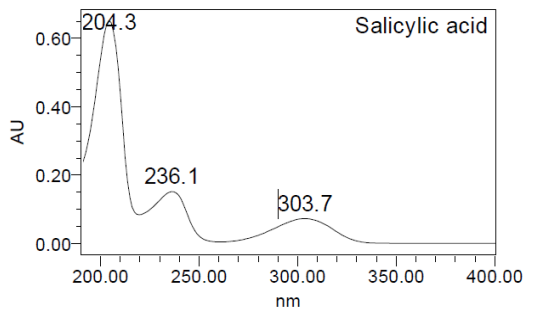
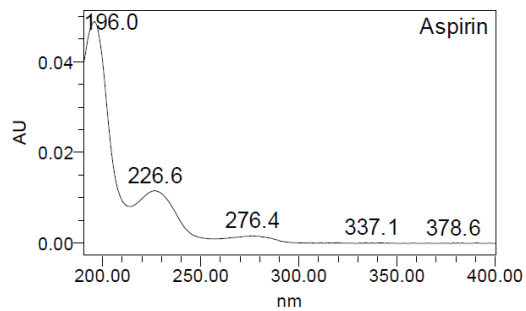
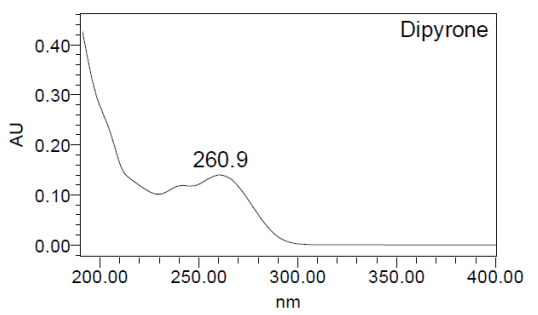
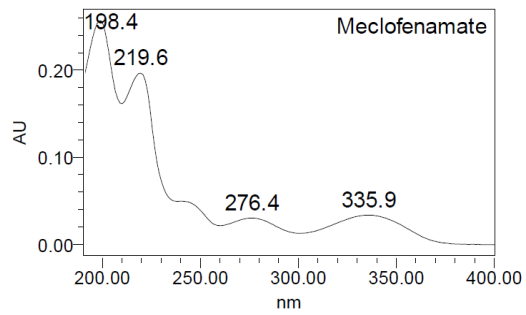
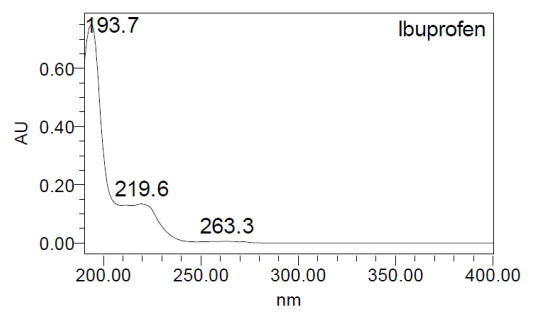
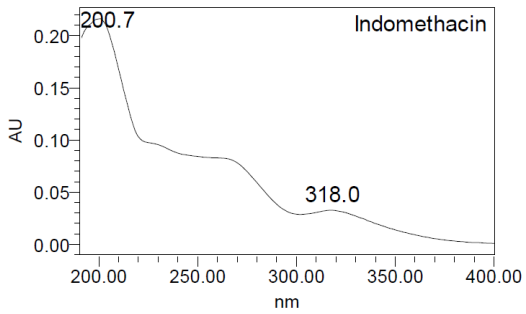
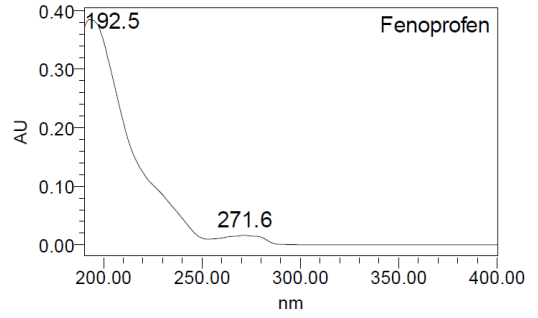
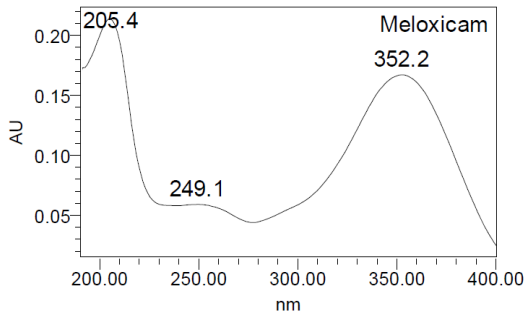
○ PDA Spectrum

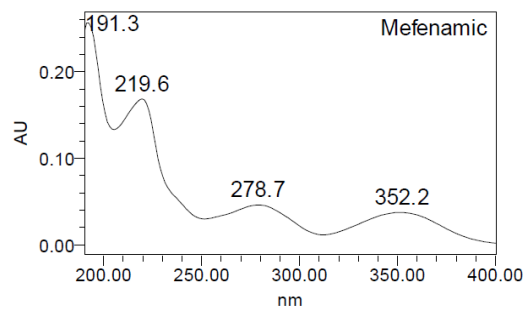
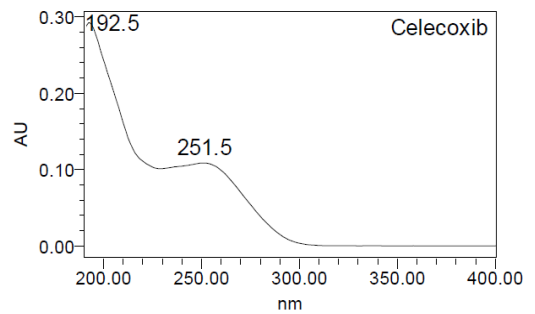
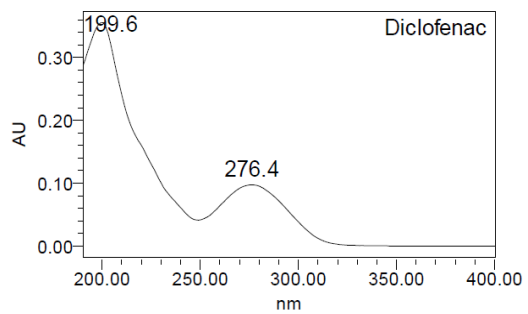
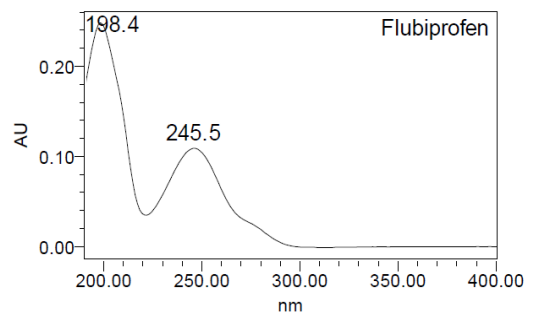
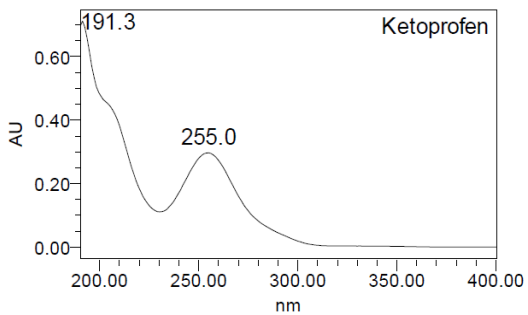
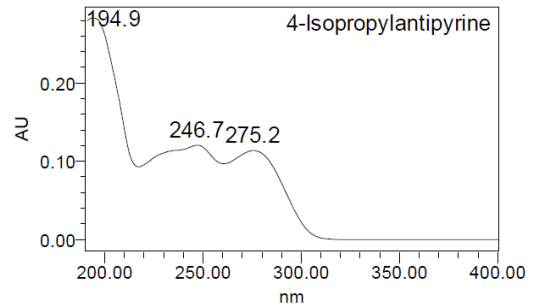
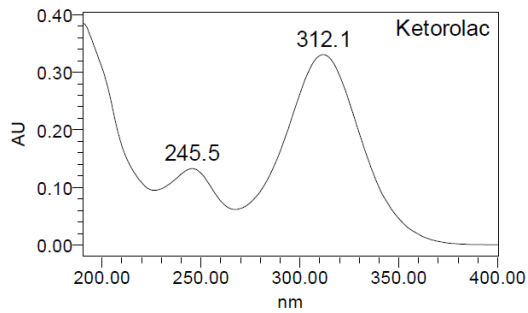


Retention Time 8.370









## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	UPLC Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS T <sub>3</sub> (2.1 mm × 100 mm, 1.8 μm)		
• Column Temp.	30℃		
• Mobile Phase	(A) 10 mM Ammonium acetate in Water (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	1.0	95	5
	3.0	30	70
	4.0	30	70
	6.0	5	95
	8.0	5	95
	8.1	95	5
	10.0	95	5
• Flow Rate	0.5 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ	
• Ionization Mode	ESI (+)	ESI (-)
• Capillary Voltage	2.5 kV	3.0 kV
• Desolvation Temp.	400℃	400℃
• Desolvation Gas Flow	700 L/Hr (N <sub>2</sub> )	700 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	20 L/Hr (N <sub>2</sub> )	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Acetaminophen	+	152.11	25	92.82	20
				109.85	15
				106.24	20
4-Dimethylaminoantipyrine	+	232.20	24	111.13	15
				113.25	12
				92.9	25
Phenacetin	+	179.98	30	109.93	20
				137.97	15
				179.10	30
Carbamazepine	+	237.13	30	194.12	20
				220.05	15
				233.18	27
Sulindac	+	357.15	42	248.18	28
				340.17	18
Ketorolac	+	256.16	27	105.12	16
				169.00	20
Naproxen	-	229.09	18	170.08	17
				185.05	6
Flurbiprofen	-	243.05	14	198.80	10
Indomethacin	-	356.14	21	297.08	21
				312.40	9
Ibuprofen	-	205.08	15	160.70	5
Meclofenamate	-	294.02	25	213.70	20
				257.70	15
4-Aminoantipyrine	+	204.00	25	145.95	15
				158.98	15
				172.95	12
Dipyron	-	310.16	24	191.07	14
				175.01	27
Aspirin	-	178.95	15	92.60	20
				136.60	10
Salicylic acid	-	136.90	10	92.60	15

표준액 1

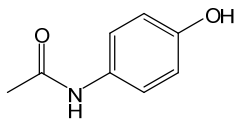
표준액 2



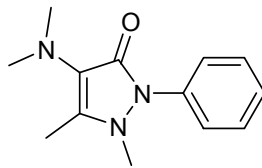
Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Piroxicam	-	330.10	15	145.60	20
				209.60	15
4-Isopropylantipyrine	+	231.00	10	189.07	20
				201.07	25
Ketoprofen	+	255.25	25	104.85	25
				209.00	15
				145.75	20
Meloxicam	-	350.01	25	209.75	15
				285.85	15
				92.60	25
Fenoprofen	-	241.05	20	196.70	7
				213.70	25
Diclofenac	-	293.91	20	249.69	12
				275.80	28
				295.80	25
Celecoxib	-	379.80	20	315.85	20
				180.07	30
Mefenamic acid	-	240.16	28	196.12	18

표준액 2

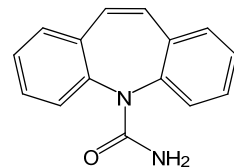
### 구조식



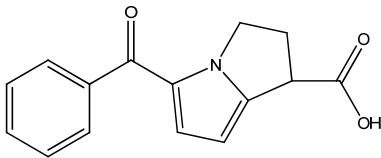
Acetaminophen  
[C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>]



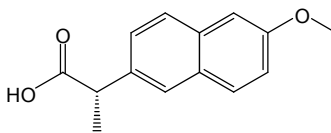
4-Dimethylaminoantipyrine  
[C<sub>13</sub>H<sub>17</sub>N<sub>3</sub>O]



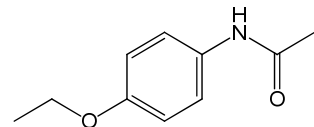
Carbamazepine  
[C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O]



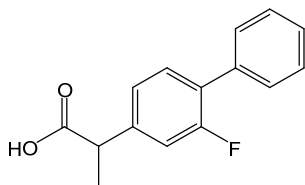
Ketorolac  
[C<sub>15</sub>H<sub>13</sub>NO<sub>3</sub>]



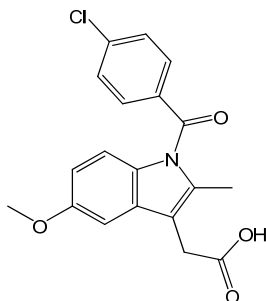
Naproxen  
[C<sub>14</sub>H<sub>14</sub>O<sub>3</sub>]



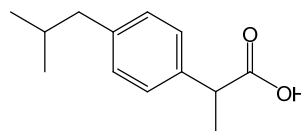
Phecacetin  
[C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub>]



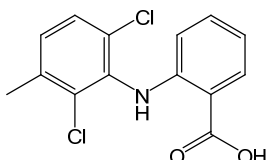
Flurbiprofen  
[C<sub>15</sub>H<sub>13</sub>FO<sub>2</sub>]



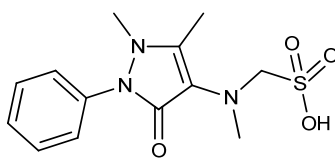
Indomethacin  
[C<sub>19</sub>H<sub>16</sub>ClNO<sub>4</sub>]



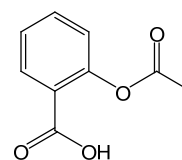
Ibuprofen  
[C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>]



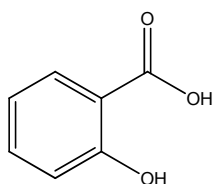
Meclofenamate  
[C<sub>14</sub>H<sub>11</sub>Cl<sub>2</sub>NO<sub>2</sub>]



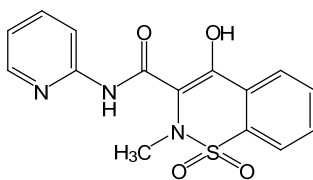
Dipyrrone  
[C<sub>13</sub>H<sub>17</sub>N<sub>3</sub>O<sub>4</sub>S]



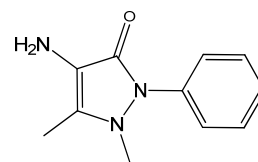
Aspirin  
[C<sub>9</sub>H<sub>8</sub>O<sub>4</sub>]



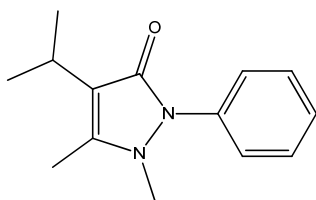
Salicylic acid  
[C<sub>7</sub>H<sub>6</sub>O<sub>3</sub>]



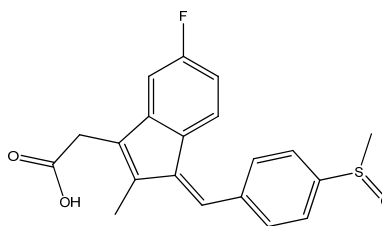
Piroxicam  
[C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>S]



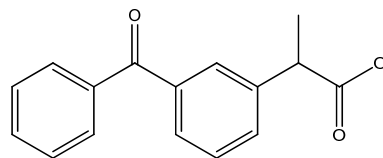
4-Aminoantipyrine  
[C<sub>11</sub>H<sub>13</sub>N<sub>3</sub>O]



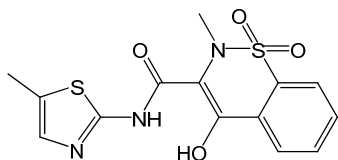
4-Isopropylantipyrine  
[C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O]



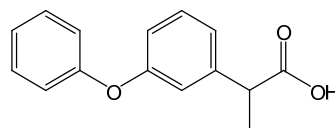
Sulindac  
[C<sub>20</sub>H<sub>17</sub>FO<sub>3</sub>S]



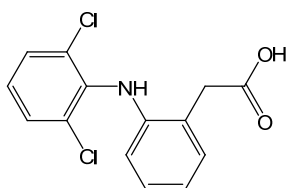
Ketoprofen  
[C<sub>16</sub>H<sub>14</sub>O<sub>3</sub>]



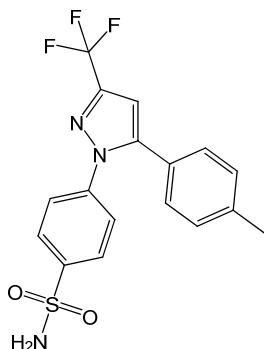
Meloxicam  
[C<sub>14</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



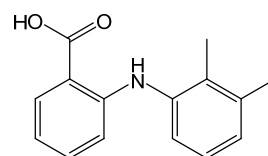
Fenoprofen  
[C<sub>15</sub>H<sub>14</sub>O<sub>3</sub>]



Diclofenac  
[C<sub>14</sub>H<sub>11</sub>Cl<sub>2</sub>NO<sub>2</sub>]



Celecoxib  
[C<sub>17</sub>H<sub>14</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub>S]



Mefenamic acid  
[C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub>]

## ■ 참고문헌

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4. M. Farré & M. Petrovi & D. Barceló, Recently developed GC/MS and LC/MS methods for determining NSAIDs in water samples, *Anal Bioanal Chem*. 387, 1203-1214, (2007)

# III-1 < 갱년기치료관련성분(9종) 분석법

## ■ 배경

- 유통기한이 경과한 폐기대상 수입식품을 갱년기 개선 제품으로 허위·과대광고 업자 적발('05)



## ■ 특 성

- 폐경과 관련 있는 에스트로젠 결핍증상, 폐경기 골다공증 등 갱년기 질환에 사용
- 에스트로젠은 갱년기치료에는 효과적이지만 자궁내막암의 위험을 증가시킬 수 있어, 장기 치료 시 의사의 지시에 따라 정기적인 검사를 받아야 함



■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 표준액 조제 : Estrone 등 9종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 1.0 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Estrone, β-Estradiol, β-Estradiol 17-valerate, 17α-Ethynylestradiol, Estropipate, β-Estradiol 17-cypionate, Norethisterone acetate, Medroxyprogesterone acetate, Raloxifene hydrochloride

○ Analytical condition of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 1 mM Ammonium acetate in Water (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	80	20
	1.0	80	20
	3.0	40	60
	6.0	0	100
	8.0	0	100
	8.1	80	20
	10.0	80	20
• Flow Rate	0.35 mL/min		
• Inj. Volume	4 µL		

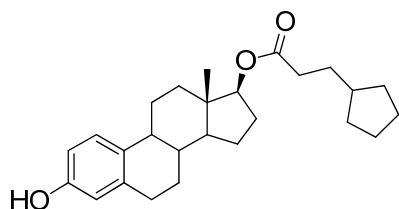
○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+), (-)
• Capillary Voltage	2.5 kV
• Desolvation Temp.	350°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

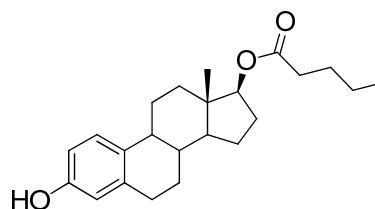
○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Estrone	-	268.95	50	144.89	40
				158.90	30
				182.92	35
β-Estradiol	-	270.98	40	144.85	35
				182.90	35
17α-Ethynylestradiol	-	294.96	40	144.85	35
				182.90	35
β-Estradiol 17-valerate	-	355.05	40	100.88	30
				252.98	30
Estropipate	-	348.90	35	144.87	40
				268.98	35
β-Estradiol 17-cypionate	-	395.05	40	140.92	35
				252.98	30
Norethisterone	+	341.05	25	108.95	25
				281.11	15
Medroxyprogesterone	+	387.07	25	285.10	20
				327.10	15
Raloxifene	+	474.97	45	111.97	30
				269.91	30

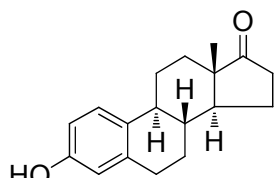
■ 구조식



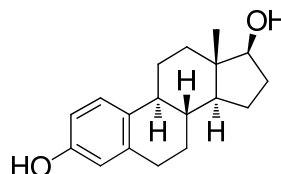
β-Estradiol 17-cypionate  
[C<sub>26</sub>H<sub>36</sub>O<sub>3</sub>]



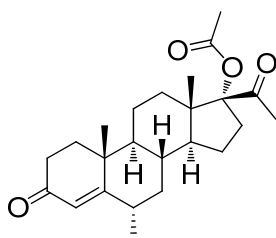
β-Estradiol 17-valerate  
[C<sub>23</sub>H<sub>32</sub>O<sub>3</sub>]



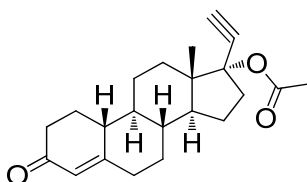
Estrone  
[C<sub>18</sub>H<sub>22</sub>O<sub>2</sub>]



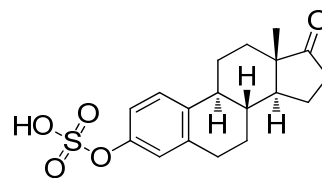
β-Estradiol  
[C<sub>18</sub>H<sub>24</sub>O<sub>2</sub>]



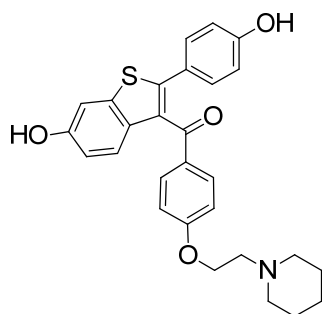
Medroxyprogesterone  
[C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>]



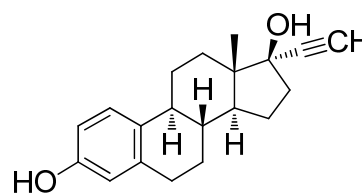
Norethisterone  
[C<sub>22</sub>H<sub>28</sub>O<sub>3</sub>]



Estropipate  
[C<sub>18</sub>H<sub>22</sub>O<sub>5</sub>S]



Raloxifene  
[C<sub>28</sub>H<sub>27</sub>NO<sub>4</sub>S]



17α-Ethinylestradiol  
[C<sub>20</sub>H<sub>24</sub>O<sub>2</sub>]

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## III-2 < 고혈압치료관련성분(34종) 분석법

### ■ 배경

- 혈압치료제 넣은 한약을 면접특효약으로 판매한 약사 적발.
- 항공사승무원 지망생 및 예능고 수험생 등에게 '면접 올림증 특효약'인 것처럼 광고하여 판매('12. 5.)
- 건강기능식품 섞은 지하수로 압 치료 거짓광고 적발('17. 6.)



### ■ 특성

- 고혈압 치료제는 혈관을 확장시켜 혈압을 낮추는 역할을 해줌
- 약의 작용에 따라 크게 이뇨제, 교감신경억제제, 혈관확장제로 나누어짐

### ■ 분석사례

- 상명탕: Propranolol hydrochloride 0.21 mg/g 검출

■ 분석법

1. HPLC법

○ 전처리 방법

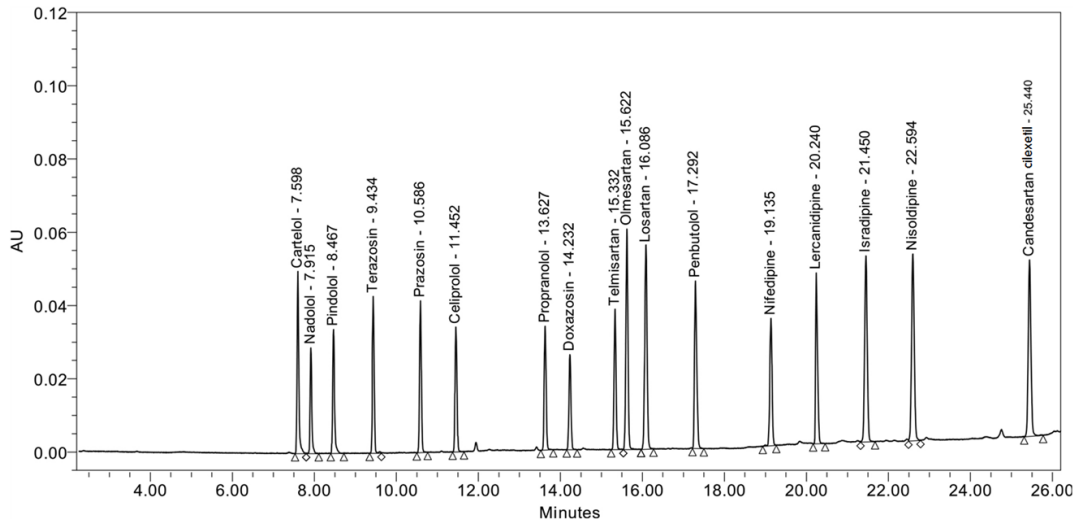
- 표준액 조제 : 표준액 1\* Cartelol hydrochloride 등 17종  
표준액 2\* Atenolol 등 17종  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 5~40 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

- \* 표준액 1 : Cartelol hydrochloride, Nadolol, Pindolol, Terazosin hydrochloride, Prazosin hydrochloride, Celiprolol, Propranolol hydrochloride, Doxazosin mesylate, Telmisartan, Olmesartan medoxomil, Losartan potassium, (±)-Penbutolol hydrochloride, Nifedipine, Lercanidipine hydrochloride, Isradipine, Nisoldipine, Candesartan cilexetil
- \* 표준액 2 : Atenolol, Clonidine hydrochloride, Minoxidil, Acebutolol hydrochloride, (±)-Metoprolol (+)-tartrate salt, Phentolamine mesylate, Betaxolol hydrochloride, Diltiazem hydrochloride, Benazepril hydrochloride, Carvedilol, Irbesartan, Amlodipine besylate, Verapamil hydrochloride, Valsartan, Nitrendipine, Nilvadipine, Felodipine

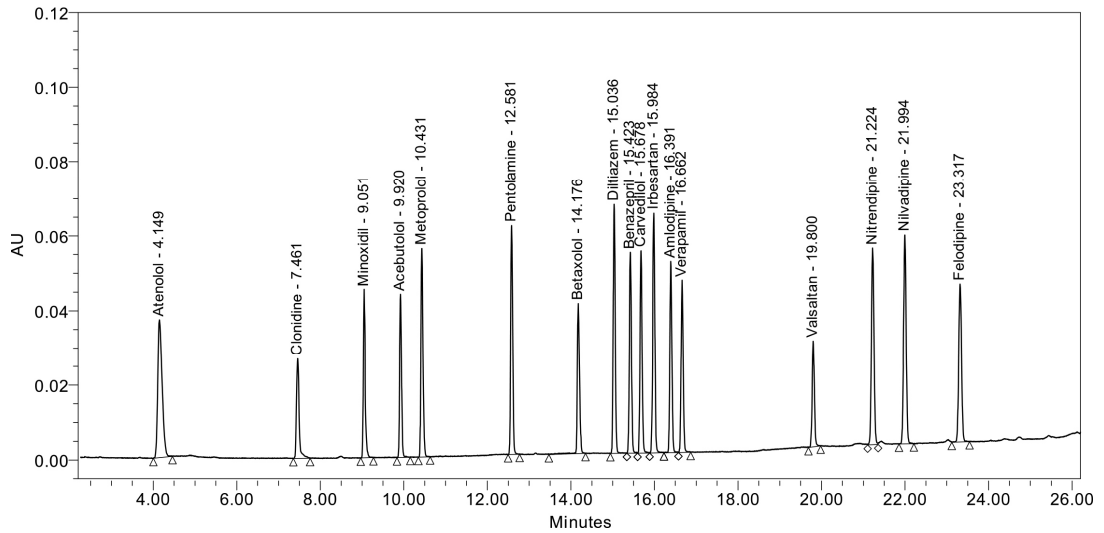
○ Analytical condition of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 150 mm, 1.8 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.5 mM Sodium-1-hexane sulfonate in Water (0.1% H <sub>3</sub> PO <sub>4</sub> ) (B) 95% Acetonitrile		
	Time (min)	A (%)	B (%)
	0.0	90	10
	1.0	90	10
	10.0	68	32
	16.0	50	50
	17.0	40	60
	24.0	18	82
	24.1	0	100
	26.0	0	100
	26.1	90	10
	30.0	90	10
• Flow Rate	0.23 mL/min		
• Inj. Volume	1 µL		
• UV Detection	205 nm		
• PDA Range	190~400 nm		

○ Chromatogram

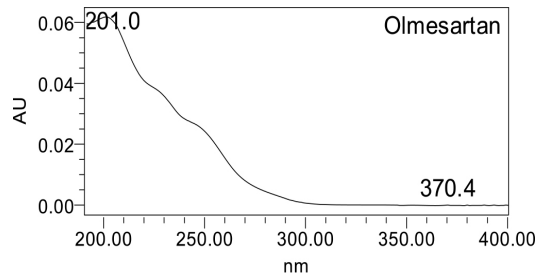
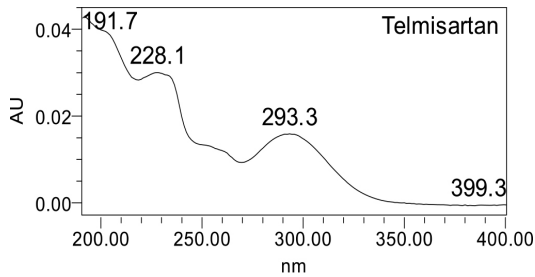
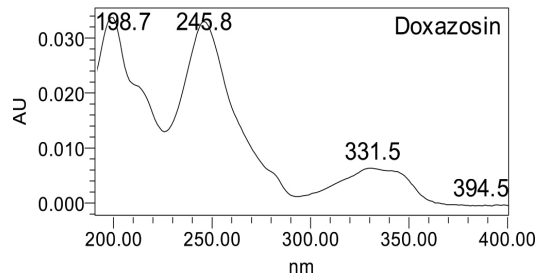
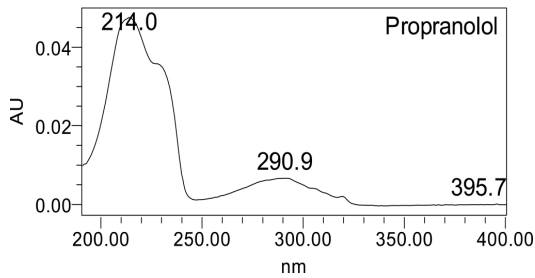
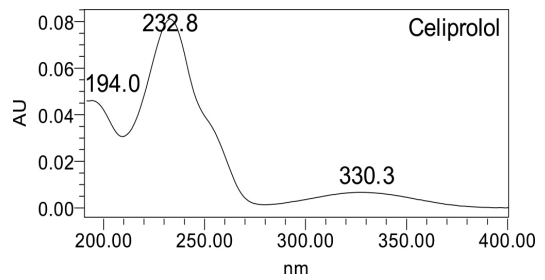
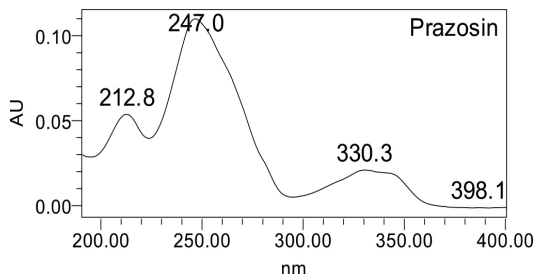
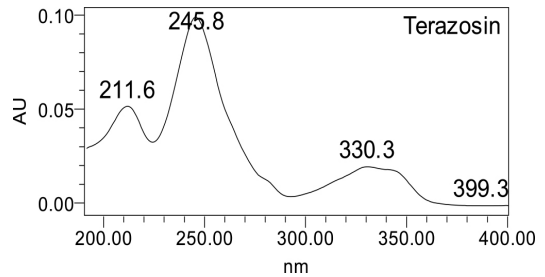
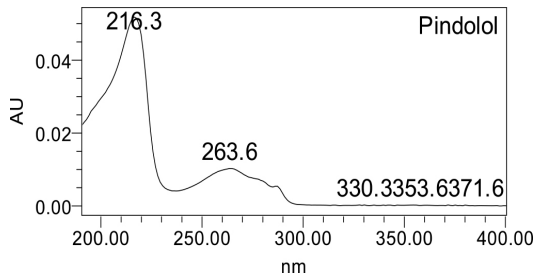
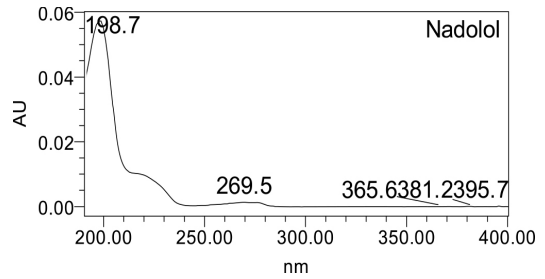
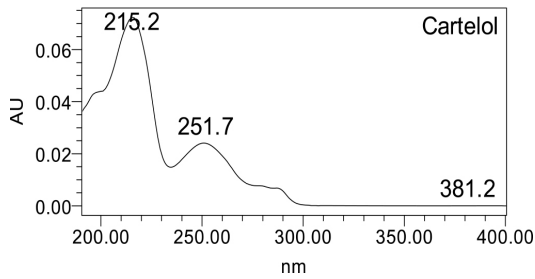


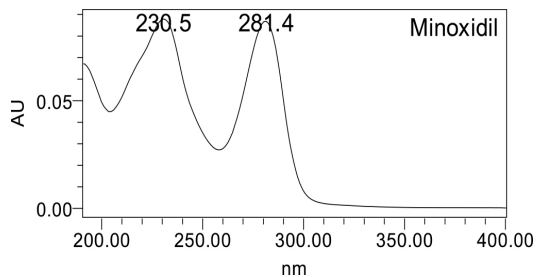
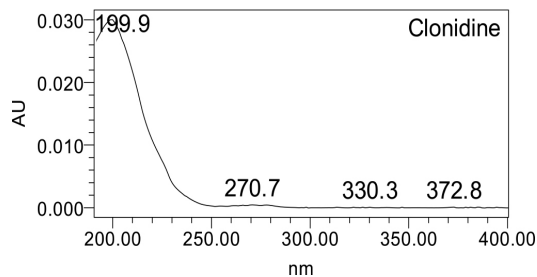
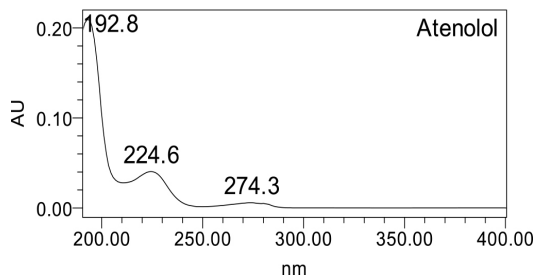
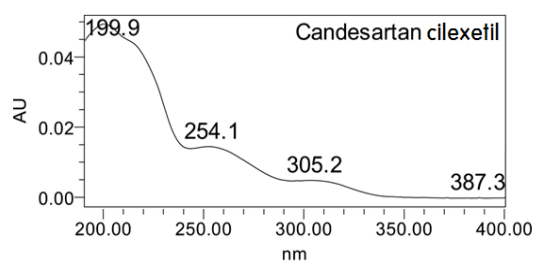
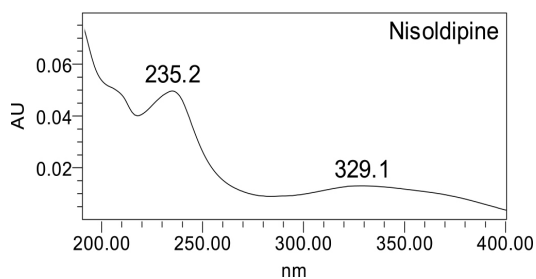
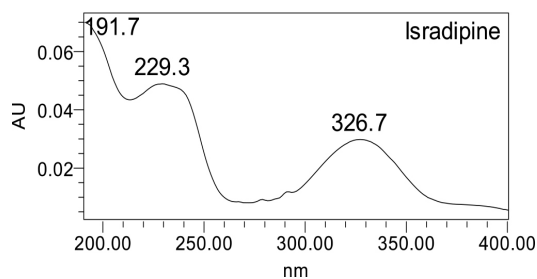
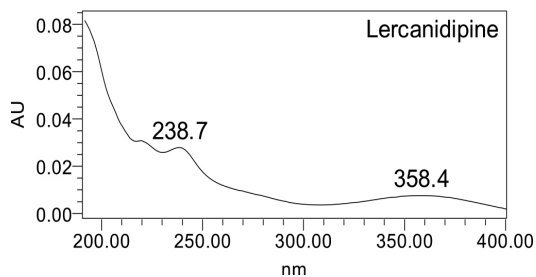
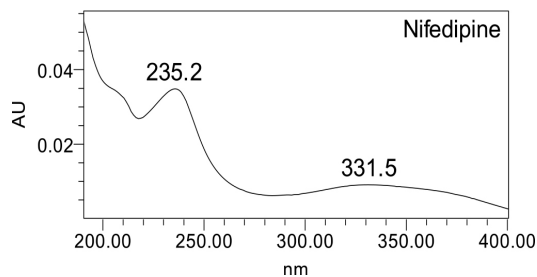
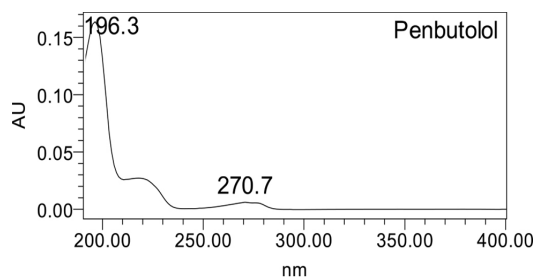
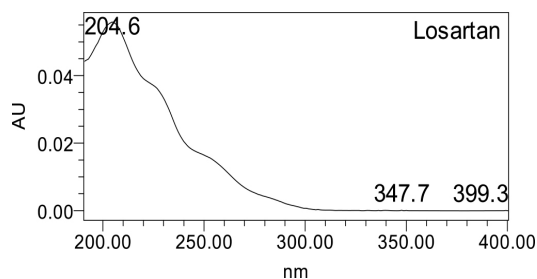
[표준액 1]



[표준액 2]

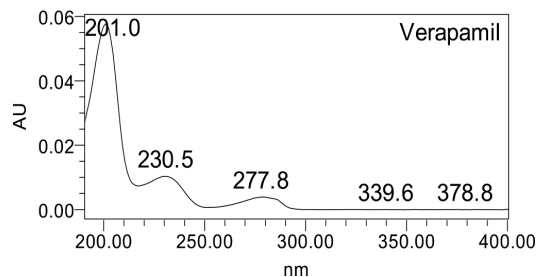
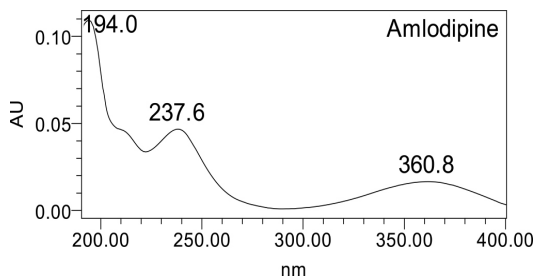
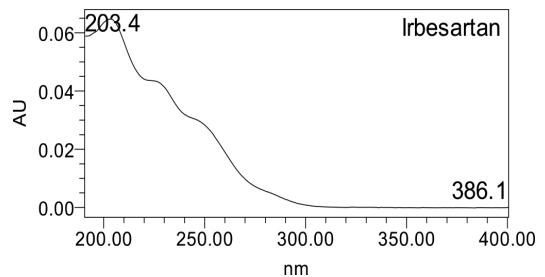
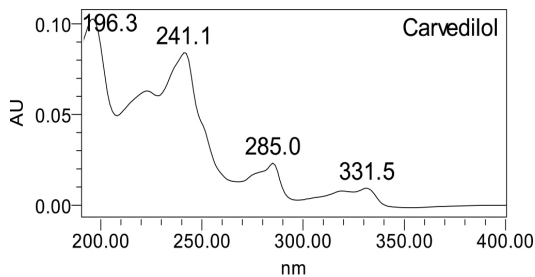
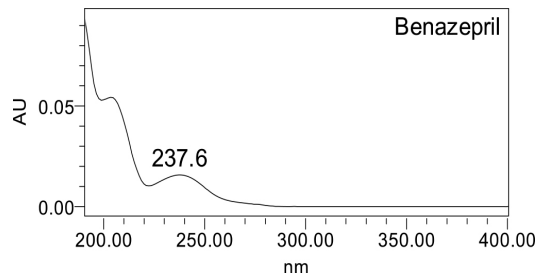
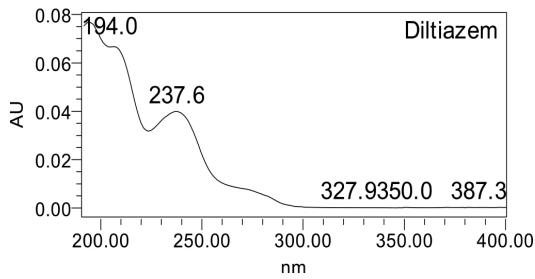
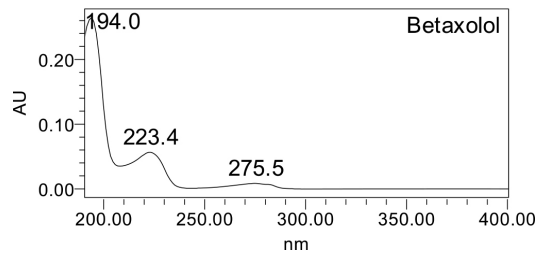
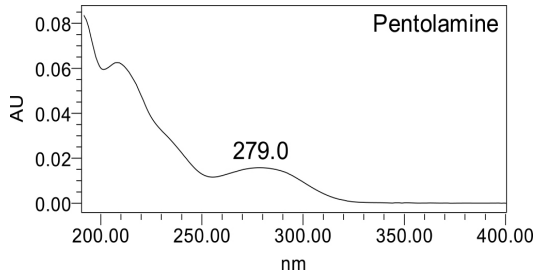
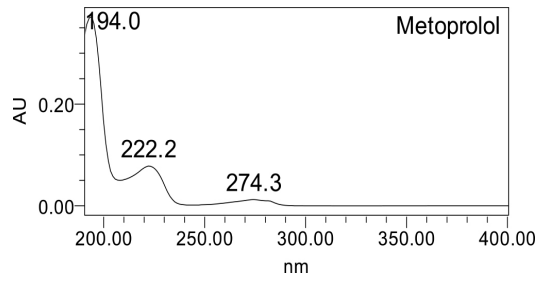
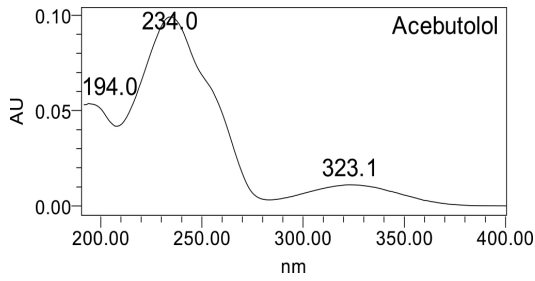
○ PDA Spectrum

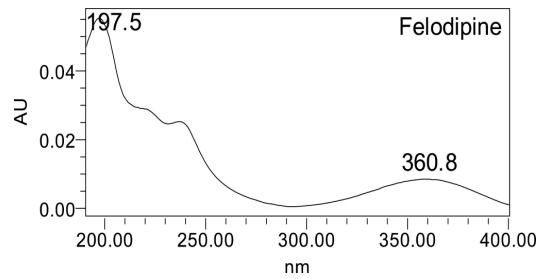
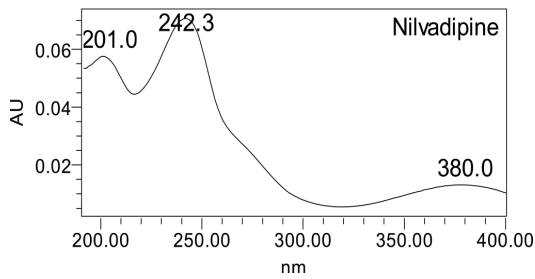
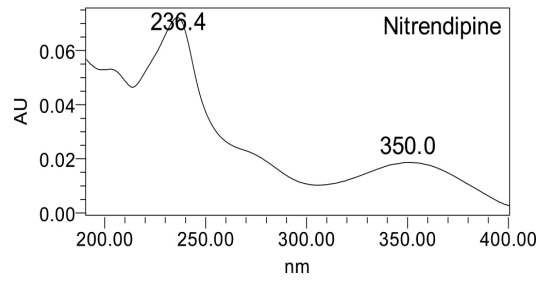
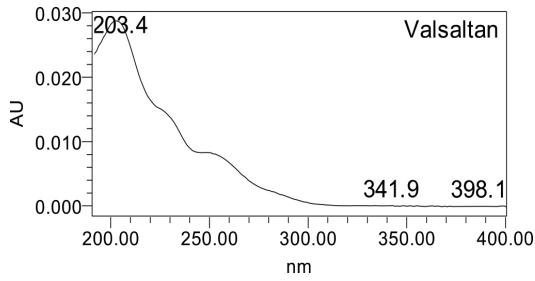






III-2. 고혈압치료관련성분(34종) 분석법





## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Shiseido SP3133		
• Column	Waters Atlantis dC <sub>18</sub> (2.1 mm × 150 mm, 3 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.5 mM Ammonium acetate in Water (B) 0.5 mM Ammonium acetate in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	3.0	95	5
	25.0	0	100
	28.0	0	100
	28.1	95	5
	30.0	95	5
• Flow Rate	0.22 mL/min		
• Inj. Volume	1 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (+)
• Curtain Gas	20 psi
• Collision Gas	10 psi
• Ion Voltage	4500 V
• Ion Source Gas 1	55 psi
• Ion Source Gas 2	60 psi
• Source Temp.	450°C

○ Analyte LC-MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (V)	CXP (V)
Carteolol	+	293.2	60	74.0	30	10
				164.1	35	10
				202.1	30	10
				237.1	20	10
Nadolol	+	310.2	65	201.1	35	10
				236.1	30	10
				254.1	25	15
Pindolol	+	249.2	65	116.0	25	10
				146.1	25	10
				172.1	25	15
Terazosin	+	388.2	65	71.0	55	15
				290.1	40	20
				95.0	65	15
Prazosin	+	384.2	85	138.0	40	15
				247.1	40	10
				233.1	35	10
Celiprolol	+	380.2	45	251.1	35	10
				307.1	25	10
				324.2	25	15
				116.1	25	15
Propranolol	+	260.1	70	155.1	35	15
				157.1	25	10
				183.0	25	15
Doxazosin	+	452.2	90	247.1	55	10
				290.1	50	10
				344.1	45	15
Telmisartan	+	515.3	25	211.1	55	10
				276.2	65	15
				305.2	45	10
Olmesartan	+	447.3	90	207.1	35	25
				235.1	30	20
Losartan	+	423.1	65	180.0	60	15
				207.1	35	10
				405.1	20	15

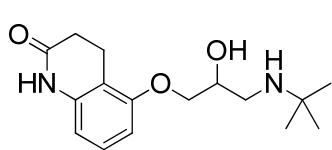
표준액 1

Compound	Ion Mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (V)	CXP (V)			
표준액 1	Penbutolol	+	292.2	50	133.0	35	10		
					201.1	30	25		
					236.1	25	10		
표준액 1	Nifedipine	+	347.1	75	195.1	25	10		
					254.1	25	10		
					315.1	15	10		
표준액 1	Lercanidipine	+	612.2	65	100.1	60	10		
					280.2	35	15		
					312.1	15	20		
표준액 1	Isradipine	+	372.3	65	340.1	20	20		
					239.1	30	15		
					315.0	15	15		
표준액 1	Nisoldipine	+	389.2	65	357.1	15	15		
					147.1	55	15		
					207.1	60	10		
표준액 1	Candesartan cilexetil	+	611.3	65	263.1	35	15		
					423.2	25	15		
					145.1	40	15		
표준액 2	Atenolol	+	267.1	35	190.1	25	15		
					225.1	25	15		
					132.9	60	15		
표준액 2	Clonidine	+	230.0	90	160.0	50	10		
					213.0	35	10		
					110.0	35	15		
표준액 2	Minoxidil	+	210.1	65	164.1	35	10		
					193.1	20	15		
					98.0	30	10		
표준액 2	Acebutolol	+	337.1	85	218.1	35	15		
					260.1	30	30		
					319.2	25	15		
표준액 2	Metoprolol	+	268.2	50	116.1	25	10		
					133.1	35	10		
					159.1	30	20		
							191.1	25	15

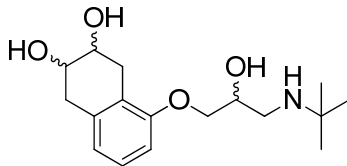
Compound	Ion Mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (V)	CXP (V)
Phentolamine	+	282.1	65	212.1	30	15
				239.1	30	10
				98.1	30	10
Betaxolol	+	308.2	65	116.1	25	15
				133.0	35	15
Diltiazem	+	415.2	40	178.1	35	10
				310.0	30	10
				118.0	60	10
Benazepril	+	425.2	75	190.1	45	15
				351.2	35	15
				100.0	40	10
Carvedilol	+	407.2	90	222.1	35	15
				224.1	30	15
				283.1	30	10
Irbesartan	+	429.3	50	180.1	65	15
				195.1	30	10
				207.1	35	10
Amlodipine	+	409.2	70	206.0	35	15
				220.0	40	10
				294.0	15	15
Verapamil	+	455.3	75	150.1	55	15
				165.1	40	5
				303.2	35	15
Valsartan	+	436.2	60	235.1	25	15
				291.1	25	15
				306.1	20	10
Nitrendipine	+	361.2	55	283.1	35	10
				315.0	15	20
				329.1	20	15
Nilvadipine	+	386.1	70	312.0	20	20
				326.0	15	10
				344.0	10	15
Felodipine	+	384.1	40	338.0	20	15
				352.1	20	15

표준액 2

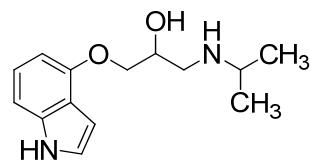
■ 구조식



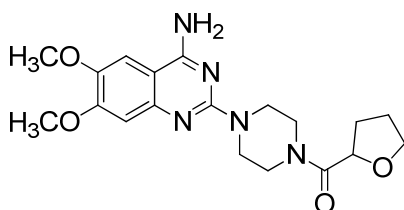
Carteolol  
[C<sub>16</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>]



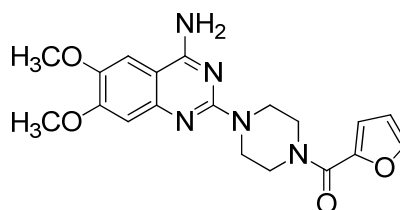
Nadolol  
[C<sub>17</sub>H<sub>27</sub>NO<sub>4</sub>]



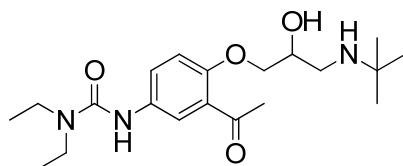
Pindolol  
[C<sub>14</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>]



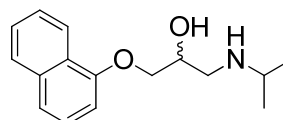
Terazosin  
[C<sub>19</sub>H<sub>25</sub>N<sub>5</sub>O<sub>4</sub>]



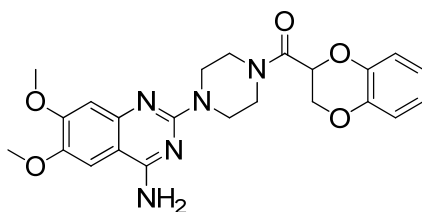
Prazosin  
[C<sub>19</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>]



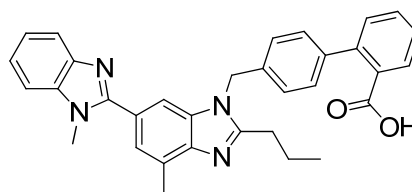
Celiprolol  
[C<sub>20</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>]



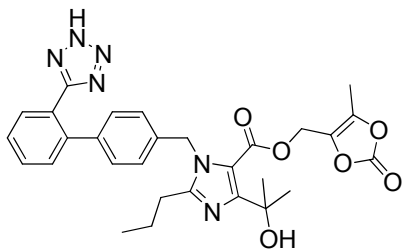
Propranolol  
[C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub>]



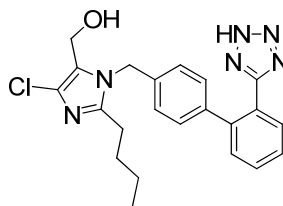
Doxazosin  
[C<sub>23</sub>H<sub>25</sub>N<sub>5</sub>O<sub>5</sub>]



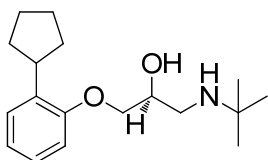
Telmisartan  
[C<sub>33</sub>H<sub>30</sub>N<sub>4</sub>O<sub>2</sub>]



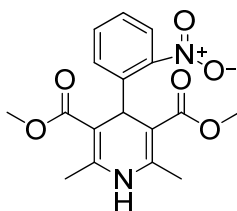
Olmesartan  
[C<sub>23</sub>H<sub>30</sub>N<sub>6</sub>O<sub>6</sub>]



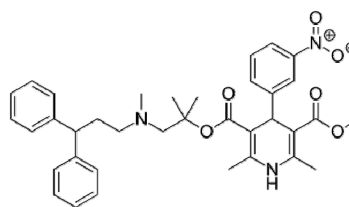
Losartan  
[C<sub>22</sub>H<sub>22</sub>ClN<sub>6</sub>O]



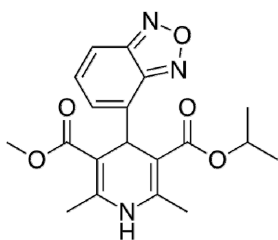
Penbutolol  
[C<sub>18</sub>H<sub>23</sub>NO<sub>2</sub>]



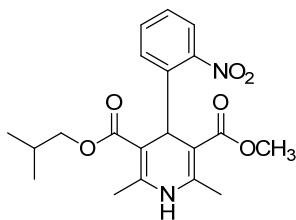
Nifedipine  
[C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>]



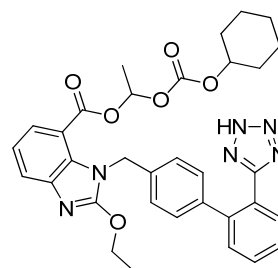
Lercanidipine  
[C<sub>36</sub>H<sub>41</sub>N<sub>3</sub>O<sub>6</sub>]



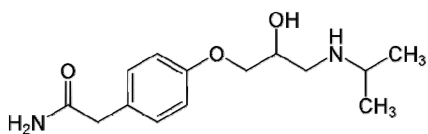
Isradipine  
[C<sub>19</sub>H<sub>21</sub>N<sub>3</sub>O<sub>5</sub>]



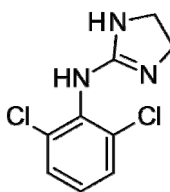
Nisoldipine  
[C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>]



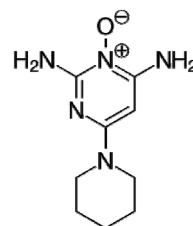
Candesartan cilexetil  
[C<sub>33</sub>H<sub>34</sub>N<sub>6</sub>O<sub>6</sub>]



Atenolol  
[C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>]

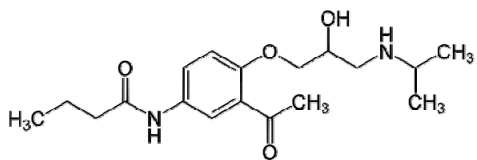


Clonidine  
[C<sub>9</sub>H<sub>9</sub>Cl<sub>2</sub>N<sub>3</sub>]

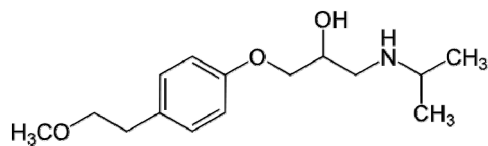


Minoxidil  
[C<sub>9</sub>H<sub>15</sub>N<sub>5</sub>O]

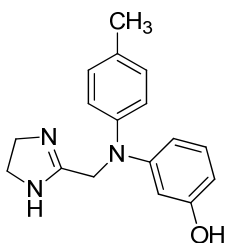




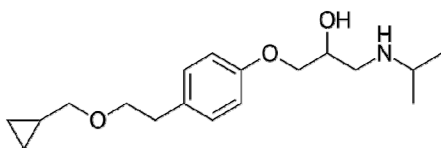
Acebutolol  
[C<sub>18</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>]



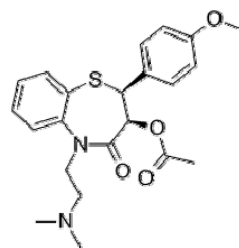
Metoprolol  
[C<sub>15</sub>H<sub>25</sub>NO<sub>3</sub>]



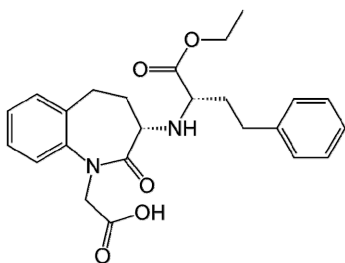
Phentolamine  
[C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O]



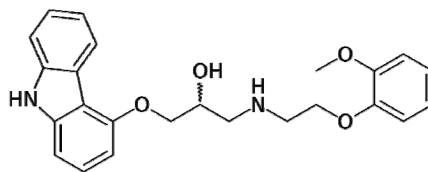
Betaxolol  
[C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>]



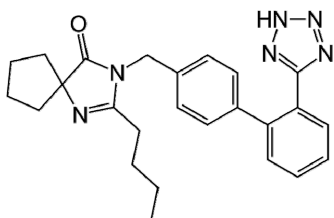
Diltiazem  
[C<sub>22</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>S]



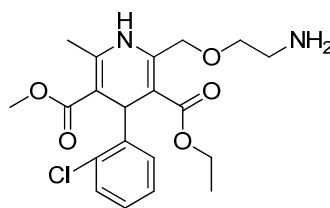
Benazepril  
[C<sub>24</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>]



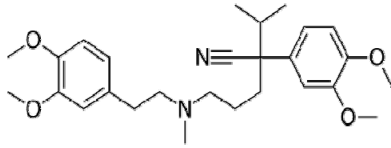
Carvedilol  
[C<sub>24</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>]



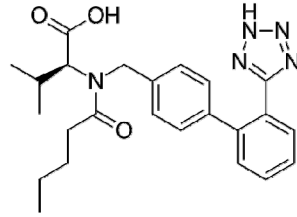
Irbesartan  
[C<sub>25</sub>H<sub>28</sub>N<sub>6</sub>O]



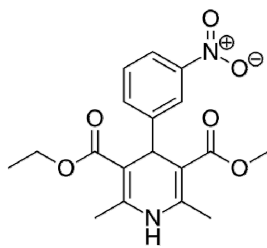
Amlodipine  
[C<sub>20</sub>H<sub>25</sub>ClN<sub>2</sub>O<sub>5</sub>]



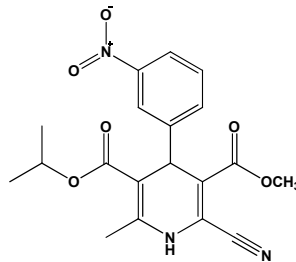
Verapamil  
[C<sub>27</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub>]



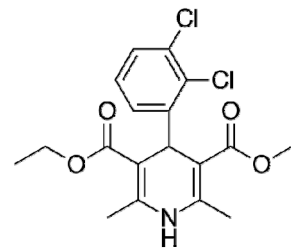
Valsartan  
[C<sub>24</sub>H<sub>29</sub>N<sub>5</sub>O<sub>3</sub>]



Nitrendipine  
[C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>6</sub>]



Nilvadipine  
[C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>6</sub>]



Felodipine  
[C<sub>18</sub>H<sub>19</sub>Cl<sub>2</sub>NO<sub>4</sub>]

## ■ 참고문헌

1. Seok Heo, Geum Joo Yoo, Ji Yeon Choi, Hyoung Joon Park, Sung-Kwan Park and Sun Young Baek. A rapid method for the simultaneous determination of 25 anti-hypertensive compounds in dietary supplements using ultra-high-pressure liquid chromatography. *Food Addit Contam Part A*. 33(11), 1627-1636 (2016)
2. Vishnuvardhan C, Srinivas R and Satheeshkumar N. Development and validation of a UPLC method for screening potentially counterfeit anti-hypertensive drugs using design of experiment. *Anal Meth*. 6 (13), 4610-4616 (2015)
3. Gonzales O, Alonso R. M. Ferreirós, Weinmann W, Zimmermann R and Dresen S. Development of an LC-MS/MS method for the quantitation of 55 compounds prescribed in combined cardiovascular therapy. *J Chromatogr B*. 879, 243-252 (2011)

# III-3 N-나이트로소디에탄올아민 분석법

## 배 경

- N-나이트로소디에탄올아민은 식품의 제조 과정 중 육류나 생선 등에 통상적으로 들어있는 2차 아민화합물과 아질산염과 같은 산화질소 화합물이 반응해 자연적으로 생성되는 니트로소 화합물질이며, 동물에 강력한 발암물질로 작용
- 식약처는 식품제조, 가공 중 자연 발생하는 유해물질인 니트로소디에탄올아민 등의 저감화 추진



## 특 성

- 유기질소, 황 화합물 등은 산성조건에서 nitrite, nitrate, nitrocompound 등과 반응하여 니트로사민류를 생성
- 니트로사민류의 발암성에 대해 국제암연구기관(IARC)에서는 니트로사민류 중 N-Nitrosodimethylamine, N-Nitrosodiethylamine 2종의 경우 그룹2A (인체 발암 추정물질)로 분류

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : NDELA (*N*-Nitrosodiethanolamine)  
→ 일정량 취함 → 물 가함 → 최종 농도(약 0.2 µg/mL)
- 검액 조제 : 수용성: 약 2 g 취함 → 물 가함 → 20 mL 정용  
지용성: 약 2.5 g 취함 → 디클로로메탄 가함  
→ to 10 mL → 물 5 mL  
→ 진탕(30분), 원심분리(10분, 19,400 g)  
→ SPE(Sep-pak C<sub>18</sub> 카트리지, 6 cc, 1 g)  
→ Condition(5 mL, 100% 메탄올) → Equilibrate(5 mL, 물)  
→ Loading(검액, 5 mL) → 초기 2 mL 버림 → Eluent, 3 mL  
→ Eluent(물 5 mL) → Eluent 8 mL → 검액으로 사용

#### ○ Analytical condition of HPLC

- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC HSS T<sub>3</sub> (2.1 mm × 150 mm, 1.8 µm)
- Column Temp. 30°C
- Mobile Phase (A) 0.01% Formic acid in Water  
(B) 100% Acetonitrile

Time (min)	A (%)	B (%)
0.0	99	1
4.0	99	1
6.0	80	20
7.0	80	20
7.1	99	1
10.0	99	1

- Flow Rate 0.3 mL/min
- Inj. Volume 10 µL

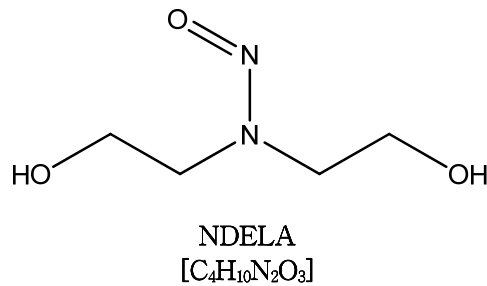
○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	3.5 kV
• Desolvation Temp.	500°C
• Desolvation Gas Flow	700 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	CV (V)	Product Ion ( <i>m/z</i> )	CE (eV)
<i>N</i> -Nitrosodiethanolamine	+	135.16	10	73.97	14
				104.04	12

■ 구조식



■ 참고문헌

1. Maria T. Matyska, Joseph J. Pesek, Li Yang. Screening method for determining the presence of *N*-nitrosodiethanolamine in cosmetics by open-tubular capillary electrochromatography. *J. Chrom A.* 887, 497-503 (2000)
2. R. C. Schothorst, H. H. J. Somers. Determination of *N*-nitrosodiethanolamine in cosmetic products by LC-MS/MS. *Anal Bio Chem.* 381, 681-685 (2005)

### III-4 < 노닐페놀 에톡시레이트 분석법

#### ■ 배 경

- 불법소포제를 쓴 감자·고구마 전분 제조업체 적발('13. 4.)
- 생감자와 생고구마 분쇄·가공시 발생하는 거품을 제거할 목적으로 기준·규격이 고시되지 않은 화학적 합성품을 소포제로 사용함



#### ■ 특 성

- 기름과 물을 섞어 오염물질을 제거하는 데 도움을 주는 계면활성제로서, 주로 주방용 세정제, 세척제, 세안제, 샴푸 등 다양한 용도로 사용
- 내분비계 장애 추정물질로 알려져 있으며, 남성에게 발기부전을 일으키거나 무정자증을 유발해 불임의 원인이 되고, 여성에게는 기형아, 성조숙증 등을 일으킬 수 있음

■ 분석법

1. HPLC법

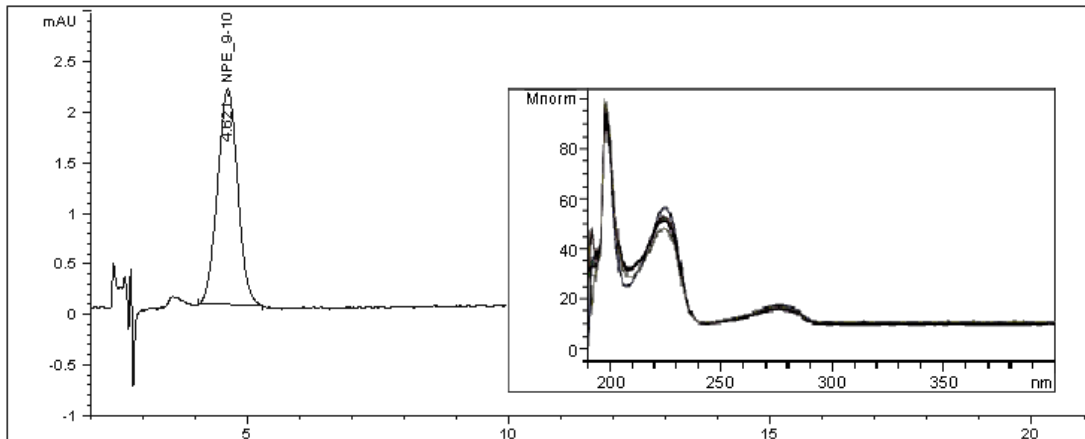
○ 전처리 방법

- 표준액 조제 : P.O.E. (9 to 10) Nonylphenol  
 → 20 mg 정도 취함 → 100% 메탄올 용액 가함  
 → 최종 농도(약 1.0 mg/mL)
- 검액 조제 : 약 10 g 취함 → 100% 메탄올 가함 → 30분 진탕 → 100 mL 정용

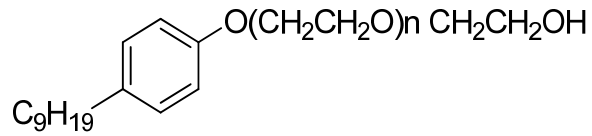
○ Analytical condition of HPLC

• Instrument	Agilent DE/1200 HPLC
• Column	Waters Sunfire C <sub>8</sub> (4.6 mm × 200 mm, 5 μm)
• Column Temp.	40°C
• Mobile Phase	80% Methanol + 5% Acetonitrile + 15% Water
• Flow Rate	1.0 mL/min
• Inj. Volume	50 μL
• UV Detection	280 nm
• PDA Range	190~400 nm

○ Chromatogram & PDA Spectrum



## ■ 구조식



Nonylphenol ethoxylates  
[C<sub>15</sub>H<sub>24</sub>O<sub>2</sub>[C<sub>2</sub>H<sub>4</sub>O]<sub>n</sub>]

## ■ 참고문헌

1. Bing Shao, Jian-ying Hu, Min Yang. Determination of nonylphenol ethoxylates in the aquatic environment by normal phase liquid chromatography -electrospray mass spectrometry. *J. Chrom. A.* 950, 167-175 (2002)
2. L. Núñez, E. Turiel, J. L. Tadeo. Determination of nonylphenol and nonylphenol ethoxylates in environmental solid samples by ultrasonic-assisted extraction and high performance liquid chromatography-fluorescence detection. *J. Chrom. A.* 1146, 157-163 (2007)



## III-5 < 당뇨병치료제성분(26종) 분석법

### ■ 배 경

- 건강기능식품중 혈당강하제인 글리베클라미드가 검출된 사례 적발('11)
- 해당제품을 당뇨병, 고혈압, 전립선 등에 효과가 있는 것처럼 광고하여 불법 판매



### ■ 특 성

- 당뇨병치료제 종류로 크게 인슐린 분비 촉진제, 인슐린 작용 증강제 등이 있음
  - 인슐린 분비 촉진제: 췌장 베타세포에서 인슐린 분비를 촉진시켜 혈당을 낮춤 (ex) Glibenclamide, Mitiglinide
  - 인슐린 작용 증강제: 간에서 당 생성 억제 및 근육과 지방 세포 흡수와 이용을 증가시킴 (ex) Metformin, Polglitazone
- 부작용: 심각한 저혈당을 유발할 수 있으며, 다른 약물과 상호작용에 의해 고혈당증을 유발하거나 혈당 조절 능력을 상실할 수 있음

### ■ 분석사례

- 베타-파워플러스 : Glibenclamide 3.26 mg/포 검출
- 회갈색 분말 : Glibenclamide 2.62 g/kg 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

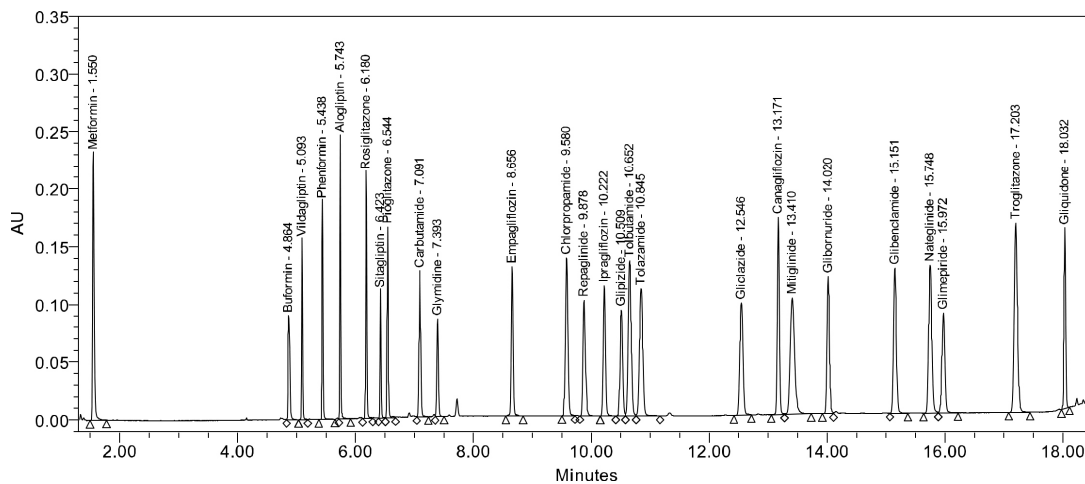
- 표준액 조제 : Metformin hydrochloride 등 26종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10~50 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Metformin hydrochloride, Buformin hydrochloride, Vildagliptin, Phenformin hydrochloride, Alogliptin, Rosiglitazone, Sitagliptin phosphate monohydrate, Pioglitazone hydrochloride, Carbutamide, Glymidine, Empagliflozin, Chlorpropamide, Repaglinide, Ipragliflozin, Glipizide, Tolbutamide, Tolazamide, Gliazide, Canagliflozin, Mitiglinide Calcium, Glibornuride, Glibenclamide, Nateglinide, Glimepiride, Troglitazone, Gliquidone

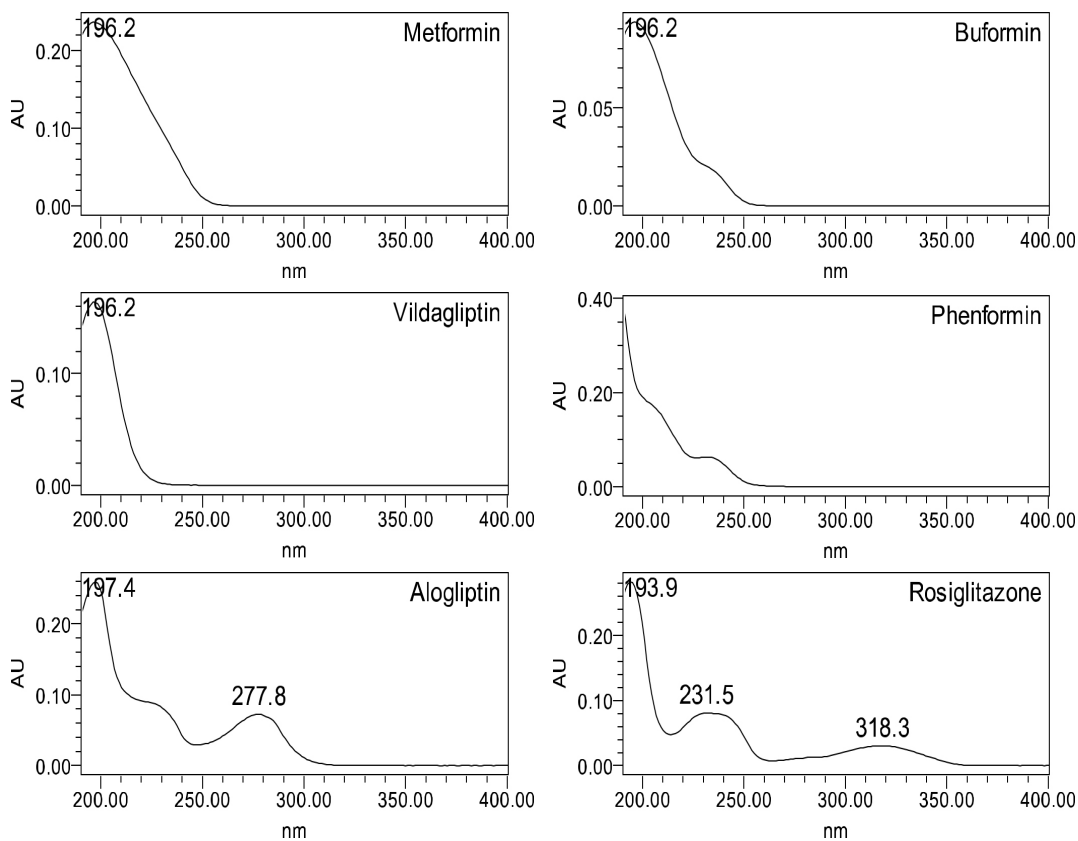
#### ○ Analytical conditions of HPLC

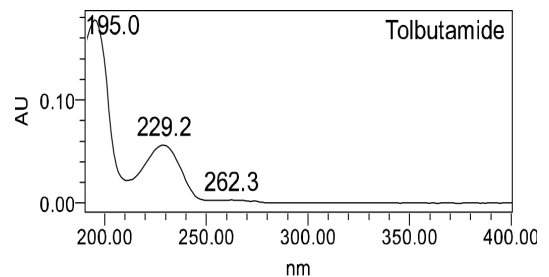
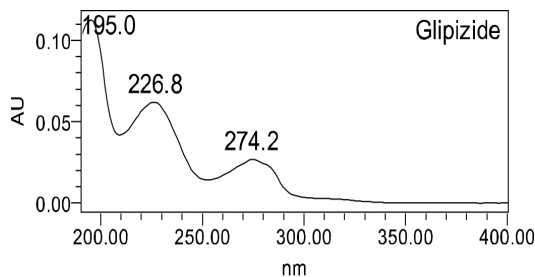
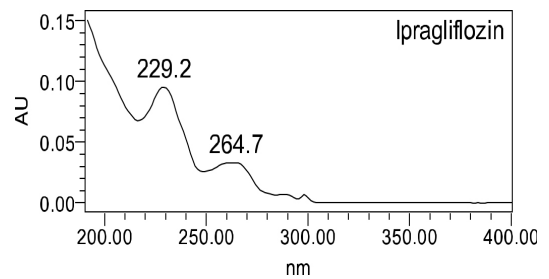
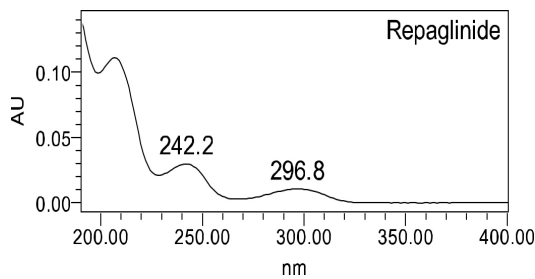
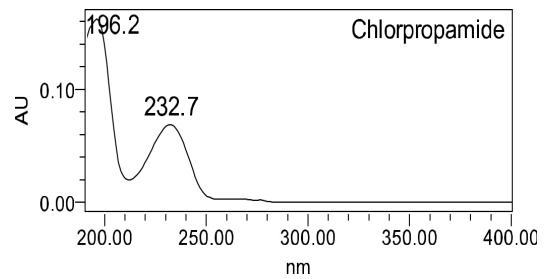
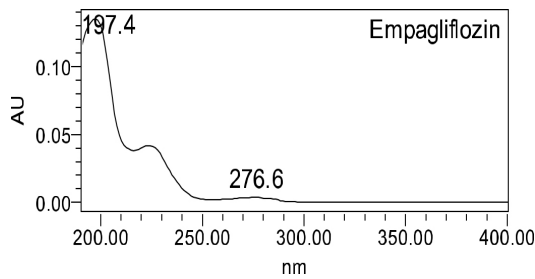
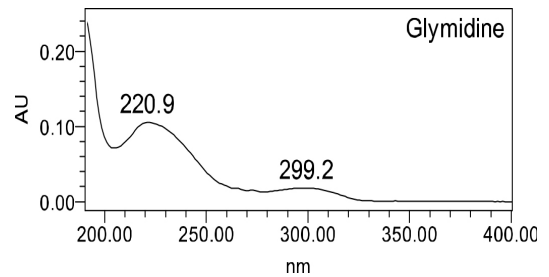
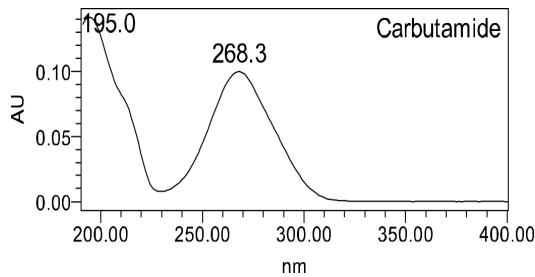
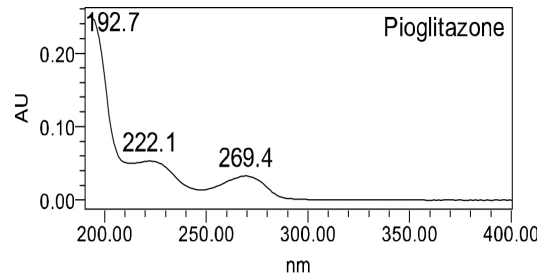
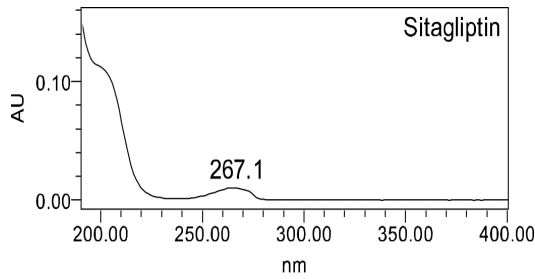
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 150 mm, 1.7 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.5 mM Sodium-1-hexane sulfonate in Water (0.1% H <sub>3</sub> PO <sub>4</sub> ) (B) 95% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	1.0	95	5
	4.5	65	35
	10.0	55	45
	12.0	45	55
	16.0	40	60
	16.5	0	100
	18.5	0	100
	19.0	95	5
	24.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 µL		
• UV Detection	200 nm		
• PDA Range	190~400 nm		

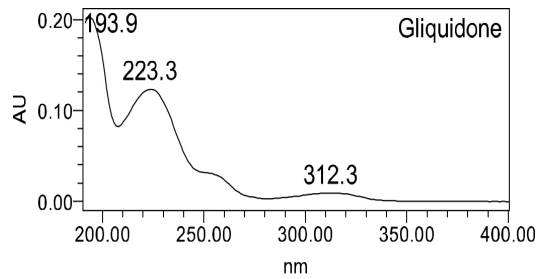
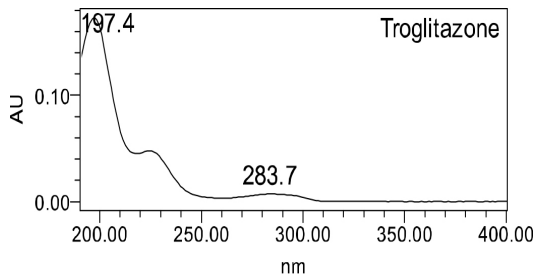
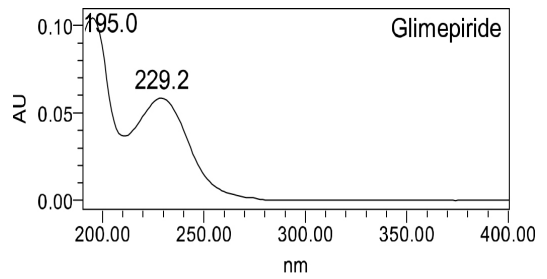
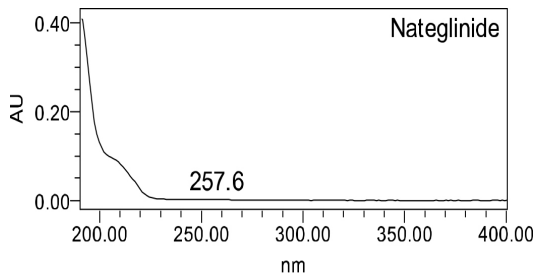
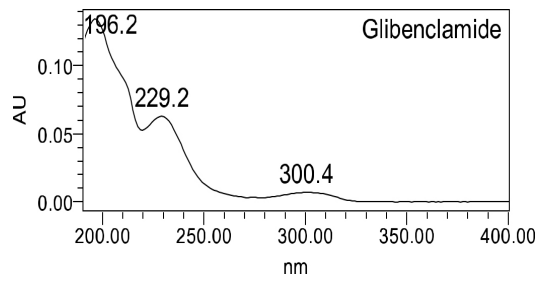
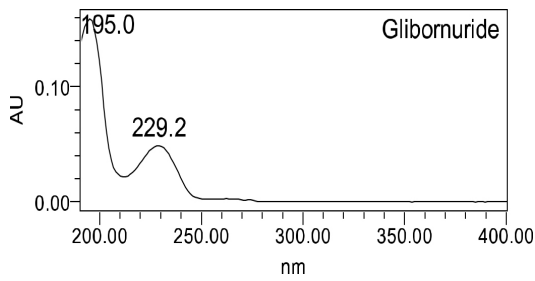
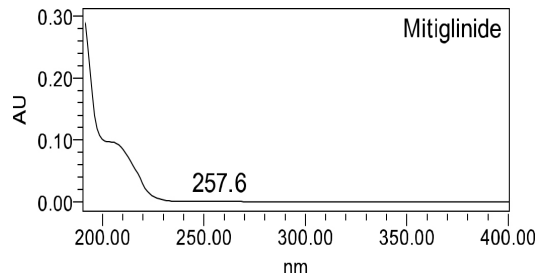
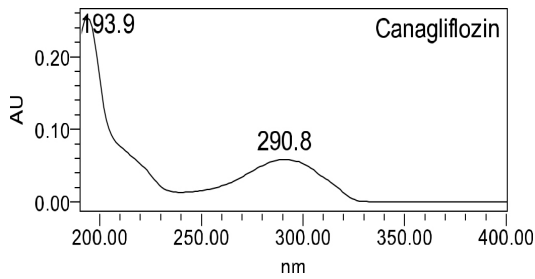
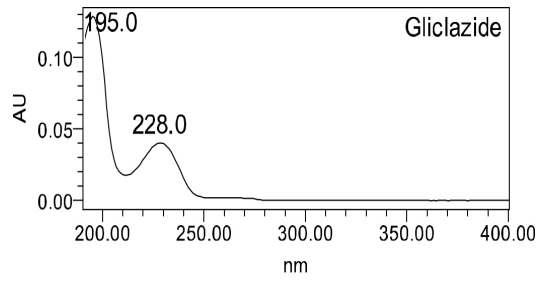
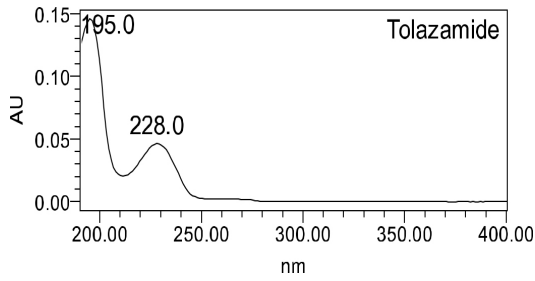
○ Chromatogram



○ PDA Spectrum







## 2. LC-MS/MS

### ○ Analytical conditions of HPLC

• Instrument	Agilent DE/1200 HPLC		
• Column	Shiseido Capcell Pak C <sub>18</sub> (MG II) (2.0 mm × 100 mm, 3 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.1% Formic acid in Water		
	(B) 0.1% Formic acid in Methanol		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	0.7	95	5
	1.0	60	40
	3.0	50	50
	8.0	10	90
	12.0	10	90
	12.1	95	5
	18.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Qtrap 4000	
• Ionization Mode	ESI (+)	ESI (-)
• Curtain Gas	30 psi	30 psi
• Collision Gas	9 psi	9 psi
• Ion Voltage	5000 V	4500 V
• Ion Source Gas 1	50 psi	50 psi
• Ion Source Gas 2	50 psi	50 psi
• Source Temp.	500°C	500°C

○ Analyte MS/MS transition

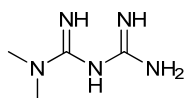
Compound	Ion mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (eV)	CXP (V)
Metformin	+	130.1	45	85.1	20	5
			45	70.9	25	10
			45	60.0	20	10
Buformin	+	158.0	66	59.9	21	10
			66	42.8	59	20
			65	154.2	25	10
Vildagliptin	+	304.2	65	151.1	30	9
			65	133.2	45	10
			60	105.1	37	20
Phenformin	+	206.2	60	164.2	25	10
			60	189.2	23	12
			35	116.1	47	22
Alogliptin	+	340.2	35	323.1	27	22
			35	266.2	31	18
			48	135.0	30	10
Rosiglitazone	+	358.2	48	119.0	78	11
			48	107.0	60	16
			45	235.0	27	15
Sitagliptin	+	408.2	45	174.0	37	10
			45	193.0	35	12
			91	134.1	39	12
Pioglitazone	+	357.0	91	119.0	65	20
			68	156.0	25	10
Carbutamide	+	272.2	68	108.1	40	10
			90	111.0	35	20
Glymidine	+	310.1	90	252.0	28	15
			50	397.0	13	10
Empagliflozin	+	451.1	50	355.1	17	8
			50	71.2	50	13
			55	192.0	19	12
Chlorpropamide	+	277.1	55	110.9	43	10
			55	175.0	25	14

Compound	Ion mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (eV)	CXP (V)
Repaglinide	+	453.2	55	230.1	38	12
			55	162.0	33	12
			55	86.0	33	13
Ipragliflozin	+	422.1	30	151.2	30	10
			30	285.1	20	18
			30	309.1	20	20
Glipizide	-	444.1	23	319.0	30	15
			23	169.9	40	8
Tolbutamide	+	271.2	61	91.20	47	17
			61	155.05	25	15
			61	74.20	20	13
Tolazamide	+	312.0	35	115.2	30	5
			35	141.1	30	10
			35	157.1	20	10
Gliclazide	-	322.2	30	169.8	35	10
			30	105.9	50	8
Canagliflozin	+	443.1	55	365.0	20	8
			55	353.0	28	10
			55	153.0	50	10
Mitiglinide	+	316.2	43	298.2	22	12
			43	145.1	36	10
			43	126.2	33	10
Glibornuride	+	367.2	25	170.1	20	10
			25	152.2	30	10
			25	349.0	20	25
Glibenclamide	+	492.1	70	169.9	35	15
			70	367.0	28	13
			70	127.0	65	10
Nateglinide	+	318.1	50	166.1	18	10
			50	125.2	22	7
			50	120.1	25	14
Glimepiride	-	489.2	55	224.9	45	10
			55	364.1	30	10
			55	349.8	25	10

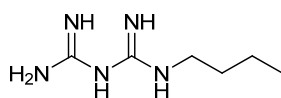


Compound	Ion mode	Precursor ion (m/z)	DP (V)	Product ion (m/z)	CE (eV)	CXP (V)
Troglitazone	+	443.1	25	165.0	25	10
			25	367.0	25	8
			25	291.0	25	20
Gliquidone	+	528.2	45	403.1	15	10
			45	386.0	31	14
			45	165.1	63	14

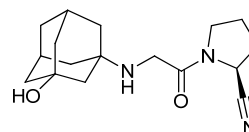
### ■ 구조식



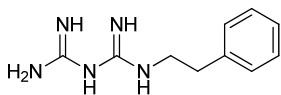
Metformin  
[C<sub>4</sub>H<sub>11</sub>N<sub>5</sub>]



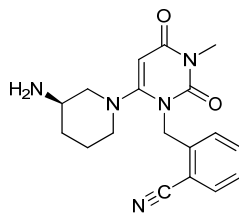
Buformin  
[C<sub>6</sub>H<sub>15</sub>N<sub>5</sub>]



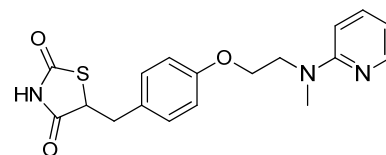
Vildagliptin  
[C<sub>17</sub>H<sub>25</sub>N<sub>3</sub>O<sub>2</sub>]



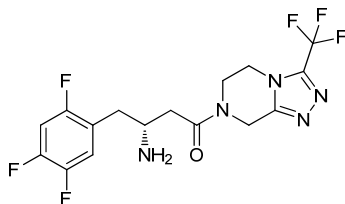
Phenformin  
[C<sub>10</sub>H<sub>15</sub>N<sub>5</sub>]



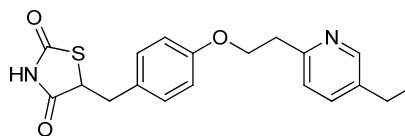
Alogliptin  
[C<sub>18</sub>H<sub>21</sub>N<sub>5</sub>O<sub>2</sub>]



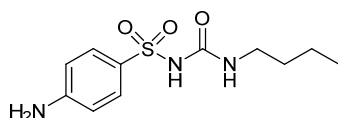
Rosiglitazone  
[C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>S]



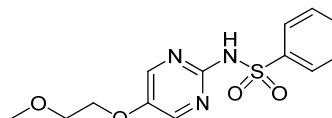
Sitagliptin  
[C<sub>16</sub>H<sub>15</sub>F<sub>6</sub>N<sub>5</sub>O]



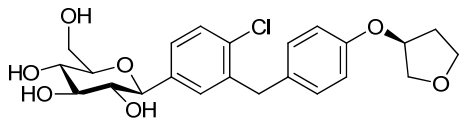
Pioglitazone  
[C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>S]



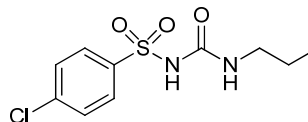
Carbutamide  
[C<sub>11</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>S]



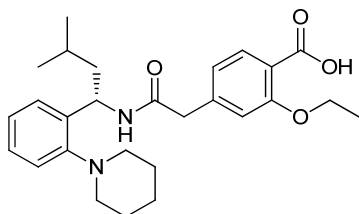
Glymidine  
[C<sub>13</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub>S]



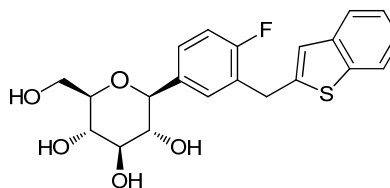
Empagliflozin  
[C<sub>23</sub>H<sub>27</sub>ClO<sub>7</sub>]



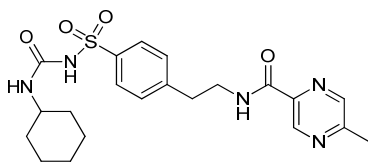
Chlorpropamide  
[C<sub>10</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>3</sub>S]



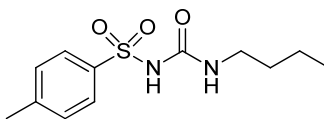
Repaglinide  
[C<sub>27</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub>]



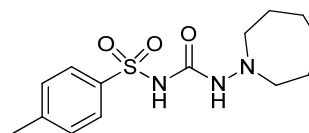
Ipragliflozin  
[C<sub>21</sub>H<sub>21</sub>FO<sub>5</sub>S]



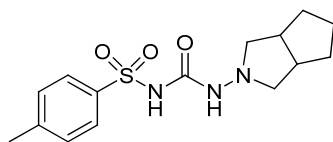
Glipizide  
[C<sub>21</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>S]



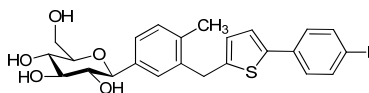
Tolbutamide  
[C<sub>12</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>S]



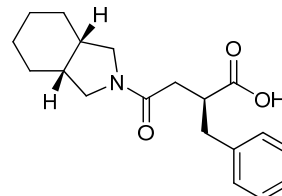
Tolazamide  
[C<sub>14</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>S]



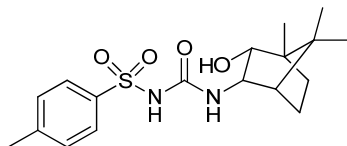
Gliclazide  
[C<sub>15</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>S]



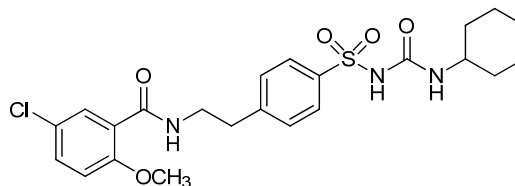
Canagliflozin  
[C<sub>24</sub>H<sub>25</sub>FO<sub>5</sub>S]



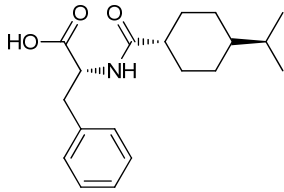
Mitiglinide  
[C<sub>19</sub>H<sub>25</sub>NO<sub>3</sub>]



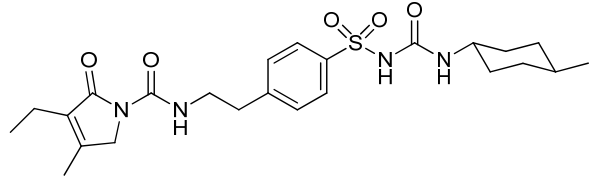
Glibornuride  
[C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>S]



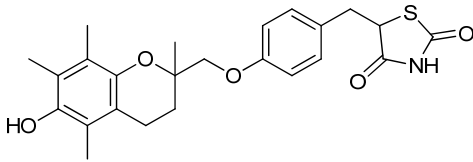
Glibenclamide  
[C<sub>23</sub>H<sub>28</sub>ClN<sub>3</sub>O<sub>5</sub>S]



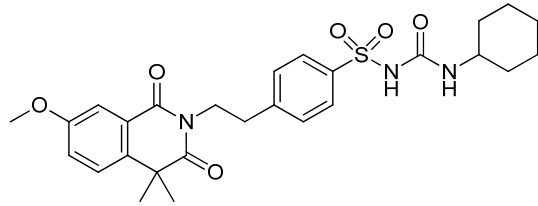
Nateglinide  
[C<sub>19</sub>H<sub>27</sub>NO<sub>3</sub>]



Glimepiride  
[C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S]



Troglitazone  
[C<sub>24</sub>H<sub>27</sub>NO<sub>5</sub>S]



Gliquidone  
[C<sub>27</sub>H<sub>33</sub>N<sub>3</sub>O<sub>6</sub>S]

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### III-6 마 및 천마 성분 분석법

#### ■ 배경

- 인삼 또는 홍삼에 값싼 마(산약)분말을 40% 혼합하여 100% 인삼 또는 홍삼제품으로 속여 고가에 불법 판매('10. 1.)
- 국내산 마는 가격이 인삼에 비해 저렴하며 혼입하더라도 냄새와 맛이 거의 없어 소비자가 구별하기 어려움



#### ■ 특성

- 디오신: 마과식물 왕마(*Dioscorea tokoro*)의 뿌리에서 얻은 스테로이드의 일종인 사포닌으로 마의 주요 성분
- 가스트로딘: 천마(*Gastrodiae elara* Blume)의 뿌리에서 얻은 폴리페놀의 일종으로 *gastrodigenin*의 배당체형인 천마의 주요 성분

#### ■ 분석사례

- 인삼제품: Dioscin 검출
- 진천마고: Gastrodin 검출

■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 표준액 조제 : Dioscin, Gastrodin
  - 일정량 취함 → 100% 메탄올 가함 → 농도(약 1,000 µg/mL)
  - 일정량 취함 → 물 가함 → 최종 농도(약 20 ng/mL)
  - SPE(solid phase extraction, HLB, 500 mg)
    - Condition(100% 메탄올, 5 mL) → Equilibrate(물, 5 mL)
    - Load(표준액, 5 mL) → Wash(5% 메탄올, 5 mL)
    - Eluent(100% 메탄올, 5 mL) → 최종 표준액
- 검액 조제 : 검체 약 2 g 취함 → 물 가함 → 진탕
  - to 50 mL → 원심분리 → 상층액 취해 검액(A액)으로 함
  - SPE(solid phase extraction, HLB, 500 mg)
    - Condition(100% 메탄올, 5 mL) → Equilibrate(물, 5 mL)
    - Load(SPE용 검액, 5 mL) → Wash(5% 메탄올, 5 mL)
    - Eluent(100% 메탄올, 5 mL) → 최종 검액

○ Analytical condition of HPLC

- Instrument Shiseido SP3133
- Column Shiseido Capcell Pak C<sub>18</sub> MGII(2.0 mm × 100 mm, 3 µm)
- Column Temp. 40°C
- Mobile Phase (A) 10 mM Ammonium acetate in Water  
(B) 100% Methanol

Time (min)	A (%)	B (%)
0.0	40	60
2.0	40	60
4.0	10	90
6.0	10	90
8.0	40	60
10.0	40	60

- Flow Rate 0.3 mL/min
- Inj. Volume 5 µL

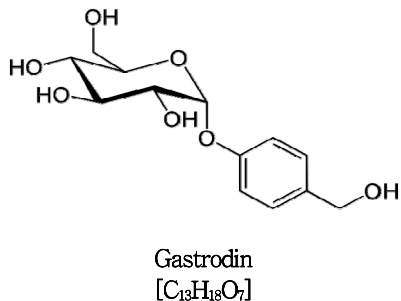
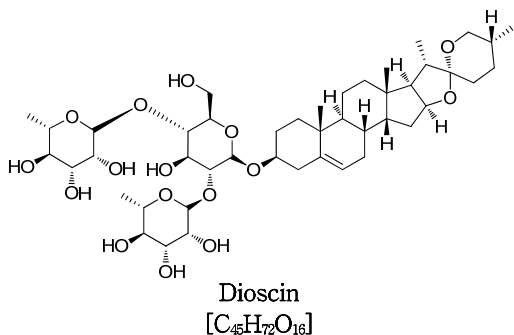
○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (-)
• Curtain Gas	25 psi
• Collision Gas	9 psi
• Ion Voltage	4500 V
• Ion Source Gas 1	55 psi
• Ion Source Gas 2	45 psi
• Source Temp.	550℃

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	DP (V)	Product Ion ( <i>m/z</i> )	CE (V)	CXP (V)
Dioscin	-	867.4	5	721.5	46	27
Gastrodin	-	285.0	50	123.0	18	11

■ 구조식



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### III-7 메칠클로로이소치아졸리논, 메칠이소치아졸리논 분석

#### ■ 배경

- 화장품·물티슈에 ‘가습기 살균제’ 성분, 회수 조치('16. 9.)  
물티슈 일부서 가습기 살균제 성분 ‘MIT/CMIT’ 검출('16. 9.)  
아기 로션에도 버젓이, ‘살균제 화장품’ 유통('16. 9.)  
CMIT/MIT 함유된 치약 회수 조치('16. 9.)
- 가습기 살균제 사건의 원인물질로 알려진 성분들이 다른 용도의 생활 화학용품에 별도의 안전기준이 없이 사용되고 있음



#### ■ 특성

- 미국에서 1998년 농약으로 분류돼 2등급 흡입독성물질로 지정  
부작용: 비염, 기관지염, 편도염, 폐질환 유발



■ 분석법

1. HPLC법

○ 전처리 방법

- 표준액 조제 : Methylchloroisothiazolinone 등 2종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10~30 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

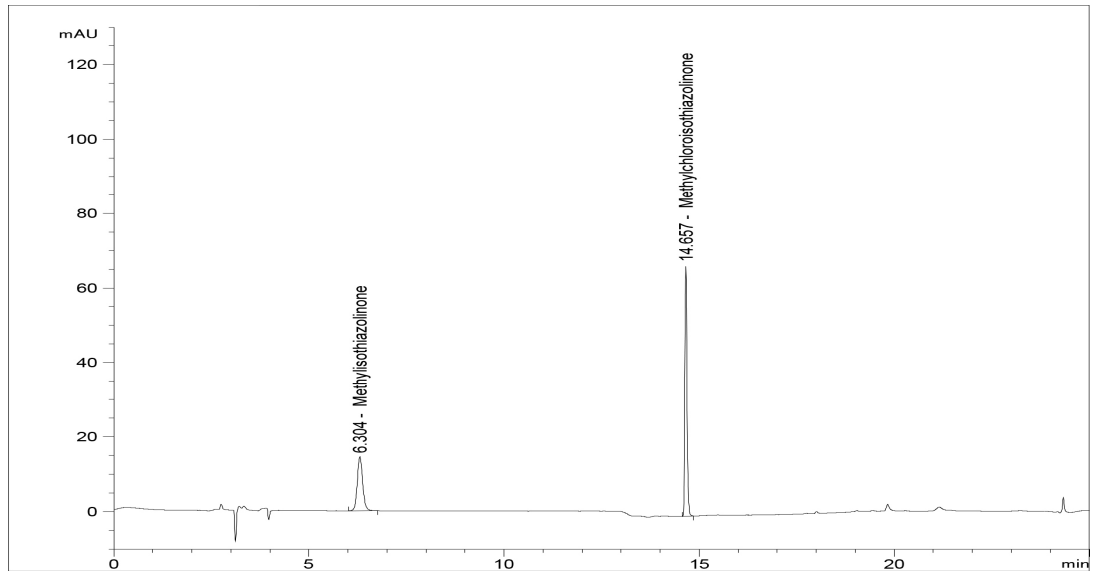
\* 표준액 : Methylchloroisothiazolinone(CMIT), Methylisothiazolinone(MIT)

○ Analytical condition of HPLC

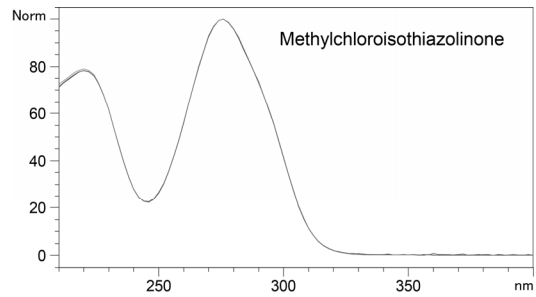
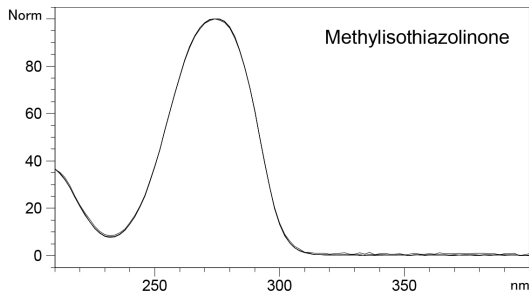
• Instrument	Agilent DE/1200 HPLC (DAD)		
• Column	Agilent Eclipse XDB C18 (4.6 mm × 250 mm, 5 µm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 0.1% 인산수용액:ACN (95:5) (B) 0.1% 인산수용액:ACN (5:95)		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	100	0
	8.0	100	0
	15.0	20	80
	20.0	20	80
	25.0	100	0
	30.0	100	0
• Flow Rate	0.80 mL/min		
• Inj. Volume	5 µL		
• UV Detection	275 nm		
• PDA Range	190~400 nm		

- 0.1% 인산수용액 : Potassium phosphate dibasic (K<sub>2</sub>HPO<sub>4</sub>) 0.2 g + Potassium phosphate monobasic (KH<sub>2</sub>PO<sub>4</sub>) 0.8 g을 증류수 1 L에 녹임.

### ○ Chromatogram



### ○ PDA Spectrum



## 2. LC-MS/MS법

## ○ Analytical condition of HPLC

• Instrument	Waters UPLC		
• Column	Waters ACQUITY UPLC HSS T <sub>3</sub> (2.1 mm× 100 mm, 1.7 μm)		
• Column Temp.	30°C		
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	100	0
	2.0	100	0
	7.0	0	100
	9.0	0	100
	9.1	100	0
	11.0	100	0
• Flow Rate	0.20 mL/min		
• Inj. Volume	1 μL		

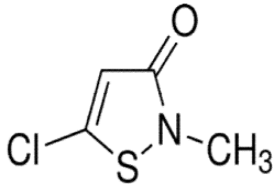
## ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	2.7 kV
• Desolvation Temp.	500°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

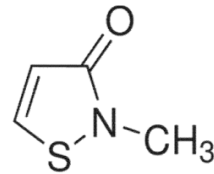
## ○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Methylchloroisothiazolinone (CMIT)	+	150.07	15	86.78	15
				95.78	20
				114.80	20
				118.74	20
Methylisothiazolinone (MIT)	+	115.97	30	70.76	15
				98.75	20
				100.79	20

## ■ 구조식



Methylchloroisothiazolinone  
[C<sub>4</sub>H<sub>4</sub>ClNOS]



Methylisothiazolinone  
[C<sub>4</sub>H<sub>5</sub>NOS]

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# III-8 모유분비촉진관련성분(5종) 분석법

## 배 경

- 발암 한약재 ‘등축’, 수유 특효약 둔갑(‘16. 10.)
- 등축 발암, 신부전증 등 부작용, 통초로 둔갑해 유통 ‘생김새 보니’ (‘16. 10.)
- 수유산모·신생아 심장 위협 ‘돔페리돈’, 산부인과서 8만건 처방 (‘16. 10.)
- [국감] 모유수유 신생아 돌연사 美 금지약물, 국내선 남용 (‘16. 10.)



## 특 성

- 등축에 함유된 아리스톨로크산(aristolochic acid): 신장장애 및 신장암 유발
  - 미국 FDA에서는 2001년부터 발암성분으로 규정
  - 우리나라에서도 2005년부터 유통과 사용 전면 금지된 약재
  - 모유 수유에 좋은 통초로 속여 파는 사례 급증
- 돔페리돈(domperidone): 오심, 구토 증상 완화에 사용하는 위장관운동촉진제
  - 투약 후 모유수유 시 산모와 신생아 급성심장사 가능성 높음
  - 부작용인 젖 분비 과다 증상을 이용해 모유 촉진제로 처방하는 경우가 급증

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Sulpiride 등 5종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10 ng/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Sulpiride, Metoclopramide hydrochloride, Domperidone, Chlorpromazine hydrochloride, Medroxyprogesterone acetate

#### ○ Analytical condition of HPLC

• Instrument	Shiseido SP3133		
• Column	Agilent Poroshell 120 SB-C <sub>18</sub> , (2.1 mm × 75 mm, 2.7 μm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 20mM Ammonium formate in Water (pH 5.4) (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90.0	10.0
	1.0	90.0	10.0
	6.0	5.0	95.0
	10.0	5.0	95.0
	10.1	90.0	10.0
	13.0	90.0	10.0
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 μL		

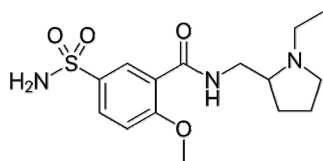
#### ○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (+)
• Curtain Gas	30 psi
• Collision Gas	8 psi
• Ion Voltage	5500 V
• Ion Source Gas 1	50 psi
• Ion Source Gas 2	50 psi
• Source Temp.	500°C

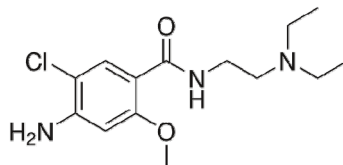
○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion ( $m/z$ )	CV (V)	Product ion ( $m/z$ )	CE (eV)	CXP (V)
Sulpiride	+	342.0	120	112.2	40	13
				84.1	40	20
Metoclopramide	+	300.1	120	227.1	2	13
				184.0	45	25
Domperidone	+	426.1	120	175.0	32	15
				147.0	45	20
Chlorpromazine	+	319.1	120	86.1	31	14
				58.2	55	14
Medroxyprogesterone acetate	+	387.0	120	327.2	21	14
				123.1	33	12

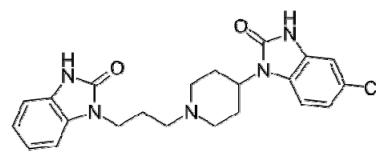
■ 구조식



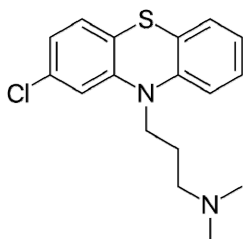
Sulpiride  
[C<sub>15</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub>S]



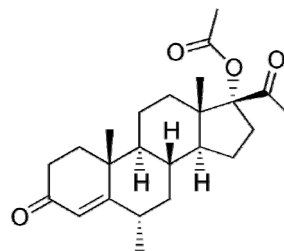
Metoclopramide  
[C<sub>14</sub>H<sub>22</sub>ClN<sub>3</sub>O<sub>2</sub>]



Domperidone  
[C<sub>22</sub>H<sub>24</sub>ClN<sub>5</sub>O<sub>2</sub>]



Chlorpromazine  
[C<sub>17</sub>H<sub>19</sub>ClN<sub>2</sub>S]



Medroxyprogesterone acetate  
[C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>]

## ■ 참고문헌

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2. Yan, M., Li, H.-D., Chen, B.-M., Liu, X.-L. & Zhu, Y.-G. Determination of metoclopramide in human plasma by LC-ESI-MS and its application to bioequivalence studies. *J Chromatogr B.* 878, 883-887 (2010)



## III-9 발모관련성분(13종) 분석법

### 배 경

- 식품에 사용할 수 없는 발모제 성분인 미녹시딜이 함유된 건강기능식품을 판매한 업자 적발 ('13. 9.)
- 국내에 허가되지 않은 탈모치료제를 불법 유통하였으며, 발모제 성분인 피나스테리드가 검출된 사례 적발.('15. 3.)
- 속눈썹감모증치료제인 전문의약품 '라티쎬'가 인터넷 불법판매 및 유통 ('16. 7.)
- 탈모치료제 프로페시아, 우울증 자살생각 '경고' ('17. 7.)



### 특 성

- 대표적인 발모제는 미녹시딜, 피나스테리드로서 FDA에 승인받은 의약품임
- 미녹시딜은 모낭혈관을 확장시켜 혈액흐름을 원활하게 하는 발모제 성분으로 과량 사용 시 부종, 부정맥, 가려움 등 부작용을 나타냄
- 속눈썹 감모증 치료제인 '라티쎬'는 녹내장치료제 성분인 비마토프로스트의 부작용으로 만든 전문의약품으로서 FDA에 승인받음

### 분석 사례

- 모리아 알지-III(베타카로틴): Minoxidil 2.47mg/캡슐 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

- 표준액 조제 : Triaminodil 등 13종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 5~100 µg/mL)
- 검액 조제 : 약 1g 취함 → 100% 메탄올 가함 → 30분 진탕 → 50 mL 정용  
→ 원심분리(3,000 rpm, 10분) → 상층액을 검액으로 함

\* 표준액 : Triaminodil, Minoxidil, Bimatoprost, Alimemazine tartrate, Diphenylcyclopropenone, Alfatradiol, Finasteride, Methyltestosterone, Spironolactone, Flutamide, Cyproterone acetate, Dutasteride, Testosterone 17-propionate

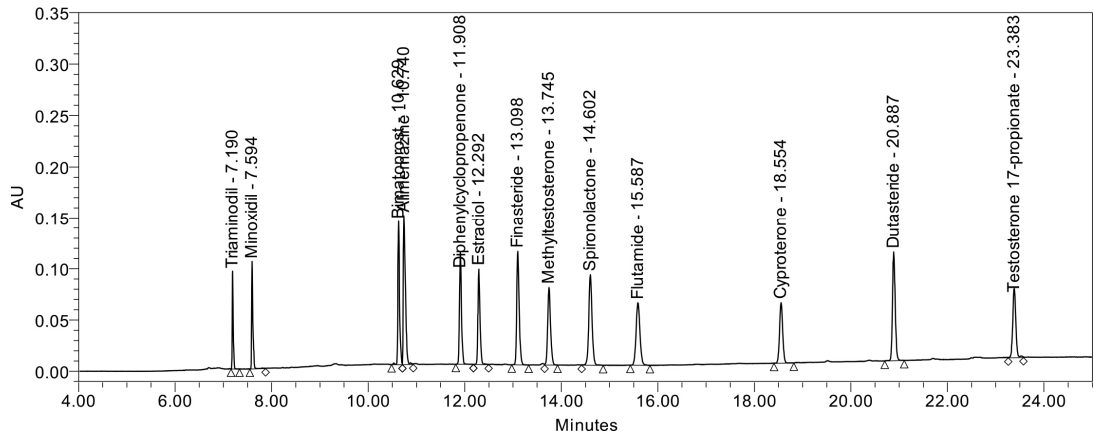
#### ○ Analytical condition of HPLC

- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC HSS T3 (2.1 mm × 150 mm, 1.8 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.5 mM Sodium-1-hexane sulfonate in Water (0.1% H<sub>3</sub>PO<sub>4</sub>)  
(B) 90% Acetonitrile

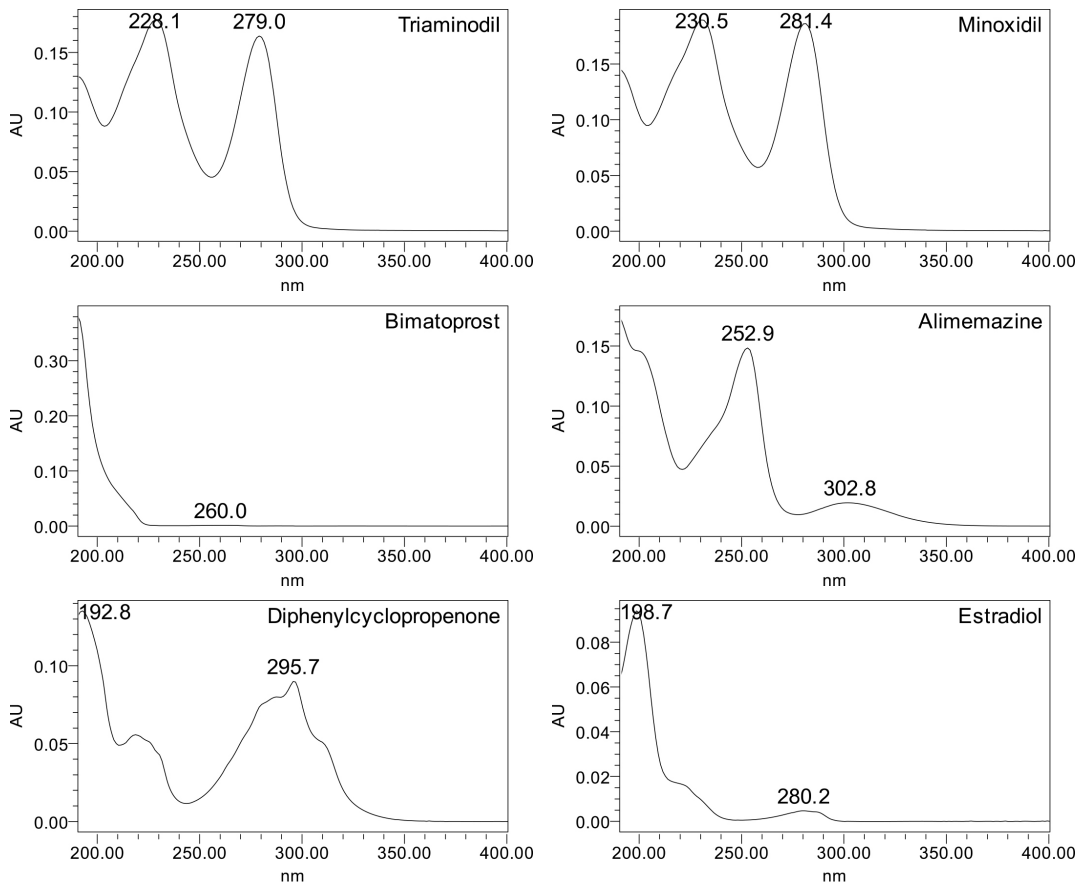
Time (min)	A (%)	B (%)
0.0	95	5
3.0	95	5
5.0	70	30
10.0	42	58
14.0	42	58
22.0	10	90
24.0	10	90
24.1	95	5
26.0	95	5

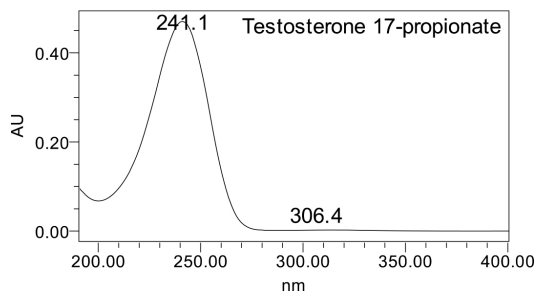
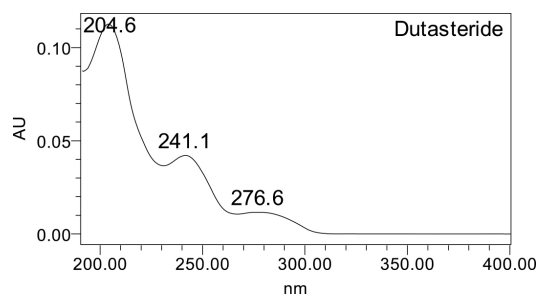
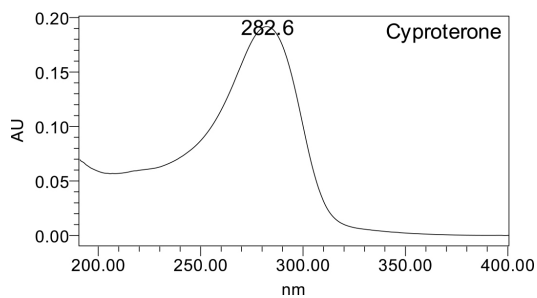
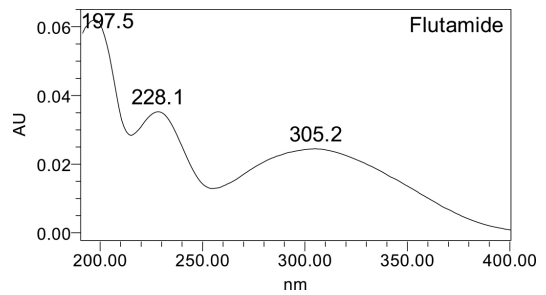
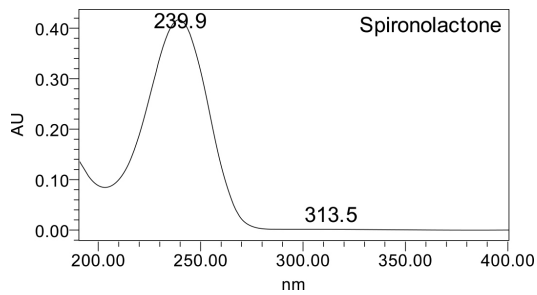
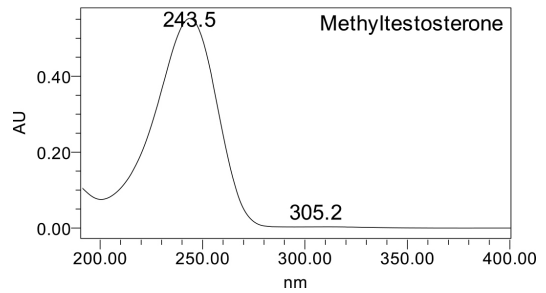
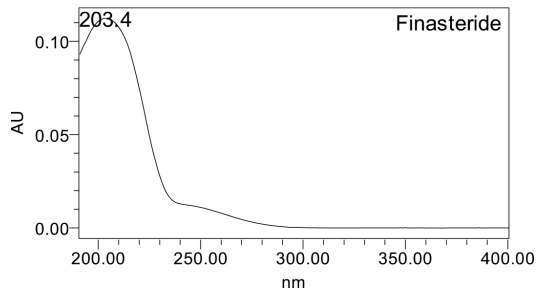
- Flow Rate 0.30 mL/min
- Inj. Volume 1 µL
- UV Detection 200 nm
- PDA Range 190~400 nm

○ Chromatogram



○ PDA Spectrum





## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC																								
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)																								
• Column Temp.	30℃																								
	(A) 1 mM Ammonium acetate in Water (B) 100% Acetonitrile																								
• Mobile Phase	· Alimemazine의 경우 (A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile																								
	<table border="1"> <thead> <tr> <th>Time (min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0.0</td> <td>90</td> <td>10</td> </tr> <tr> <td>1.0</td> <td>90</td> <td>10</td> </tr> <tr> <td>3.0</td> <td>50</td> <td>50</td> </tr> <tr> <td>8.0</td> <td>10</td> <td>90</td> </tr> <tr> <td>10.0</td> <td>10</td> <td>90</td> </tr> <tr> <td>10.1</td> <td>90</td> <td>10</td> </tr> <tr> <td>12.0</td> <td>90</td> <td>10</td> </tr> </tbody> </table>	Time (min)	A (%)	B (%)	0.0	90	10	1.0	90	10	3.0	50	50	8.0	10	90	10.0	10	90	10.1	90	10	12.0	90	10
Time (min)	A (%)	B (%)																							
0.0	90	10																							
1.0	90	10																							
3.0	50	50																							
8.0	10	90																							
10.0	10	90																							
10.1	90	10																							
12.0	90	10																							
• Flow Rate	0.3 mL/min																								
• Inj. Volume	1 μL																								

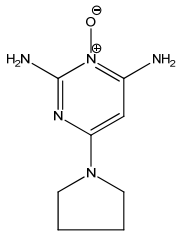
### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+),(-)
• Capillary Voltage	2.5 kV
• Desolvation Temp.	400℃
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	off

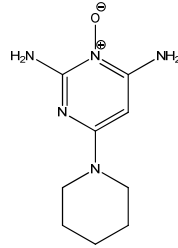
○ Analyte LC-MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Triaminodil	+	196.20	25	137.15	20
				151.15	20
				179.20	15
Minoxidil	+	210.20	10	110.10	25
				164.20	25
				193.20	15
Biamtoprost	+	398.39	20	317.28	15
				362.25	10
				100.00	20
Alimemazine tartrate	+	299.08	30	179.95	40
				211.90	25
				77.05	35
Diphenylcyclopropenone	+	207.18	35	152.13	35
				178.20	25
				144.95	35
Alfatradiol	-	271.10	40	182.97	40
				305.35	30
Finasteride	+	373.35	35	317.30	25
				97.10	25
Methyltestosterone	+	303.30	30	109.10	25
				107.15	25
Spironolactone	+	341.13	50	187.20	20
				174.95	30
Flutamide	-	274.85	40	181.95	30
				201.97	25
				165.13	50
Cyproterone acetate	+	417.28	35	279.30	25
				357.30	15
Dutasteride	+	529.30	45	133.20	45
				461.32	35
Testosterone 17-propionate	+	345.30	30	97.10	20
				109.10	25
				253.30	15

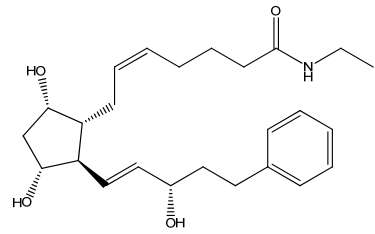
■ 구조식



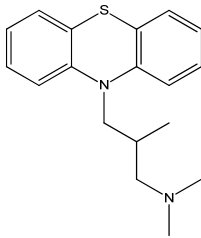
Triaminodil  
[C<sub>8</sub>H<sub>13</sub>N<sub>5</sub>O]



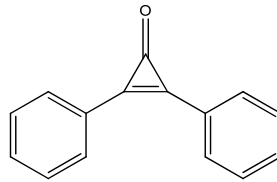
Minoxidil  
[C<sub>9</sub>H<sub>15</sub>N<sub>5</sub>O]



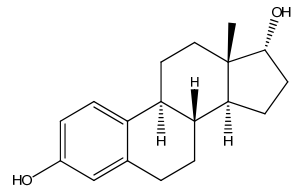
Bimatoprost  
[C<sub>28</sub>H<sub>37</sub>NO<sub>4</sub>]



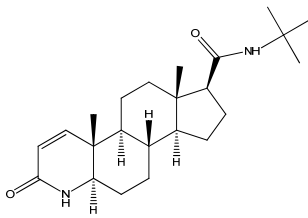
Alimemazine  
[C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>S]



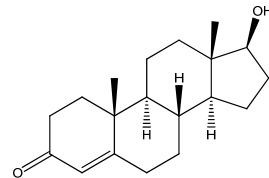
Diphenylcyclopropenone  
[C<sub>15</sub>H<sub>10</sub>O]



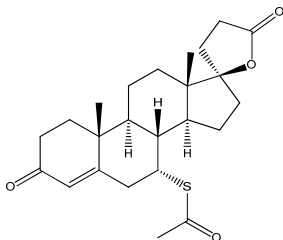
Alfatradiol  
[C<sub>18</sub>H<sub>24</sub>O<sub>2</sub>]



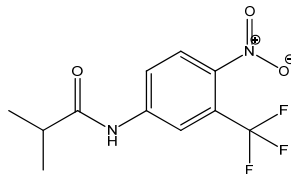
Finasteride  
[C<sub>23</sub>H<sub>36</sub>N<sub>2</sub>O<sub>2</sub>]



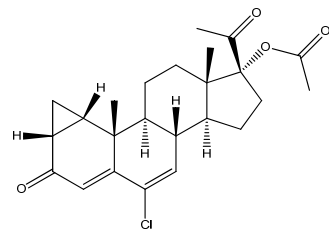
Methyltestosterone  
[C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>]



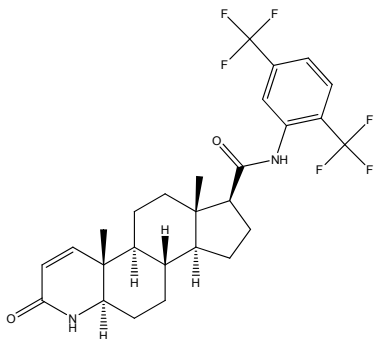
Spironolactone  
[C<sub>24</sub>H<sub>32</sub>O<sub>4</sub>S]



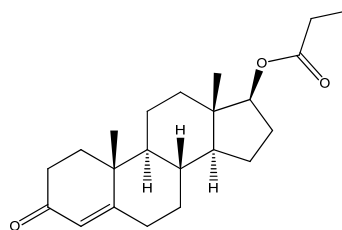
Flutamide  
[C<sub>11</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>O<sub>3</sub>]



Cyproterone  
[C<sub>24</sub>H<sub>28</sub>ClO<sub>4</sub>]



Dutasteride  
[C<sub>27</sub>H<sub>30</sub>F<sub>6</sub>N<sub>2</sub>O<sub>2</sub>]



Testosterone 17-propionate  
[C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>]

## ■ 참고문헌

1. Gavin Gibson, Tore Ramstad, Kent A Mills, Michael J Dunn, A method for the determination of minoxidil in hair-regrowth formulations by micellar electrokinetic capillary chromatography, *Il Farmaco*, 10, 847 - 853(2005)
2. Nivedita Patel and Dhananjay Meshram, Development and Validation of Analytical Method for Simultaneous Determination of Minoxidil and Finasteride in Pharmaceutical Dosage Form by RP-HPLC Method, *IJPSR*, 6(11),4882-4885(2015)



## III-10 <복어독(테트로도톡신) 분석법

### ■ 배 경

- 14알 먹으면 사망 ‘복어독 환’ 불법 제조 암 환자에 판매('17. 4.)
- 복어독 불법 의약품이 ‘암 특효약’으로 둔갑('17. 4.)



### ■ 특 성

- 복에 함유되어 있는 맹독(tetrodotoxin)으로 물에 잘 녹지 않고 동시에 내열성이므로 보통의 조리 조건으로는 무독화 되지 않으며 존재 여부를 관능적으로 감지할 수 없음
- 흡수된 tetrodotoxin은 신경근 접합부에 작용, 신경의 흥분에 동반하는 Na<sup>+</sup>의 세포 내로의 유입을 선택적으로 억제하는 특이한 작용을 나타내어 자율운동신경의 흥분전도를 차단하게 되어 강한 독성을 나타냄
- 중독증상(제1도)은 섭취 후 2~3 시간 내에 먼저 입술, 혀끝, 손끝이 저리고 두통, 복통, 구토가 계속되며 이어서 불완전 운동마비의(제2도) 상태가 되어 지각마비, 언어장애, 혈압이 떨어진 후 완전 운동마비의(제3도) 운동 불능의 상태인 호흡곤란(cyanosis)이 나타나고 전신마비를 보이며 의식소실(제4도)의 단계로 진행되어 의식을 잃고, 호흡과 심장박동이 정지됨

### ■ 분석사례

- 복어환 : 테트로도톡신 0.531mg/g 검출

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Tetrodotoxin  
→ 일정량 취함 → 0.1% acetic acid 가함 → 최종 농도(약 10 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

#### ○ Analytical conditions of UPLC

- Instruments Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC Hilic (2.1 mm × 100 mm, 1.7 µm)
- Column Temp. 35°C
- Mobile Phase (A) 0.1% Acetic acid in Water  
(B) 100% Acetonitrile

Time (min)	A (%)	B (%)
0.0	90	10
3.0	50	50
4.0	50	50
4.1	90	10
6.0	90	10

- Flow Rate 0.4 mL/min
- Inj. Volume 2 µL

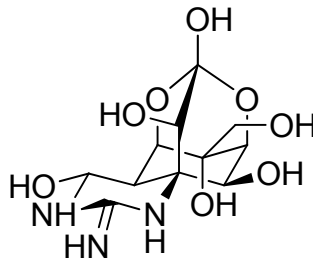
#### ○ Analytical conditions of LC-MS/MS

- Instrument Waters Xevo TQ
- Ionization Mode ESI (+)
- Capillary Voltage 3.5 kV
- Desolvation Temp. 350°C
- Desolvation Gas Flow 600 L/Hr (N<sub>2</sub>)
- Cone Gas Flow 50 L/Hr (N<sub>2</sub>)

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Tetrodotoxin	+	320.1	45	302.1	37
				284.2	29
				162.0	25

■ 구조식



Tetrodotoxin  
[C<sub>11</sub>H<sub>17</sub>N<sub>3</sub>O<sub>8</sub>]

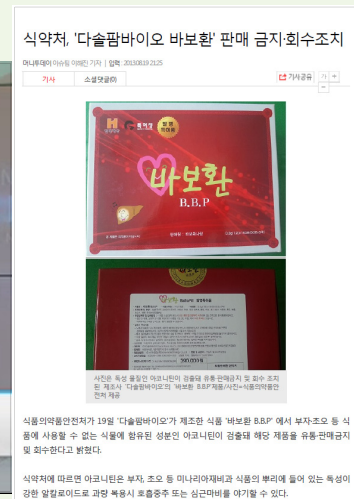
■ 참고문헌

1. Hong-Nan, Huang Jie Lina, Hong-Lin Lina, Identification and quantification of tetrodotoxin in the marine gastropod Nassarius by LC - MS, *Toxicol.* 51(5), 774-779 (2008)

### III-11 < 부자성분 분석법

#### ■ 배경

- 부자·초오 등 식품에 사용할 수 없는 식물에 함유된 성분인 아코니틴이 검출되어 해당 제품을 유통·판매금지 및 회수('13. 8.)
- 식품에 금지된 아코니틴을 포함한 식품을 만병통치약으로 속여 판매된 제품 적발('14. 6.)



#### ■ 특성

- 아코니틴: 부자, 초오 등 미나리아재비과 식품의 뿌리에 들어 있는 알칼로이드
- 부작용: 독성이 강하여 과량 복용 시 호흡중추 또는 심근마비를 야기할 수 있음

#### ■ 분석사례

- 바보환 B.B.P: Aconitine 검출
- 인삼성분함유미삼정: Aconitine 검출

■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 표준액 조제 : Aconitine 등 3종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 1.0 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Aconitine, Mesaconitine, Hypaconitine

○ Analytical condition of HPLC

- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC BEH C<sub>18</sub> (2.1 mm × 100 mm, 1.7 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1% Formic acid in Water  
(B) 100% Methanol

Time (min)	A (%)	B (%)
0.0	60	40
1.0	60	40
5.0	35	65
5.5	35	65
6.0	10	90
7.0	10	90
7.1	60	40
10.0	60	40

- Flow Rate 0.25 mL/min
- Inj. Volume 2 µL

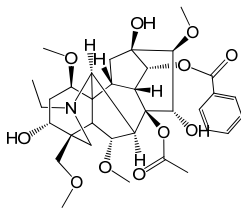
○ Analytical conditions of LC-MS/MS

- Instrument Waters Xevo TQ
- Ionization Mode ESI (+)
- Capillary Voltage 2.5 kV
- Desolvation Temp. 150°C
- Desolvation Gas Flow 550 L/Hr (N<sub>2</sub>)
- Cone Gas Flow off

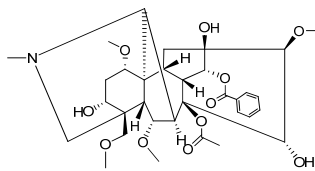
○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Aconitine	+	646.56	35	526.51	40
				586.50	35
Mesaconitine	+	632.54	52	354.27	42
				572.49	38
				338.27	42
Hypaconitine	+	616.54	52	524.45	36
				556.50	34

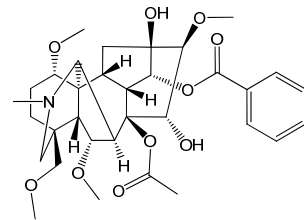
■ 구조식



Aconitine  
[C<sub>34</sub>H<sub>47</sub>NO<sub>11</sub>]



Mesaconitine  
[C<sub>33</sub>H<sub>45</sub>NO<sub>11</sub>]



Hypaconitine  
[C<sub>33</sub>H<sub>45</sub>NO<sub>10</sub>]

■ 참고문헌

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## Ⅲ-12 비만치료주사제(PPC, 5종) 분석법

### ■ 배 경

- 일반화장품으로 수입·제조된 PPC 제품을 살빼는 의약품 주사제로 둔갑시켜 무허가로 불법 판매함('10. 3.)
  - ※ PPC 주사제는 세포막의 구성성분으로 다수의 비만클리닉 등에서 피하지방에 직접 주사하는 '지방분해주사'로 사용



### ■ 특 성

- PPC 주사제의 지방분해 주사로 사용하는 기전은 '직접적인 독성 또는 계면활성 효과에 의한 피하지방의 감소'인 것으로 추정되나 이러한 요법은 식약처에서 허가한 효능·요법은 아니며 특히 의약품주사제로 허가 받지 않은 일반화장품을 인체에 직접 주사 할 경우 무균, 불용성 이물 시험검사를 실시하지 않아 끊거나 피부괴사 등 부작용이 나타날 수 있음

### ■ 분석사례

- PPC Impact Sliming Cream : Phosphatidylcholine 7.80 mg/g 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

- 표준액 조제 : Phosphatidylinositol 등 5종  
 → 각각 일정량 취함  
 → IPA:아세톤(50:50) 가함(Phosphatidylinositol에는 물 소량첨가)  
 → 최종 농도(약 20~160  $\mu\text{g}/\text{mL}$ )
- 검액 조제 : 약 1 g 취함 → IPA:아세톤(50:50) 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Phosphatidylinositol, Phosphatidylethanolamine, Phosphatidylserine, Phosphatidylcholine, Sphingomyelin

#### ○ Analytical conditions of HPLC

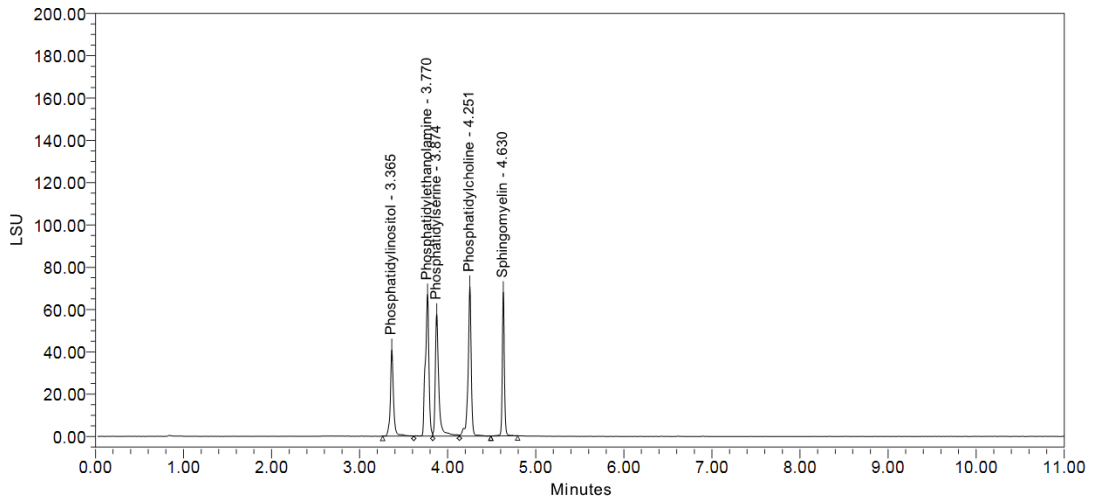
- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC BEH HILIC (2.1 mm × 100 mm, 1.7  $\mu\text{m}$ )
- Column Temp. 50°C
- Mobile Phase (A) 50% Acetonitrile (1.5% Acetic acid, 0.08% Triethylamine)  
(B) Acetonitrile:Acetone (9:1) (1.5% Acetic acid, 0.08% Triethylamine)

Time (min)	A (%)	B (%)
0.0	5	95
2.0	5	95
3.5	35	65
6.5	50	50
6.6	5	95
10.0	5	95

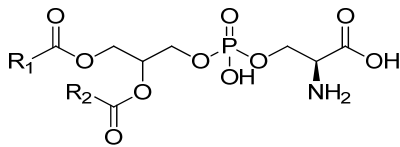
- Flow Rate 0.3 mL/min
- Inj. Volume 5  $\mu\text{L}$
- Detector ELSD (Gain: 100, Gas ( $\text{N}_2$ ): 50 psi, Drift tube: 55°C)



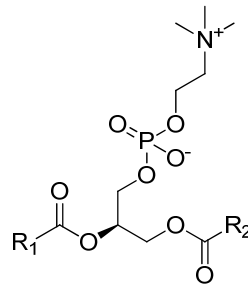
○ Chromatogram



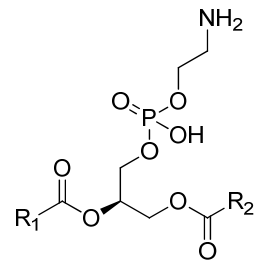
■ 구조식



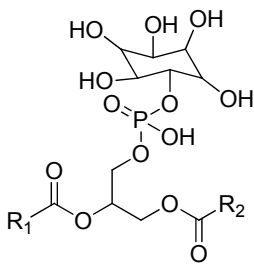
Phosphatidylserine  
[C<sub>13</sub>H<sub>24</sub>NO<sub>10</sub>P]



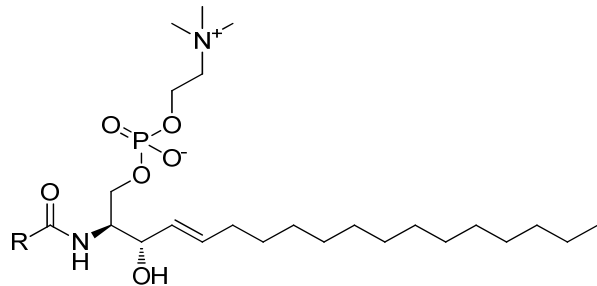
Phosphatidylcholine  
[C<sub>42</sub>H<sub>82</sub>NO<sub>8</sub>P]



Phosphatidylethanolamine  
[C<sub>40</sub>H<sub>80</sub>NO<sub>8</sub>P]



Phosphatidylinositol  
[C<sub>47</sub>H<sub>83</sub>O<sub>13</sub>P]



Sphingomyelin  
[C<sub>41</sub>H<sub>84</sub>N<sub>2</sub>O<sub>6</sub>P]

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2. Mark E. Benvenuti, Jennifer A. Burgess Monitoring Sugar Content of Fruit Juice Using ACQUITY UPLC H-Class and BEH Amide Column Chemistry with Evaporative Light Scattering Detection (ELSD). *Waters Application Note, 720004404en.* (2014)
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# III-13 식물스테롤(4종) 분석법

## 배 경

- 피자에 모조·가공 치즈를 사용하고 '100% 자연산 치즈'라 피자박스나 전단지 등에 표시해 판매한 프랜차이즈 업체 9곳과 치즈 제조업체 3곳 적발
- 100% 자연산 치즈만을 사용했다고 광고 전단지 등에 표시했으나 테두리 속 치즈에 가공 치즈를 사용함

**SBS 뉴스**  
 뉴스 프로그램 기자스페셜 이슈 + 취재파일 5858 뉴스 생방송

**경향신문**  
 The Kyungyang Shinmun

**100% 자연산이라더니... '식용유 치즈' 적발**  
 신승이 기자 | 2012.02.16 19:31 | 수정 : 2012.02.16 21:58

신승이 기자입니다.

자연을 100% 이렇게 적힌 피자 광고 많이 보셨죠. 식약청 조사결과, 이렇게 알한 업체들 가운데 일부가 물과 식용유로 만든 모조 치즈를 사용한 것으로 드러났습니다.

자연을 100% 사용하고 실제로는 모조 가공 치즈를 써온 유명 피자업체들이 무더기로 적발됐다. 식용유와 물만 섞은 16일 '모조 치즈와 가공 치즈를 사용하면서 100% 자연산 치즈만 사용한 것처럼 표시해 판매한 유명 피자 프랜차이즈 업체 12곳을 적발했다'고 밝혔다. 식약청은 치즈 원재료명을 허위로 표시한 9곳과 **식품위생법**을 위반한 3곳을 검찰에 고발했다.

자연산 치즈는 주원료인 우유를 톱고 발효해 만든다. 그러나 가공 치즈는 자연산 치즈에 **식품첨가물**을 넣는다. 두 가지 이상 첨가물이 섞이기 때문에 품질은 당연히 떨어질 수밖에 없다. 모조 치즈는 아예 우유를 사용하지 않는다. 식용유 등에 첨가물을 더해 치즈와 비슷한 색 모양만 흉내 낸 것이다.

적발된 피자업체인 **피자스쿨 69점자**, 피자머루, 난타5000, 피자가가락해, 슈퍼지아엔트피자 등 6곳은 피자 도우(빵)에 견본, 식용유, 산도 조절제 등을 첨가한 가공 치즈를 사용했다. 그러나 광고 **천연**이나 포장용 상자에는 자연산 치즈만 사용한다고 허위 광고를 했다. 피자스쿨 측은 '이런에 문제가 된 것은 치즈크러스트 피자에서 빵의 테두리 부분에 들어가는 치즈인데 '위에 얹는 토핑용 치즈는 100% 자연산만 사용하고 있다고 밝혔다.

수타올밀치즈피자와 치즈마늘밀치즈피자, 밀실치즈&79피자 등 업체 3곳은 피자의 토핑용 치즈에 모조 치즈를 섞어 먹었다. 그러나 **가방정 카푸카** 포장용 상자에는 자연산 치즈만 사용한다고 적어 놓았다.

## 특 성

- 식물스테롤은 식물성 기름, 곡류, 채소류 등에 널리 존재하고 있는 천연물질로 정제되지 않은 식물성 유지 내에 다량 함유
- 식물스테롤은 자연적으로 200여 종이나 되는 식물군에 존재하고 있고 그 양은 대략 0.3~0.8% 수준임

## ■ 분석법

### 1. GC-MS법

#### ○ 전처리 방법

• 표준액 조제 : Brassicasterol 등 4종\*

- 각각 일정량 취함 → 100% 에탄올 가함
- 유도체화 → 내부표준용액(50  $\mu\text{g}/\text{mL}$ ) 50  $\mu\text{L}$  가함 → 진탕
- 질소농축(60 $^{\circ}\text{C}$ , 약 1.5 hr) → 300  $\mu\text{L}$  정도 시료 남음
- BSFTA(1% TMCS 함유) 500  $\mu\text{L}$  가함 → 진탕
- 반응(60 $^{\circ}\text{C}$ , 30 min) → 5 min 상온 방치 → 진탕
- 최종 농도(약 5  $\mu\text{g}/\text{mL}$ )

• 검액 조제 : 균질화

- 약 25 g 취함
- Folch(클로로포름:메탄올=2:1) 25 mL 가함
- 균질화 30분 → 원심분리(4,000 rpm, 25 min, -4 $^{\circ}\text{C}$ )
- 상층액 취함 → 감압농축(45 $^{\circ}\text{C}$ , 180 rpm)
- 검화
- 100% 에탄올 40 mL 가함
- 내부표준용액(50  $\mu\text{g}/\text{mL}$ ) 50  $\mu\text{L}$  가함
- 0.1N 수산화칼륨(에탄올성) 10 mL 가함
- 환류추출(95 $^{\circ}\text{C}$ , 1 hr)
- 100% 에탄올 40 mL 가함 → 냉각관을 wash함
- 추출
- 분액여두로 옮김 → 포화 나트륨 용액 25 mL
- Hexane 50 mL 가함, 3회 반복 추출
- 무수황산나트륨과 filter paper 이용하여 여과
- 감압농축(45 $^{\circ}\text{C}$ , 180 rpm)
- 100% 에탄올 3.0 mL 가함, 용해(1 mL씩 3회) → 여과
- 유도체화
- 질소농축(60 $^{\circ}\text{C}$ , 약 1.5 hr)
- BSFTA(1% TMCS 함유) 50-500  $\mu\text{L}$  가함 → 진탕
- 반응(60 $^{\circ}\text{C}$ , 30 min) → 5 min 상온 방치 → 진탕
- 검액

\* 표준액 : Brassicasterol, Campesterol, Stigmasterol,  $\beta$ -sitosterol,

\*\* 내부표준용액 : 5 $\alpha$ -cholestane

○ Analytical conditions of GC

• Instrument	Agilent 7890A
• Column	Agilent HP 5MS (30 mm × 0.25 mm, 0.25 μm)
• Oven Temp.	200°C (1 min) → 10°C/min → 280°C (11 min) → 4°C/min → 300°C (5 min)
• Inj. Temp.	300°C
• Inj. Mode	Split 10:1
• Carrier Gas Flow	He, 1 mL/min
• Inj. Volume	1 μL
• FID Detector Temp.	300°C

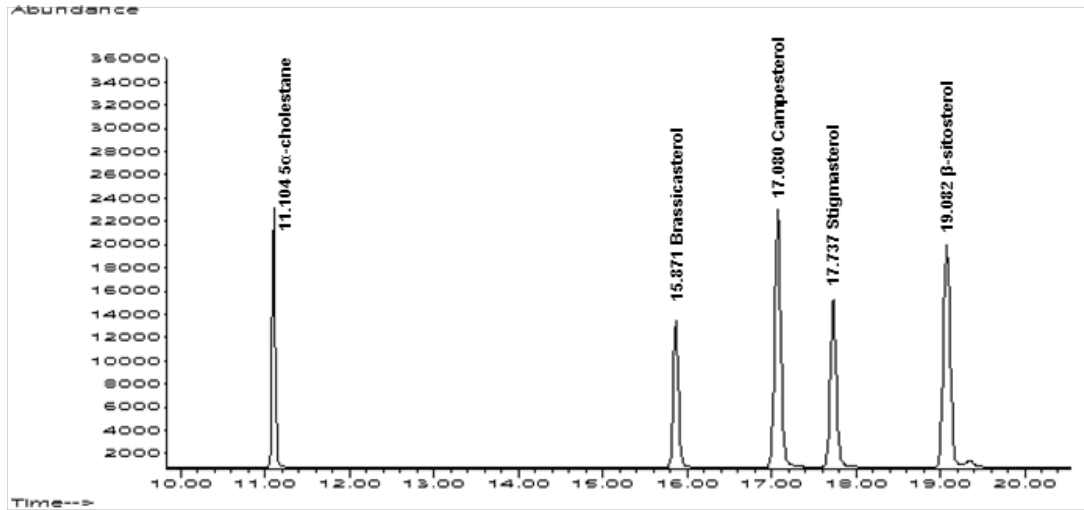
○ Analytical condition of GC/MS: SIM

• Instrument	Agilent GC/MSD 5975C
• Ionization Mode	EI
• Ionization Energy	70 eV
• Source Temp.	230°C
• Quad Temp.	150°C
• Mass Mode	SIM
• Scan Range	50~500 amu
• SIM Dwell Time	50 ms

- SIM ions

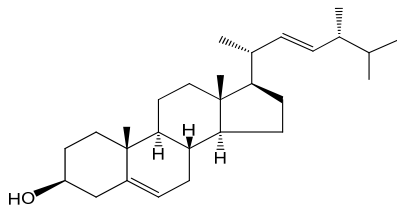
Compound	Precursor Ion ( <i>m/z</i> )	Product Ion ( <i>m/z</i> )	
Brassicasterol	255	380	470
Campesterol	382	367	472
Stigmasterol	255	394	484
β-Sitosterol	396	381	486
5α-Cholestane (I.S)	217	357	372

### ○ Chromatogram

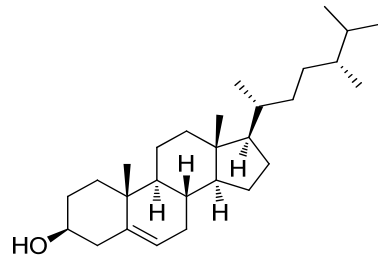


\* Internal standard : 5 $\alpha$ -cholestane

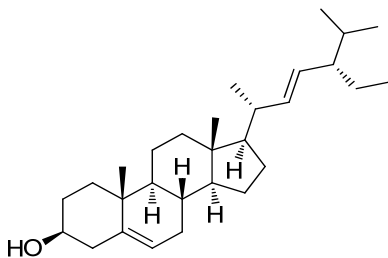
### ■ 구조식



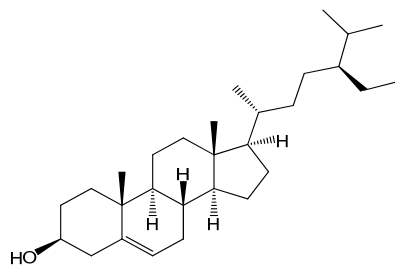
Brassicasterol  
[C<sub>28</sub>H<sub>46</sub>O]



Campesterol  
[C<sub>28</sub>H<sub>48</sub>O]



Stigmasterol  
[C<sub>29</sub>H<sub>48</sub>O]



$\beta$ -sitosterol  
[C<sub>29</sub>H<sub>50</sub>O]

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### III-14 스테로이드류(53종) 분석법

#### ■ 배 경

- 스테로이드 성분을 첨가하여 인터넷을 통해 관절염, 신경통 등 각종 통증에 특효제인 것처럼 허위·과대 광고하여 판매한 판매업자 적발 ('13. 4.)
- 국내 유통이 금지된 헬스 보조제에서 스테로이드 성분 검출 ('16. 5)



#### ■ 특 성

- 스테로이드
  - 스테로이드 핵인 cyclopentanoperhydrophenanthrene을 갖는 화합물군의 총칭
  - 지금까지 개발된 물질 중 가장 강력한 항염증제로 류마티스성 관절염, 천식, 루푸스, 장기이식후의 부작용 억제 등 여러 가지 질병치료제로 쓰임
  - 장기 복용할 경우 부신에서 호르몬 생산 억제, 소화성궤양 등 소화기계 이상, 심근경색 등 부작용이 나타날 수 있음

#### ■ 분석 사례

- 관절제품: Dexamethasone 21-acetate 42.88  $\mu\text{g/g}$  검출  
Dexamethasone 1.99  $\mu\text{g/g}$  검출



■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 표준액 조제 : Prednisolone 등 53종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 1 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Prednisolone, Hydrocortisone, Betamethasone, Dexamethasone, Prednisone 21-acetate, Cortisone 21-acetate, Prednisolone-21-acetate, Hydrocortisone 21-acetate, Hydrocortisone 17-acetate, Beclomethasone, Budesonide, Betamethasone 21-acetate, Dexamethasone 21-acetate, Triamcinolone acetonide, 6a-Methylprednisolone, Hydrocortisone 17-valerate, Hydrocortisone 21-valerate, Beclomethasone 21-acetate, Beclomethasone-21-propionate, Beclomethasone 17-valerate, Clobetasol 17-propionate, Betamethasone 17-valerate, Betamethasone 21-valerate, Triamcinolone diacetate, Dexamethasone 21-hemisuccinate, Betamethasone 21-hemisuccinate, Betamethasone 17,21-dipropionate, Beclomethasone 21-hemisuccinate, Beclomethasone 17,21-dipropionate, Medroxyprogesterone 17-acetate, Norethisterone acetate, Testosterone, Testosterone 17-propionate, Testosterone 17-valerate, Megesterol acetate, 11α-OH-progesterone-hemisuccinate, 6a-Methylprednisolone aceponate, D(-)-norgestrel, Fluticasone furoate, Norethisterone, Prednisone, Stanozolol C-3, Clobetasone butyrate, Dichlorisone diacetate, Diflorasone acetate, Flucinolone acetonide, Flurandrenolide, Hydrocortisone butyrate, Hydrocortisone 21-hemisuccinate, Mometasone furoate, Amcinonide, Fludrocortisone acetate, Fluticasone propionate

○ Analytical conditions of HPLC

- Instrument UPLC Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC BEH C<sub>18</sub> (2.1 mm × 100 mm, 1.8 µm)
- Column Temp. 35°C
- Mobile Phase A: 0.1% Formic acid in Water  
B: 0.1% Formic acid in Acetonitrile

Time (min)	A (%)	B (%)
0.0	80	20
3.0	80	20
13.0	40	60
17.0	0	100
22.0	0	100
22.1	80	20
25.0	80	20

- Flow Rate 0.25 mL/min
- Inj. Volume 2 µL

○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	2.7 kV
• Desolvation Temp.	500 °C
• Desolvation Gas Flow	400 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	60 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion mode	Precursor ion (m/z)	CV (v)	Product Ion (m/z)	CE (eV)
Testosterone	+	289.43	30	96.80	20
				108.84	20
				253.05	20
Norethisterone	+	299.43	30	108.85	20
				170.95	20
				231.05	20
D(-)-norgestrel	+	313.45	30	108.85	20
				144.90	20
				245.05	20
Stanozolol C-III	+	329.50	40	106.85	35
				108.85	35
				120.90	35
Norethisterone acetate	+	341.44	30	90.83	40
				108.85	25
				281.08	15
Testosterone 17-propionate	+	345.48	30	96.83	20
				108.85	25
				253.05	20
Prednisone	+	359.40	20	146.90	20
				170.92	25
				265.03	15
Prednisolone	+	361.44	15	307.07	10
				325.09	10
				343.09	10

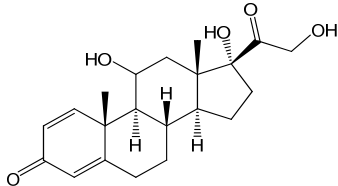
Compound	Ion mode	Precursor ion ( $m/z$ )	CV (v)	Product Ion ( $m/z$ )	CE (eV)
Hydrocortisone	+	363.45	25	120.85	25
				309.07	15
				327.07	15
Testosterone 17-valerate	+	373.50	25	108.85	25
				253.08	20
				271.08	15
6 $\alpha$ -methylprednisolone	+	375.46	15	321.10	13
				339.10	10
				357.10	10
Megesterol acetate	+	385.50	25	224.02	25
				267.05	20
				325.12	15
Medroxyprogesterone 17-acetate	+	387.50	25	122.85	25
				285.10	15
				327.10	15
Betamethasone	+	393.46	20	279.05	20
				355.10	10
				373.08	10
Dexamethasone	+	393.20	15	237.00	15
				355.11	10
				373.12	10
Prednisone 21-acetate	+	401.45	18	313.05	15
				341.05	10
				383.06	10
Prednisolone 21-acetate	+	403.48	15	307.04	15
				325.10	10
				385.10	10
Cortisone 21-acetate	+	403.48	30	162.90	25
				325.10	20
				343.10	20
Hydrocortisone 21-acetate	+	405.50	25	241.00	20
				309.10	15
				327.05	15

Compound	Ion mode	Precursor ion ( $m/z$ )	CV (v)	Product Ion ( $m/z$ )	CE (eV)
Hydrocortisone 17-acetate	+	405.50	25	309.10	15
				327.05	15
				345.10	15
Beclomethasone	+	409.43	20	279.05	20
				373.10	10
				391.05	10
Fludrocortisone acetate	+	423.46	25	239.00	25
				325.10	20
				343.05	20
Budesonide	+	431.50	20	323.05	16
				395.10	10
				413.10	10
11 $\alpha$ -OH-progesterone-hemisuccinate	+	431.50	20	253.05	20
				295.09	20
				313.13	10
Hydrocortisone 17-butyrate	+	433.50	25	309.05	20
				327.10	15
				345.10	15
Betamethasone 21-acetate	+	435.45	15	237.00	20
				279.10	15
				397.10	10
Dexamethasone 21-acetate	+	435.45	15	237.00	20
				309.05	15
				397.10	10
Triamcinolone acetonide	+	435.45	20	339.10	15
				397.10	15
				415.10	15
Flurandrenolide	+	437.50	30	225.00	25
				341.10	20
				361.10	20
Hydrocortisone 21-valerate	+	447.50	25	309.10	20
				327.10	20
				345.10	20

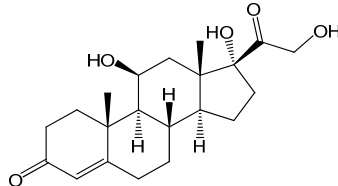
Compound	Ion mode	Precursor ion ( $m/z$ )	CV (v)	Product Ion ( $m/z$ )	CE (eV)
Hydrocortisone 17-valerate	+	447.50	25	120.85	25
				309.10	20
				345.10	15
Beclomethasone 21-acetate	+	451.45	20	319.05	15
				397.10	10
				433.10	10
Fluocinolone acetonide	+	453.45	20	337.05	15
				413.10	10
				433.10	10
Dichlorisone acetate	+	455.09	15	237.00	20
				305.05	15
				419.05	10
Hydrocortisone 21-hemisuccinate	+	463.50	25	309.05	15
				327.05	15
				445.10	10
Beclomethasone 21-propionate	+	465.45	15	319.05	20
				411.10	10
				447.10	10
Beclomethasone 17-propionate	+	465.45	15	337.10	15
				355.10	10
				447.10	10
Clobetasol 17-propionate	+	467.45	15	355.10	15
				373.05	10
				447.10	10
6a-Methylprednisolone aceponate	+	473.52	15	303.10	15
				381.10	10
				455.10	10
Betamethasone 21-valerate	+	477.52	15	279.07	15
				355.10	10
				457.15	10
Betamethasone 17-valerate	+	477.52	15	279.07	15
				355.10	10
				457.15	10

Compound	Ion mode	Precursor ion ( $m/z$ )	CV (v)	Product Ion ( $m/z$ )	CE (eV)
Clobetasone butyrate	+	479.45	25	279.07	15
				343.10	15
				371.05	15
Triamcinolone diacetate	+	479.45	15	399.10	15
				441.10	10
				459.10	10
Dexamethasone 21-hemisuccinate	+	493.50	15	319.05	15
				337.05	15
				455.10	10
Betamethasone 21-hemisuccinate	+	493.50	15	319.05	15
				455.10	10
				475.15	10
Diflorasone diacetate	+	495.50	20	279.05	15
				317.05	15
				335.05	15
Fluticasone propionate	+	501.45	15	275.05	25
				293.05	15
				313.05	15
Amcinonide	+	503.52	15	339.05	15
				399.10	10
				483.15	10
Betamethasone 17,21-dipropionate	+	505.54	15	355.10	15
				411.15	10
				485.15	10
Beclomethasone 21-hemisuccinate	+	509.45	15	319.10	15
				437.10	10
				491.10	10
Mometasone furoate	+	521.42	15	279.10	20
				355.05	15
				503.05	10
Beclomethasone 17,21-dipropionate	+	521.42	15	319.10	15
				429.10	10
				503.15	10
Fluticasone furoate	+	539.45	15	204.90	20
				265.00	20
				275.00	20

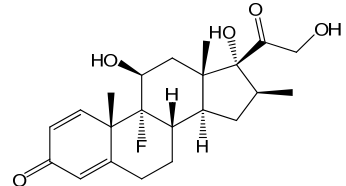
■ 구조식



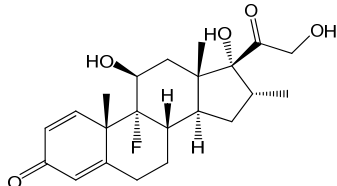
Prednisolone  
[C<sub>21</sub>H<sub>28</sub>O<sub>5</sub>]



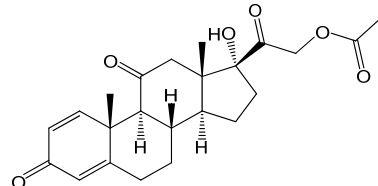
Hydrocortisone  
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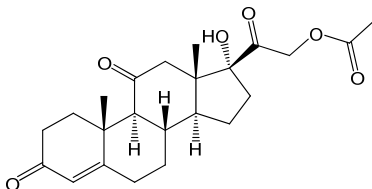
Betamethasone  
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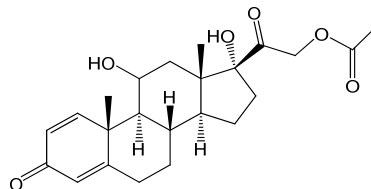
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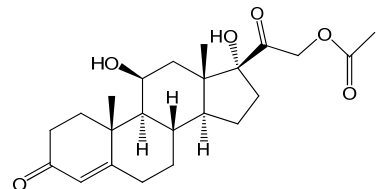
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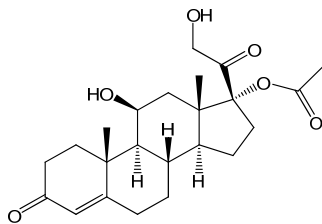
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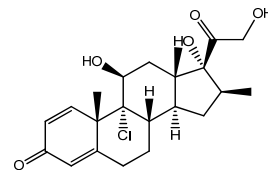
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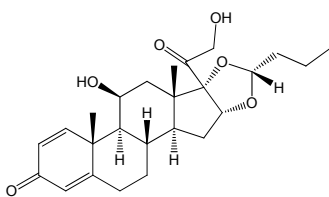
Hydrocortisone 21-acetate  
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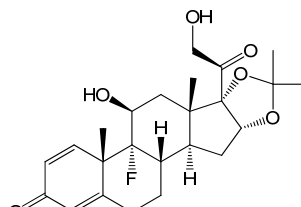
Hydrocortisone 17-acetate  
[C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>]



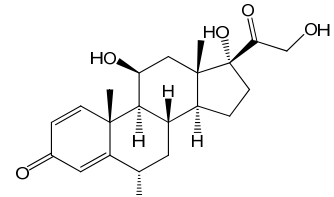
Beclomethasone  
[C<sub>22</sub>H<sub>29</sub>ClO<sub>5</sub>]



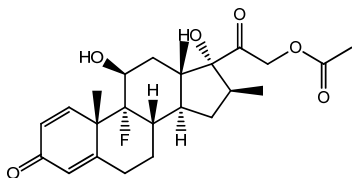
Budesonide  
[C<sub>25</sub>H<sub>34</sub>O<sub>6</sub>]



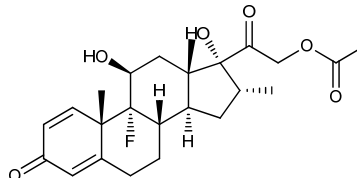
Triamcinolone acetonide  
[C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>]



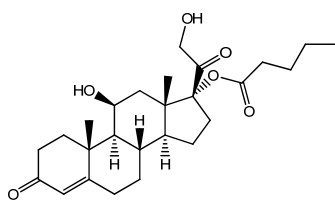
6α-Methylprednisolone  
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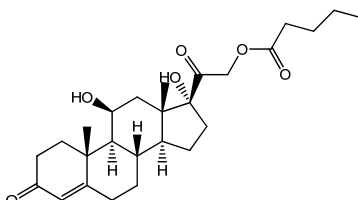
Betamethasone 21-acetate  
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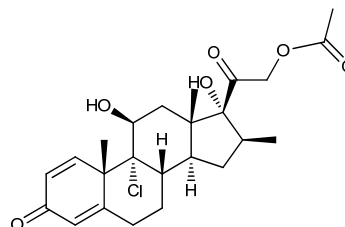
Dexamethasone 21-acetate  
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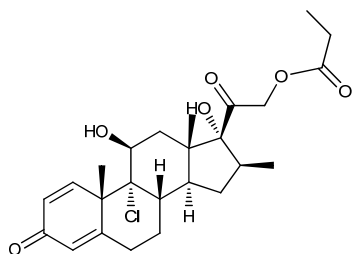
Hydrocortisone 17-valerate  
[C<sub>26</sub>H<sub>38</sub>O<sub>6</sub>]



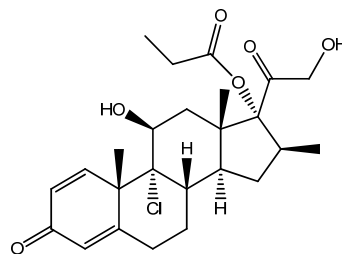
Hydrocortisone 21-valerate  
[C<sub>26</sub>H<sub>38</sub>O<sub>6</sub>]



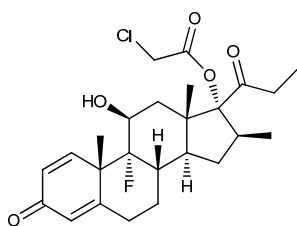
Beclomethasone 21-acetate  
[C<sub>24</sub>H<sub>31</sub>ClO<sub>6</sub>]



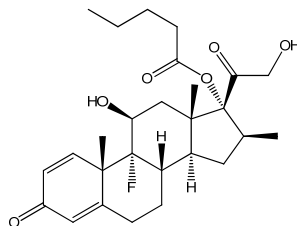
Beclomethasone 21-propionate  
[C<sub>25</sub>H<sub>33</sub>ClO<sub>6</sub>]



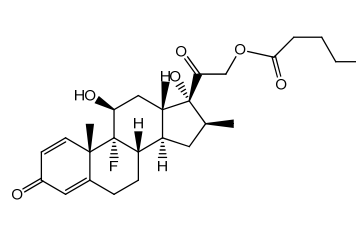
Beclomethasone 17-propionate  
[C<sub>25</sub>H<sub>33</sub>ClO<sub>6</sub>]



Clobetasol 17-propionate  
[C<sub>25</sub>H<sub>32</sub>ClFO<sub>5</sub>]

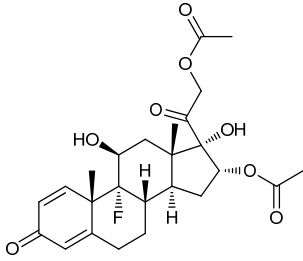


Betamethasone 17-valerate  
[C<sub>27</sub>H<sub>37</sub>FO<sub>6</sub>]

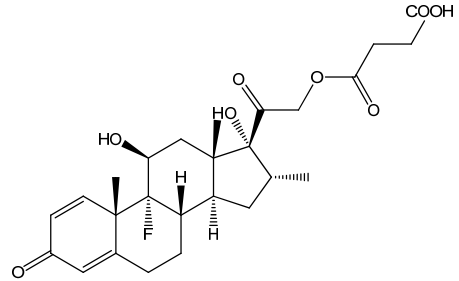


Betamethasone 21-valerate  
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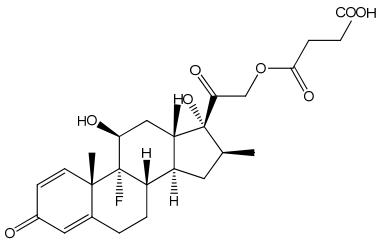




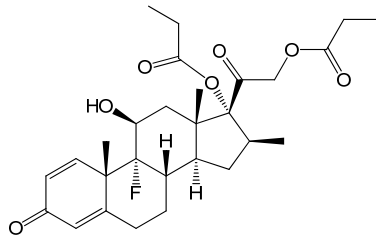
Triamcinolone diacetate  
[C<sub>25</sub>H<sub>31</sub>FO<sub>8</sub>]



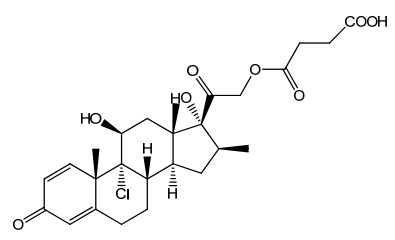
Dexamethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>FO<sub>8</sub>]



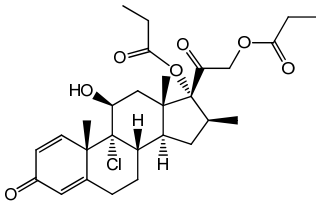
Betamethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>FO<sub>8</sub>]



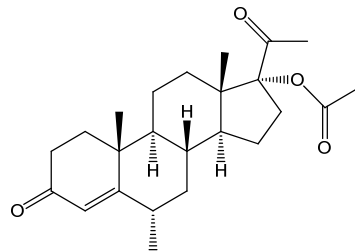
Betamethasone 17,21-dipropionate  
[C<sub>28</sub>H<sub>37</sub>FO<sub>7</sub>]



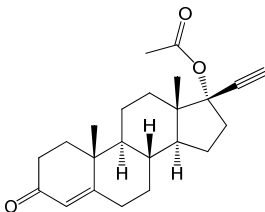
Beclomethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>ClO<sub>8</sub>]



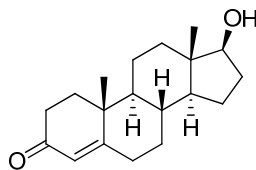
Beclomethasone 17,21-dipropionate  
[C<sub>28</sub>H<sub>37</sub>ClO<sub>7</sub>]



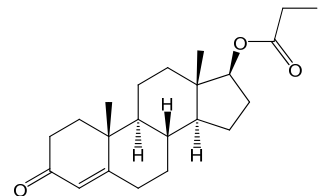
Medroxyprogesterone 17-acetate  
[C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>]



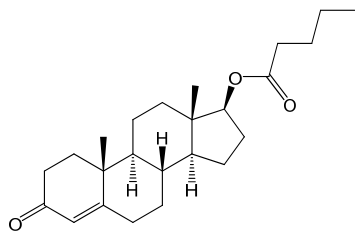
Norethisterone acetate  
[C<sub>22</sub>H<sub>28</sub>O<sub>3</sub>]



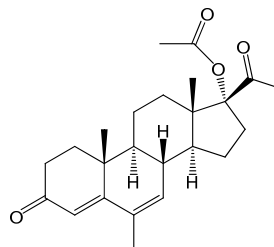
Testosterone  
[C<sub>19</sub>H<sub>28</sub>O<sub>2</sub>]



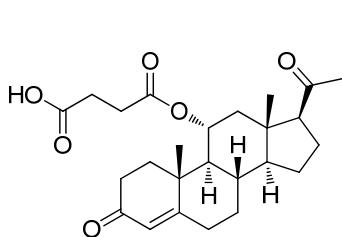
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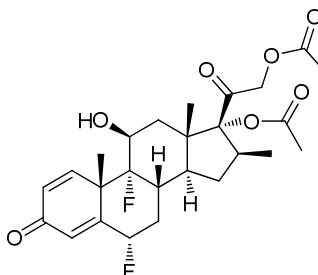
Testosterone 17-valerate  
[C<sub>24</sub>H<sub>36</sub>O<sub>3</sub>]



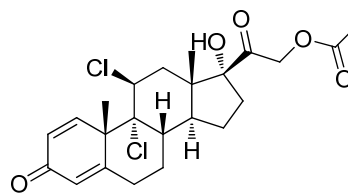
Megestrol acetate  
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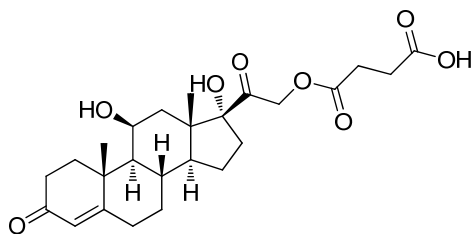
11α-OH-progesterone-hemisuccinate  
[C<sub>25</sub>H<sub>34</sub>O<sub>6</sub>]



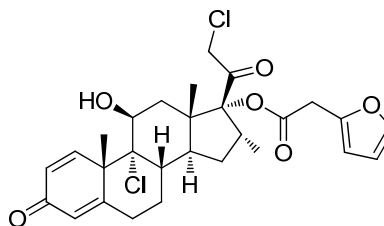
Diflorasone diacetate  
[C<sub>26</sub>H<sub>32</sub>F<sub>2</sub>O<sub>7</sub>]



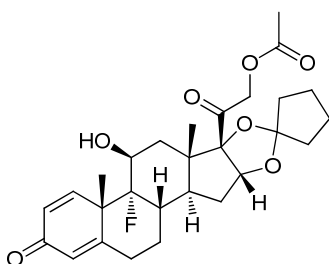
Dichlorisone acetate  
[C<sub>23</sub>H<sub>28</sub>Cl<sub>2</sub>O<sub>5</sub>]



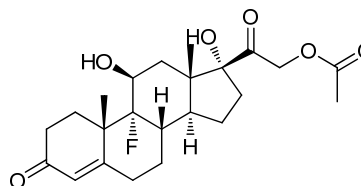
Hydrocortisone 21-hemisuccinate  
[C<sub>25</sub>H<sub>34</sub>O<sub>8</sub>]



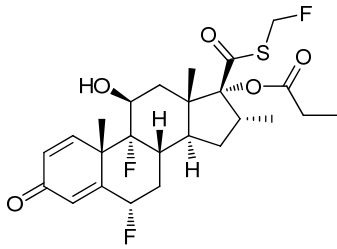
Mometasone furoate  
[C<sub>28</sub>H<sub>32</sub>O<sub>6</sub>Cl<sub>2</sub>]



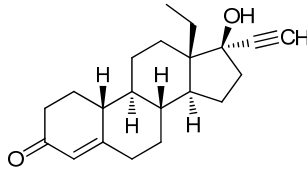
Amcinonide  
[C<sub>28</sub>H<sub>35</sub>FO<sub>7</sub>]



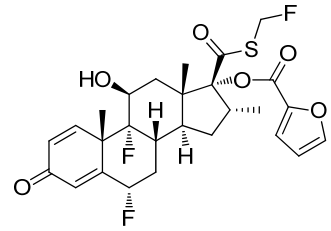
Fludrocortisone acetate  
[C<sub>23</sub>H<sub>31</sub>FO<sub>6</sub>]



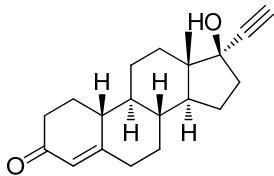
Fluticasone propionate  
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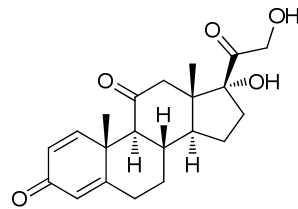
D(-)-Norgestrel  
[C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>]



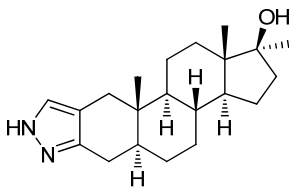
Fluticasone furoate  
[C<sub>27</sub>H<sub>29</sub>F<sub>3</sub>O<sub>6</sub>S]



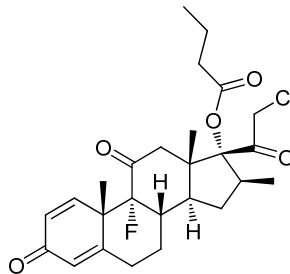
Norethisterone  
[C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>]



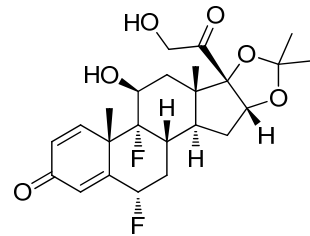
Prednisone  
[C<sub>21</sub>H<sub>28</sub>O<sub>5</sub>]



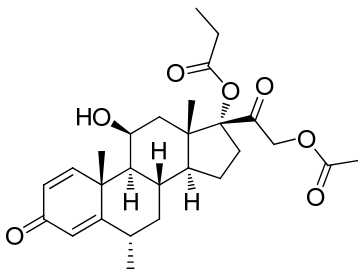
Stanozolol  
[C<sub>21</sub>H<sub>32</sub>N<sub>2</sub>O]



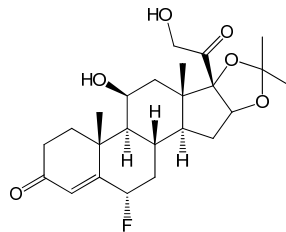
Clobetasone butyrate  
[C<sub>26</sub>H<sub>32</sub>ClFO<sub>5</sub>]



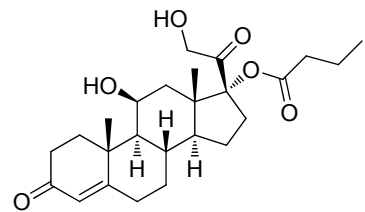
Fluocinolone acetonide  
[C<sub>24</sub>H<sub>30</sub>F<sub>2</sub>O<sub>6</sub>]



6α-Methylprednisolone aceponate  
[C<sub>27</sub>H<sub>36</sub>O<sub>7</sub>]



Flurandrenolide  
[C<sub>24</sub>H<sub>33</sub>FO<sub>6</sub>]



Hydrocortisone-17-butyrate  
[C<sub>25</sub>H<sub>36</sub>O<sub>6</sub>]

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3. Guan, F., Uboh, C., Soma, L., Hess, A., Luo, Y. & Tsang, D. S. Sensitive liquid chromatographic/tandem mass spectrometric method for the determination of beclomethasone dipropionate and its metabolites in equine plasma and urine. *J Mass Spectrom.* 38(8), 823-838 (2003)
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## III-15 여드름치료관련성분(11종) 분석법

### 배 경

- 화장품법 위반 5개 업체 행정처분('16. 9.)
- 여드름 증상 완화 효과를 높이기 위해 사용이 제한되어 있는 살균보존제 '트리클로산'을 다른 화장품 원료(일명 '그린컴플렉스')인 것처럼 사용하여 기준을 초과한化妆품을 제조·유통시킨 업체 대표 적발('16. 2.)



### 특 성

- 트리클로산: 화장품 중 배합한도성분 분석법 가이드라인 살균보존제 성분(2015.7.10.)에 따르면 세정용 제품 등 일부를 제외하고는 사용을 금지하고 있음.

### 분석 사례

- 야다 안티-티 스팟 크림: Triclosan 0.3 ~ 1.7% 검출
- 닥터에스리안티세범인텐시브케어젤: 트리클로산 0.2% 이상 검출

## ■ 분석법

### 1. HPLC법

#### ○ 전처리 방법

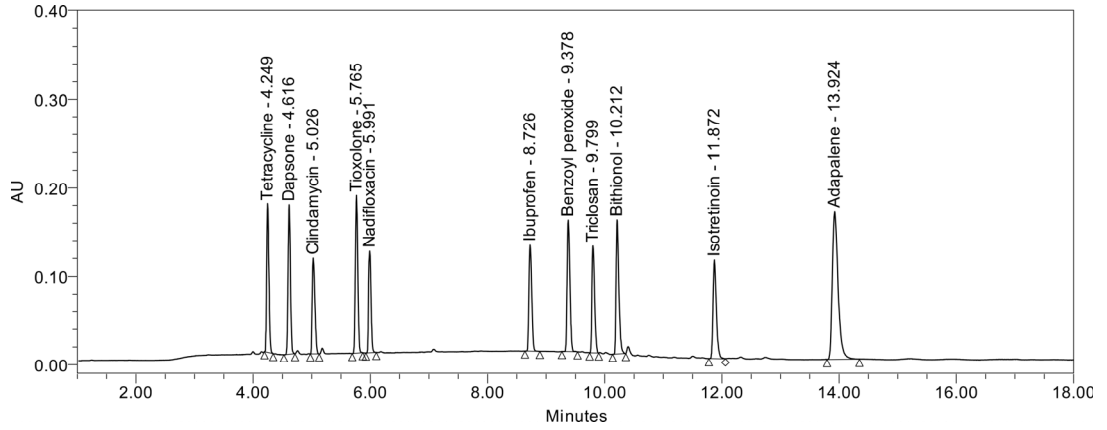
- 표준액 조제 : Tetracycline hydrochloride 등 11종\*  
→ 각각 일정량 취함 → 100% 에탄올 가함 → 최종 농도(약 10~200 µg/mL)
- 검액 조제 : 약 1 g 취함 → 100% 에탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Tetracycline hydrochloride, Dapsone, Clindamycin hydrochloride, 6-Hydroxy-1,3-benzoxathiol-2-one(=Tioxolone), Nadifloxacin, Ibuprofen, Benzoyl peroxide, Triclosan, Bithionol, Isotretinoin, Adapalene

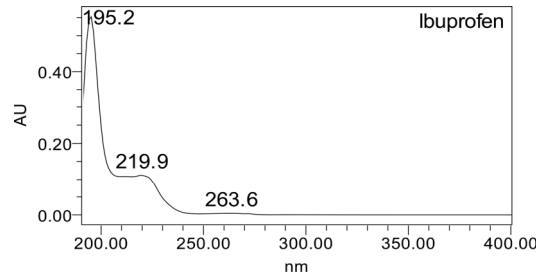
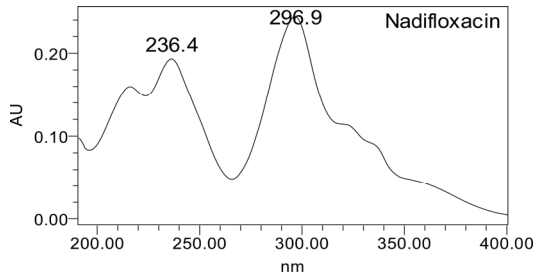
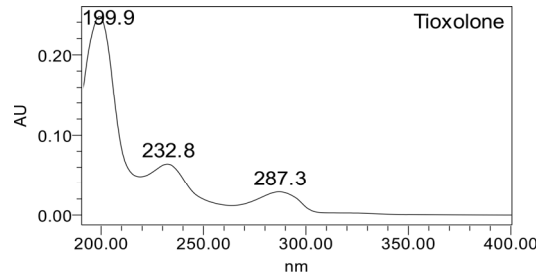
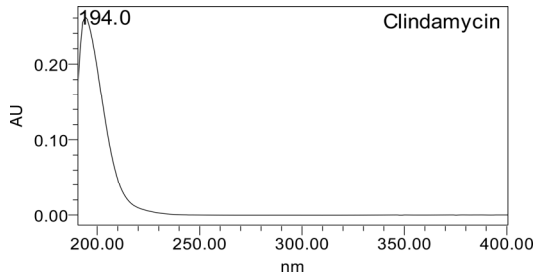
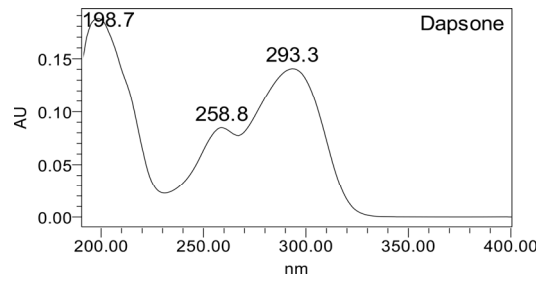
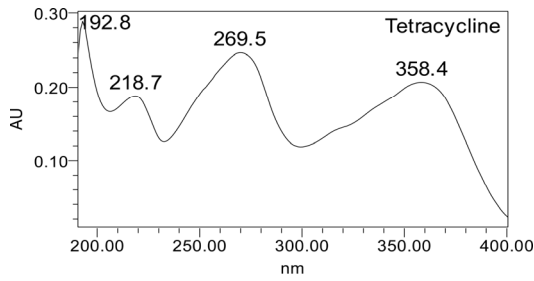
#### ○ Analytical condition of HPLC

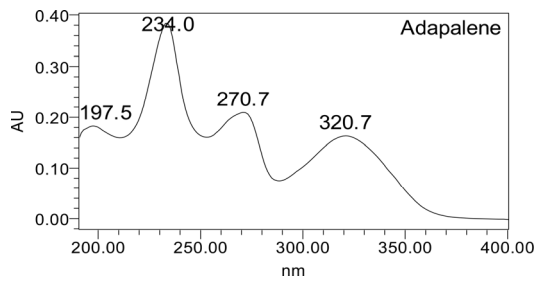
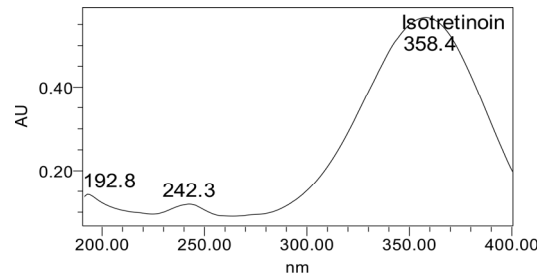
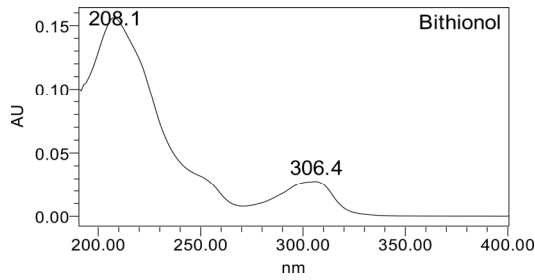
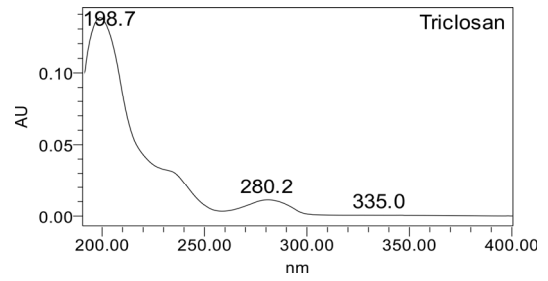
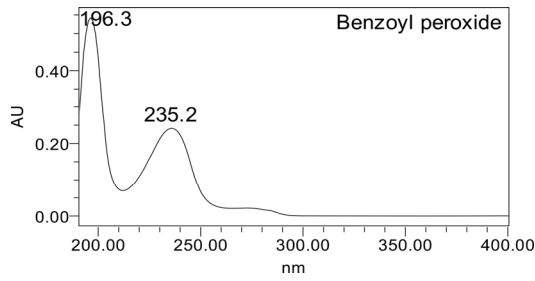
• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC HSS C <sub>18</sub> (2.1 mm × 100 mm, 1.8 µm)		
• Column Temp.	40℃		
• Mobile Phase	(A) 0.01% Trifluoroacetic acid in Water (B) 0.01% Trifluoroacetic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	2.0	90	10
	10.0	15	85
	17.0	15	85
	17.1	0	100
	19.0	0	100
	19.1	90	10
	22.0	90	10
• Flow Rate	0.3 mL/min		
• Inj. Volume	1.0 µL		
• UV Detection	205 nm		
• PDA Range	190~400 nm		

○ Chromatogram



○ PDA Spectrum







## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	35°C		
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	2.0	90	10
	7.0	0	100
	10.0	0	100
	10.1	90	10
	12.0	90	10
• Flow Rate	0.3 mL/min		
• Inj. Volume	2 μL		

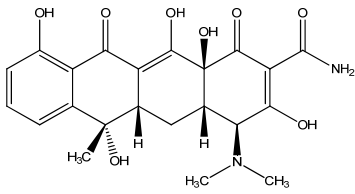
### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+),(-)
• Capillary Voltage	2.5 kV
• Desolvation Temp.	400°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

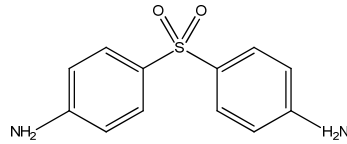
○ Analytical conditions of LC-MS/MS

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Clindamycin	+	425.38	30	81.80	55
				125.90	25
				377.05	20
Dapsone	+	249.20	25	64.80	35
				107.80	25
				155.80	15
Nadifloxacin	+	361.35	30	282.95	40
				343.03	25
				153.90	25
Tetracycline	+	445.35	25	410.03	20
				427.05	15
				428.00	15
				352.00	45
Adapalene	-	411.40	35	367.00	25
				160.70	20
				191.70	20
Bithionol	-	353.00	35	316.70	15
				160.90	5
				118.85	25
Ibuprofen	-	205.23	10	239.00	20
				255.05	15
				138.73	10
Tioxolone	-	167.05	25	122.75	15
				110.75	20
				34.70	5
Triclosan	-	287.10	15	34.70	5

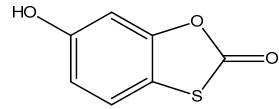
■ 구조식



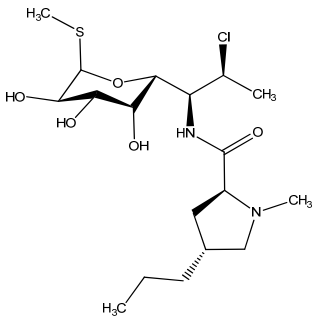
Tetracycline  
[C<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>8</sub>]



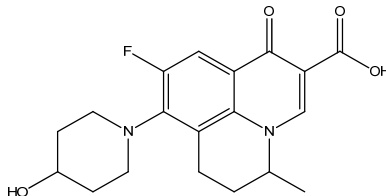
Dapsone  
[C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S]



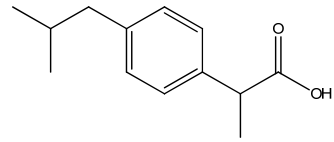
Tioxolone  
[C<sub>7</sub>H<sub>4</sub>O<sub>3</sub>S]



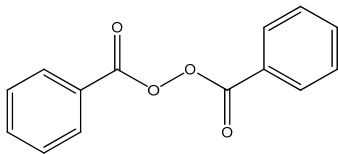
Clindamycin  
[C<sub>18</sub>H<sub>33</sub>ClN<sub>2</sub>O<sub>5</sub>S]



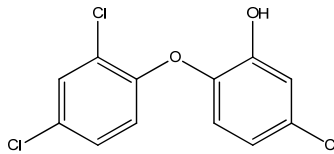
Nadifloxacin  
[C<sub>19</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>4</sub>]



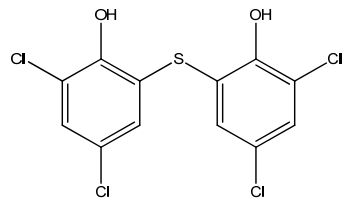
Ibuprofen  
[C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>]



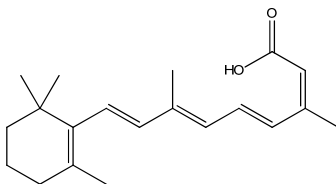
Benzoyl peroxide  
[C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>]



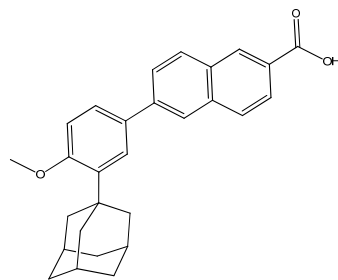
Triclosan  
[C<sub>12</sub>H<sub>7</sub>Cl<sub>3</sub>O<sub>2</sub>]



Bithionol  
[C<sub>12</sub>H<sub>6</sub>Cl<sub>4</sub>O<sub>2</sub>S]



Isotretinoin  
[C<sub>20</sub>H<sub>28</sub>O<sub>2</sub>]



Adapalene  
[C<sub>28</sub>H<sub>28</sub>O<sub>3</sub>]

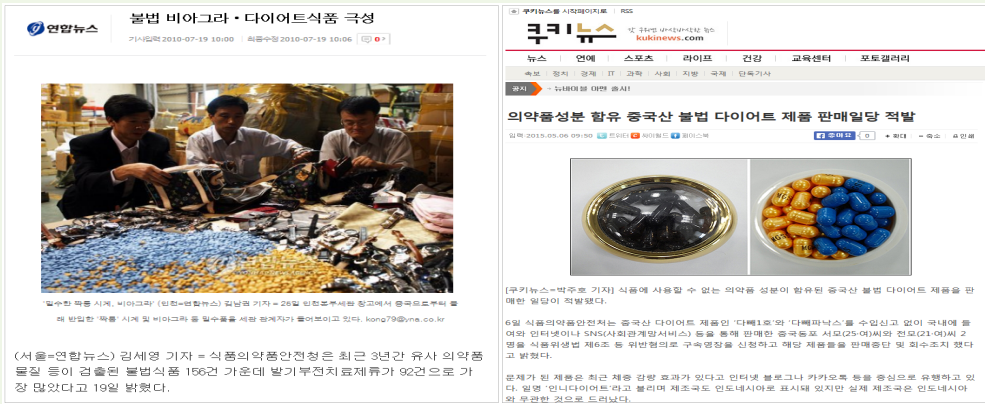
## ■ 참고문헌

1. Tashtoush, B. M., Jacobson, E. L., Jacobson, M. K. A rapid HPLC method for simultaneous determination of tretinoin and isotretinoin in dermatological formulations. *J Pharm Biomed Anal.* 43, 859-864 (2007)
2. Gue, Liang., Chen, Yiqiang., Zhang Liying., Yang, Wenjun., He, Pingli. Development and validation of a liquid chromatographic/tandem mass spectrometric method for determination of chlortetracycline, oxytetracycline, tetracycline, and doxycycline in animal feeds. *J AOAC International.* 95, 1010-1015 (2012)
3. VLADIMIR DOBRIČIĆ, NATAŠA BUBIĆ PAJIĆ, BOJAN MARKOVIĆ, SOTE VLADIMIROV, SNEŽANA SAVIĆ, GORDANA VULETA. Development and validation of an LC-MS/MS method for the determination of adapalene in pharmaceutical forms for skin application. *J. Serb. Chem. Soc.* 81, 1 - 14 (2016)

# III-16 체중감량성분\_이뇨관련성분(23종) 분석법

## 배 경

- 이뇨제 성분이 포함된 불법 다이어트 의약품 적발('10, 11)
- 지네환 복용한 장대높이뛰기 선수 도핑테스트에서 이뇨제 성분 검출('15. 1.)
- 식품에 사용할 수 없는 의약품 성분이 함유된 중국산 불법 다이어트 제품에서 이뇨제인 '푸로세미드' 검출('15. 5.)
- '다이어트·성기능 개선' 해외직구 식품서 유해물질 검출('17, 03)



## 특 성

- 뇨량을 증대시켜 체내의 불필요한 수분을 배출하는 의약품으로 대표적인 이뇨제로 하이드로클로로티아지드, 푸로세미드, 스피로노락톤 등이 있음
- 부작용으로 순간적인 탈수증에 빠질 수 있고, 수분과 함께 칼륨이나 마그네슘 등 전해질이 몸 밖으로 빠져나가므로 심장의 정상적인 박동이 어려워지기도 함

## 분석 사례

- 다빠 1호: Furosemide 79.5 mg/캡슐 검출
- 이뇨제 불법의약품: Hydrochlorothiazide 16.6 mg/정 검출

## ■ 분석법

### 1. HPLC법

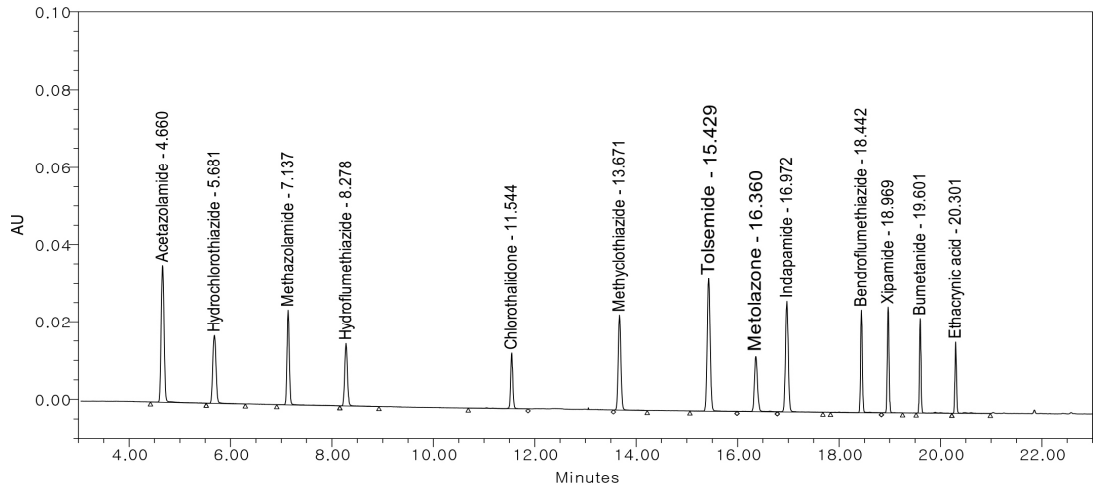
#### ○ 전처리 방법

- 표준액 조제 : 표준액 1\* Acetazolamide 등 13종  
                   표준액 2\* Chlorothiazide 등 10종  
                   → 각각 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10~20 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용
- \* 표준액 1 : Acetazolamide, Hydrochlorothiazide, Methazolamide, Hydroflumethiazide, Chlorthalidone, Methyclothiazide, Metolazone, Torsemide, Indapamide, Bendroflumethiazide, Xipamide, Bumetanide, Ethacrynic acid
- \* 표준액 2 : Chlorothiazide, Amiloride hydrochloride, Triamterene, Trichlormethiazide, Furosemide, Eplerenone, Cyclothiazide, Azosemide, Piretanide, Spironolactone

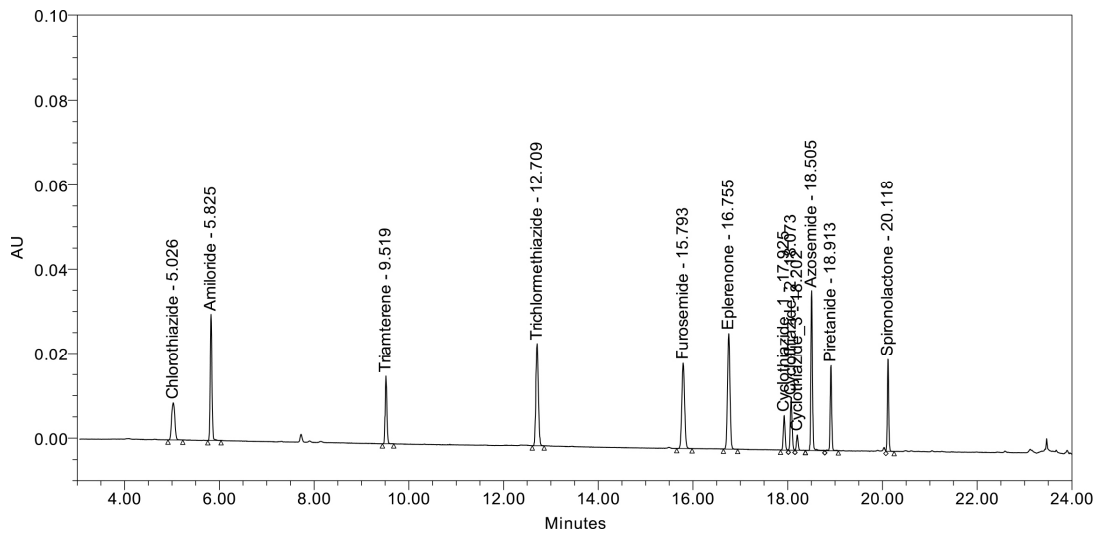
#### ○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 150 mm, 1.7 µm)		
• Column Temp.	40°C		
• Mobile Phase	(A) 0.15% Trifluoroacetic acid in Water (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	95	5
	2.0	95	5
	13.5	70	30
	15.0	70	30
	22.0	25	75
	22.1	0	100
	24.0	0	100
	24.1	95	5
	28.0	95	5
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 µL		
• UV Detection	254 nm		
• PDA Range	190~400 nm		

○ Chromatogram

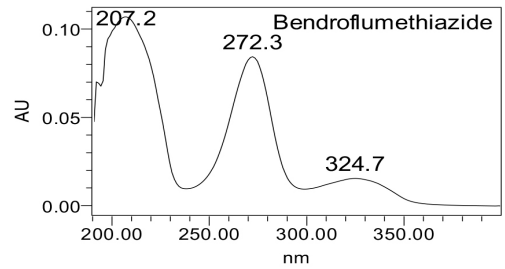
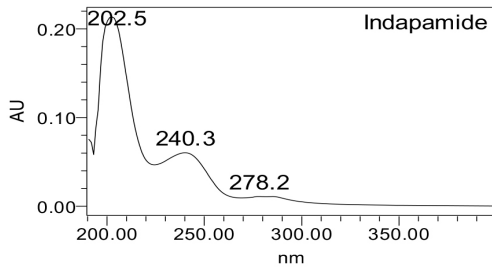
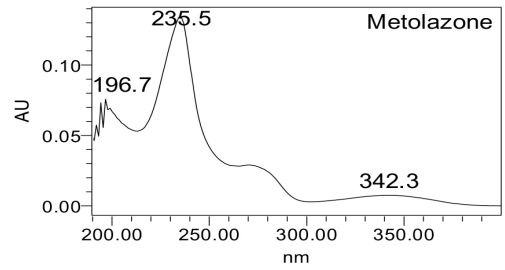
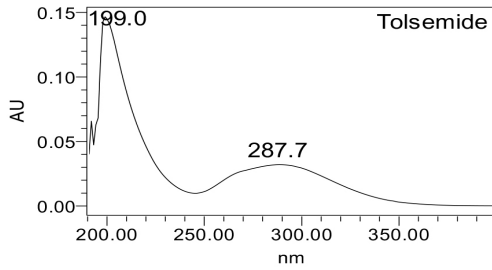
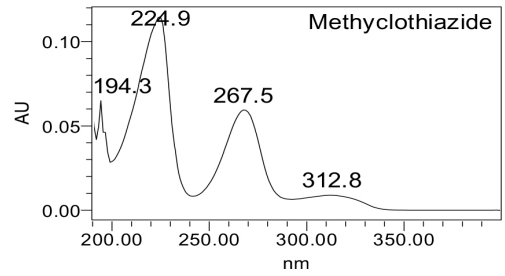
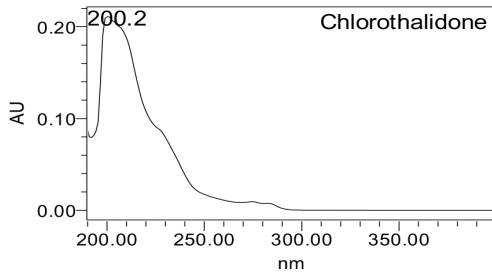
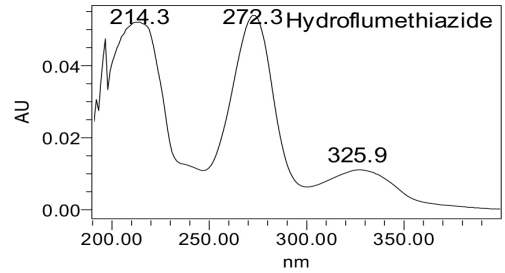
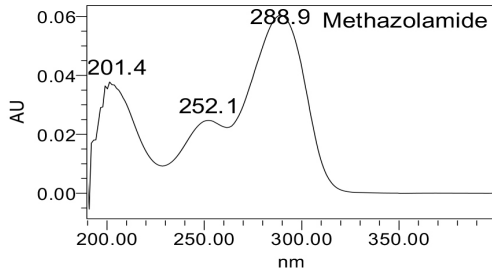
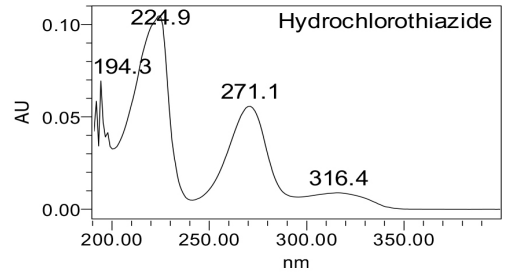
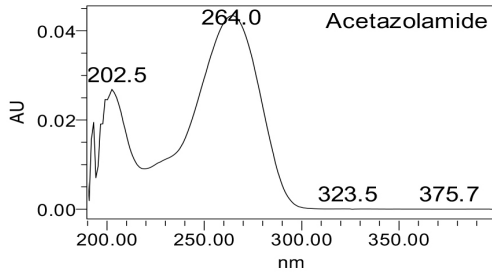


[표준액 1]



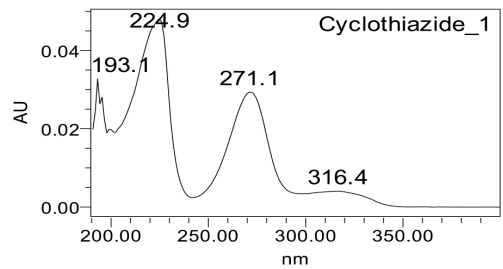
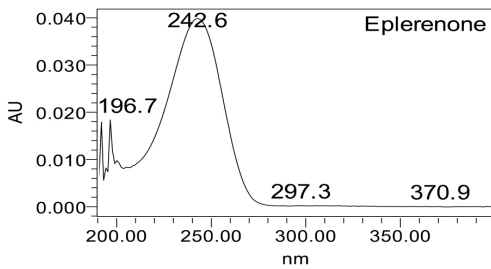
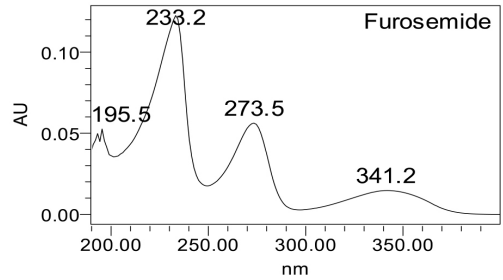
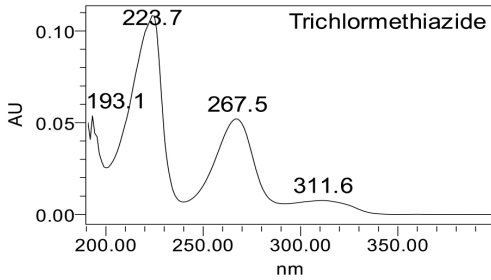
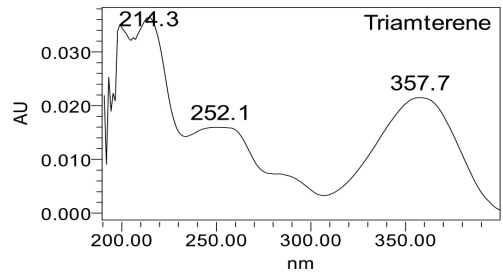
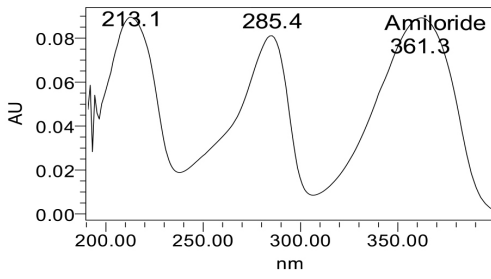
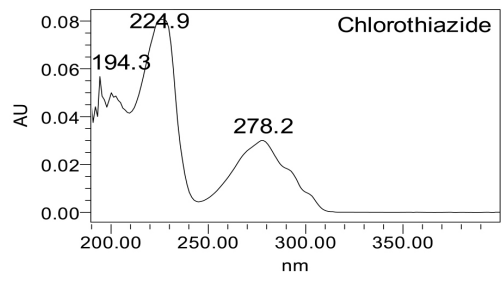
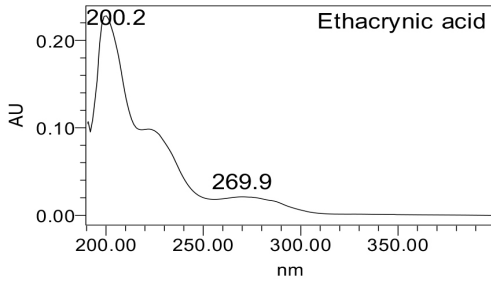
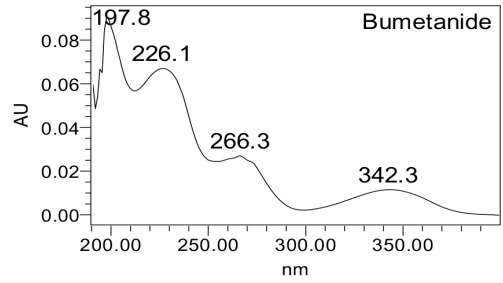
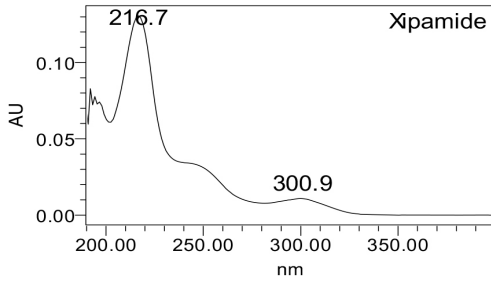
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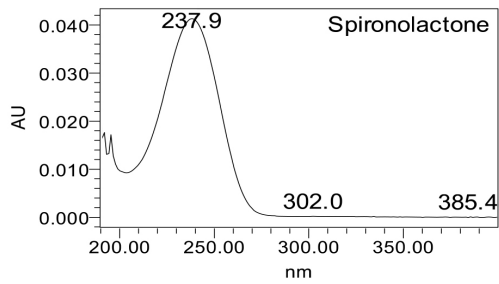
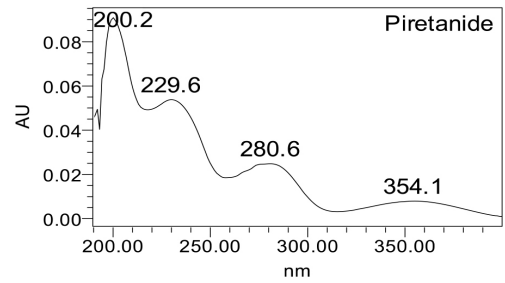
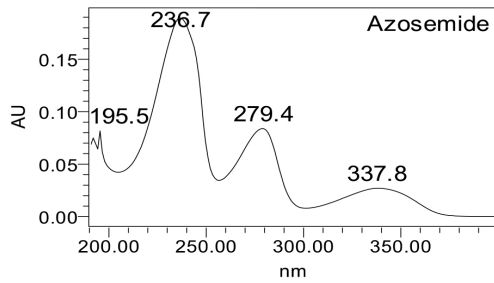
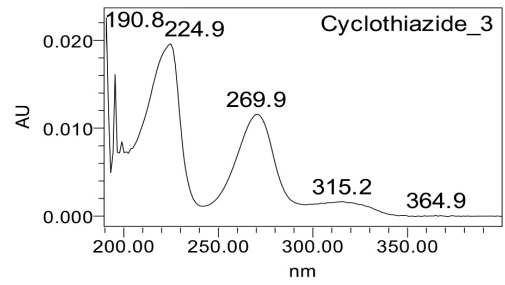
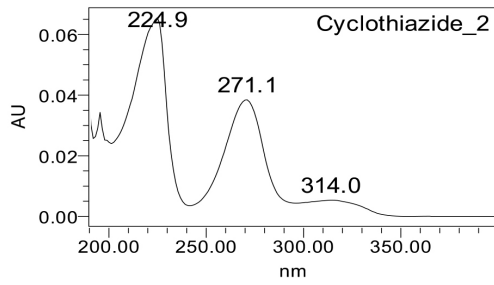
○ PDA Spectrum





III-16. 체중감량성분\_이뇨관련성분(23종) 분석법





## 2. LC-MS/MS법

### ○ Analytical conditions of HPLC

• Instrument	Waters UPLC		
• Column	Waters ACQUITY UPLC HSS T <sub>3</sub> (2.1 mm× 100 mm, 1.8 μm)		
• Column Temp.	35℃		
• Mobile Phase	(A) 10 mM Ammonium acetate in Water (B) 100% Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	100	0
	2.0	100	0
	6.0	0	100
	8.0	0	100
	8.1	100	0
	10.0	100	0
• Flow Rate	0.5 mL/min		
• Inj. Volume	2 μL		

### ○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ	
• Ionization Mode	ESI (+)	ESI (-)
• Capillary Voltage	2.5 kV	2.5 kV
• Desolvation Temp.	400℃	500℃
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )	800 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Acetazolamide	-	221.06	25	57.90	15
				82.95	15
Hydrochlorothiazide	-	295.90	42	204.96	22
				268.94	18
Methazolamide	-	235.11	20	57.70	15
				77.70	15
Hydroflumethiazide	-	329.98	40	238.99	22
				302.87	20
Chlorothalidone	-	336.97	34	146.12	24
				190.00	18
Methyclothiazide	-	357.92	32	257.98	20
				321.91	12
Metolazone	-	366.03	48	232.98	24
				258.98	24
Torsemide	-	347.05	26	262.06	20
Indapamide	-	363.90	42	131.89	24
				188.84	24
Bendroflumethiazide	-	419.99	44	288.98	22
				327.93	22
Xipamide	-	353.30	40	77.70	30
				121.75	35
				169.75	30
				273.88	25
Bumetanide	-	363.01	28	79.81	24
				206.99	18
Ethancrynic acid	-	300.92	16	191.84	30
				242.88	16
Chlorothiazide	-	294.02	30	178.97	40
				213.95	25
Amiloride	-	228.15	25	142.75	15
				185.80	15
Trichlormethiazide	-	378.00	30	241.99	20
				305.98	10

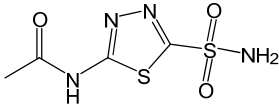
표준액  
1

Compound	Ion Mode	Precursor Ion ( $m/z$ )	CV (V)	Product Ion ( $m/z$ )	CE (eV)
Furosemide	-	329.10	25	204.93	25
				285.02	15
				122.80	35
Eplerenone	-	413.40	30	334.90	25
				353.03	20
				268.95	28
Cyclothiazide	-	388.00	52	321.88	22
				196.80	30
				284.76	20
Azosemide	-	369.23	30	325.83	20
				79.70	25
				204.85	25
Piretanide	-	361.30	30	316.93	15
				104.01	34
				141.01	42
Triamterene	+	254.08	46	236.99	26
				107.20	25
				187.10	20
Spironolactone	+	341.01	55		

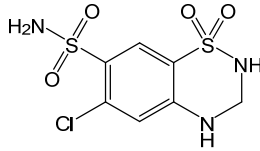
표준액 1

표준액 2

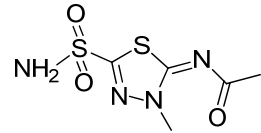
■ 구조식



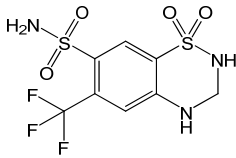
Acetazolamide  
[C<sub>4</sub>H<sub>6</sub>N<sub>4</sub>O<sub>3</sub>S<sub>2</sub>]



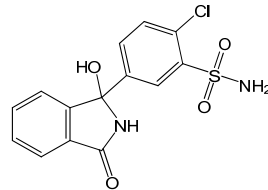
Hydrochlorothiazide  
[C<sub>7</sub>H<sub>8</sub>ClN<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



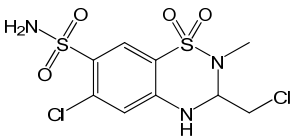
Methazolamide  
[C<sub>5</sub>H<sub>8</sub>N<sub>4</sub>O<sub>3</sub>S<sub>2</sub>]



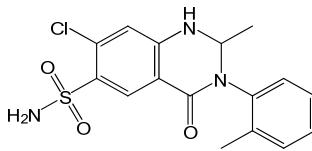
Hydroflumethiazide  
[C<sub>8</sub>H<sub>8</sub>F<sub>3</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



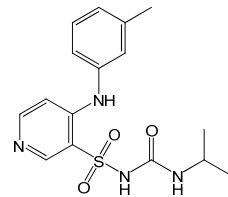
Chlorthalidone  
[C<sub>14</sub>H<sub>11</sub>ClN<sub>2</sub>O<sub>4</sub>S]



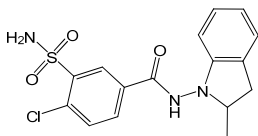
Methyclothiazide  
[C<sub>9</sub>H<sub>11</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



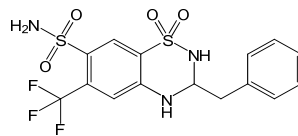
Metolazone  
[C<sub>16</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>3</sub>S]



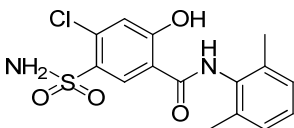
Torsemide  
[C<sub>16</sub>H<sub>20</sub>N<sub>4</sub>O<sub>3</sub>S]



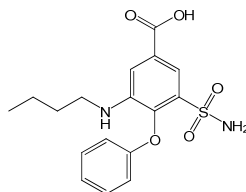
Indapamide  
[C<sub>16</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>3</sub>S]



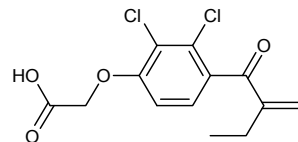
Bendroflumethiazide  
[C<sub>15</sub>H<sub>14</sub>F<sub>3</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



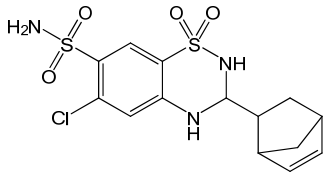
Xipamide  
[C<sub>15</sub>H<sub>15</sub>ClN<sub>2</sub>O<sub>4</sub>S]



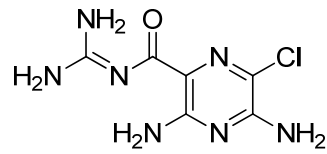
Bumetanide  
[C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub>S]



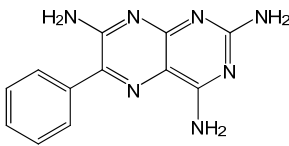
Ethacrynic acid  
[C<sub>13</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>4</sub>]



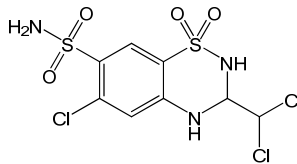
Cyclothiazide  
[C<sub>14</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



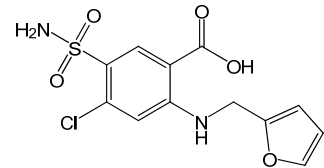
Amiloride  
[C<sub>8</sub>H<sub>8</sub>ClN<sub>7</sub>O]



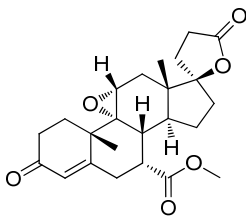
Triamterene  
[C<sub>12</sub>H<sub>11</sub>N<sub>7</sub>]



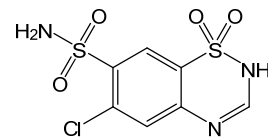
Trichlormethiazide  
[C<sub>8</sub>H<sub>8</sub>Cl<sub>3</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



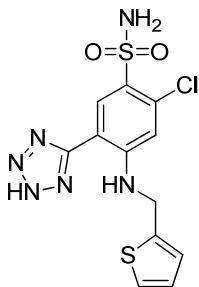
Furosemide  
[C<sub>12</sub>H<sub>11</sub>ClN<sub>2</sub>O<sub>5</sub>S]



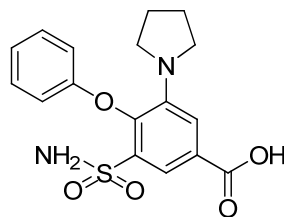
Eplerenone  
[C<sub>24</sub>H<sub>30</sub>O<sub>6</sub>]



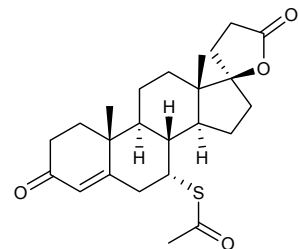
Chlorothiazide  
[C<sub>7</sub>H<sub>6</sub>ClN<sub>3</sub>O<sub>4</sub>S<sub>2</sub>]



Azosemide  
[C<sub>12</sub>H<sub>11</sub>ClN<sub>6</sub>O<sub>2</sub>S<sub>2</sub>]



Piretanide  
[C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O<sub>5</sub>S]



Spironolactone  
[C<sub>24</sub>H<sub>32</sub>O<sub>4</sub>S]

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1. Sevinc Kurbanoglu, Paula Rodringuez San Miguel, Bengi Uslu, Sibel A. Ozkan. Stability-indicating UPLC method for the determination of bisoprolol fumarate and hydrochlorothiazide: application to dosage forms and biological sample. *Chromatographia*. 44(3-4) 365-371 (2014)
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5. K. Deventer, F. T. Delbeke, K. Roels and P. Van Eenoo. Screening for 18 diuretics and probenecid in doping analysis by liquid chromatography- tandem mass spectrometry. *Biomed Chromatog*. 16, 529-535 (2002)



# III-17 진세노사이드 분석법

## 배 경

- 홍삼농축액 대신 홍삼향과 카라멜색소를 사용하여 가짜 홍삼음료 등을 제조 판매한 사례('15. 9)
- 영업등록을 하지 않은 제조시설에서 홍삼유사제품 불법제조 판매 ('15. 2.)



## 특 성

- 홍삼·인삼의 정의
  - 인삼: 인삼의 뿌리로서 그대로 또는 가는 뿌리와 코르크 층을 제거한 것
  - 홍삼: 인삼의 뿌리를 껍질째 증기로 찌서 건조한 담황갈색 인삼
- 홍삼·인삼의 규격
  - 식품공전의 인삼·홍삼음료 규격: 인삼·홍삼성분 확인되어야 함
  - 건강기능식품공전 중 기능성 원료의 인삼, 홍삼규격
    - 인삼
      - 제조기준 기능성분의 함량: 진세노사이드 Rg1과 Rb1 합하여 0.8~34 mg/g 함유
      - 진세노사이드 Rg1과 Rb1의 합(최종제품: 표시량의 80% 이상)
    - 홍삼
      - 제조기준 기능성분의 함량: 진세노사이드 Rg1, Rb1 및 Rg3를 합하여 2.5~34 mg/g 함유
      - 진세노사이드 Rg1, Rb1 및 Rg3의 합(최종제품: 표시량의 80% 이상)

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Ginsenoside Rg1 등 3종\* → 각각 일정량 취함 → 메탄올 가함  
→ 최종농도(약 1 µg/L)
- 검액 조제 : 약 1 g 취함 → 70 % 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Ginsenoside Rb1, Ginsenoside Rg1, Ginsenoside Rg3

#### ○ Analytical conditions of LC-MS/MS

• LC System	Water ACQUITY UPLC	
• Column	Waters ACQUITY UPLC HSS T <sub>3</sub> (2.1 × 100 mm, 1.8 µm)	
• Column temp.	40°C	
• Inj. Vol.	2 µL	
• Mobile Phase	A: 0.1% formic acid in D.W. B: 0.1% formic acid in MeOH	
	<b>Time (min)</b>	<b>A (%)</b>
	0.0	80
	1.5	80
	3.0	50
	4.0	30
	11.5	10
	12.0	10
	13.0	80
	15.0	80
	<b>B (%)</b>	
	20	
	20	
	50	
	70	
	90	
	90	
	20	
	20	
• Flow Rate	0.25 mL/min	
• MS system	Waters Xevo TQ	
• Ionization mode	ESI(+)	
• Capillary voltage	2.5 kV	
• Desolvation Temp.(°C)	150°C	
• Desolvation Gas Flow	300 L/Hr(N <sub>2</sub> )	
• Cone Gas Flow	off	

○ Analyte MS/MS transition

Compound	Ion Mode	Parent ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Ginsenoside Rg1	+	823.63	50	203.18	40
				643.44	40
Ginsenoside Rb1	+	1131.62	60	365.23	60
				789.51	60
Ginsenoside Rg3	+	807.64	55	245.18	55
				365.18	50

2. TLC

○ 전처리 방법

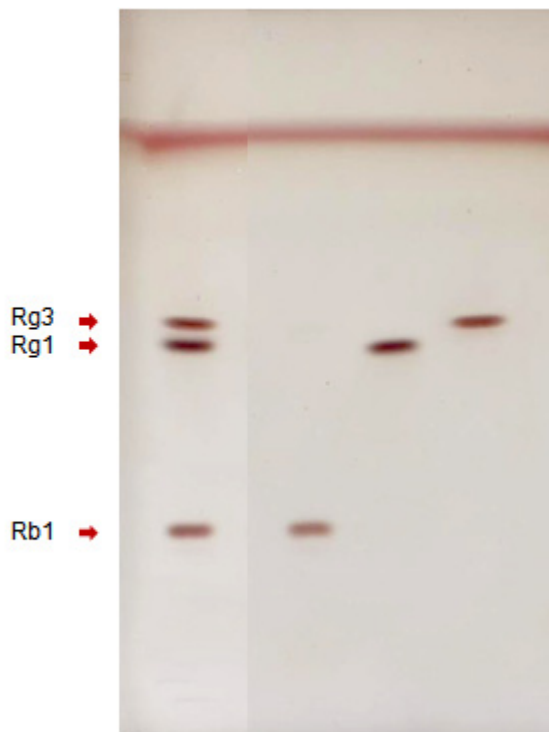
- 표준액 조제 : Ginsenoside Rg1 등 3종\*  
→ 각각 일정량 취함 → 100% 메탄올 가함
- 검액 조제 : 검체 약 50 g 취함  
→ 80℃에서 60분 동안 환류추출  
→ 감압농축  
→ 농축한 것을 물에 녹인 뒤 에테르로 지방 등의 불순물 제거  
→ 물층을 불포화 부탄올로 추출하여 감압농축  
→ 메탄올에 녹인 후 시험용액으로 함

\* 표준액 : Ginsenoside Rb1, Ginsenoside Rg1, Ginsenoside Rg3

○ Analytical condition of TLC

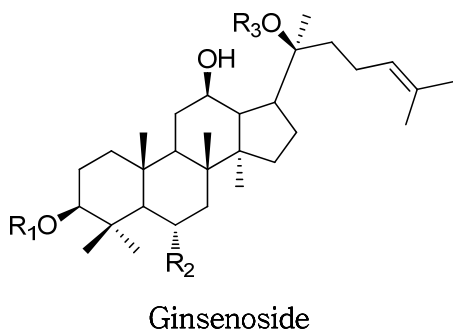
• Instrument	Camag TLC System
• TLC plate	HPTLC Silica gel 60 F <sub>254</sub> (200 μm)
• Mobile Phase	Chloroform : Methanol : Water = 65 : 35 : 10
• Dosage Speed	50 nL/s
• Loading Volume	20 μL
• Detection	10% H <sub>2</sub> SO <sub>4</sub> 용액을 분무하여 110℃에서 10분간 가열하여 발색시킨 뒤 육안으로 확인

○ Chromatogram



■ 구조식

○ 진세노사이드 (3종)



	R1	R2	R3
Rg1	H	O-Glc	Glc
Rb1	Glc <sup>2</sup> -Glc	H	Glc <sup>6</sup> -Glc
Rg3	Glc <sup>2</sup> -Glc	H	H

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3. Zongwei Cai, Tianxiu Qian, Ricky N.S. Wong, Zhi-Hong Jiang. Liquid chromatography-electrospray ionization mass spectrometry for megtabolism and pharmacokinetic studies of ginsenoside Rg3. *Analytica Chimica Acta*, 492, 283-293 (2003)

### III-18 < 칩 성분 분석법

#### ■ 배 경

- 칩냉면에 칩을 넣지 않거나 적게 넣어 함량을 허위로 표시한 식품 제조업체 적발('11. 7.)
- 칩 성분이 들어가지 않은 가짜 '칩 냉면'을 제조 유통시킨 업자 적발, 보관중인 가짜 칩냉면 등 압류('10. 4.)



#### ■ 특 성

- 칩 뿌리에는 이소플라빈 화합물인 푸에라린, 다이드제인, 다이드진 쿠마린 등의 성분을 함유
- 푸에라린: 칩(Puerariae Radix)에서 발견되는 대표적인 Isoflavone이며, 혈액순환을 활발하게 하여 동맥경화를 예방하고 고혈압, 협심증 등에 효능이 있으며 원기회복을 돕고 음주 뒤 숙취 유발물질인 아세트알데히드의 분해를 촉진함  
또한, 다양한 기전을 통해 신경세포를 보호하는 것이 보고됨

#### ■ 분석사례

- 비썬세스 비타민 E : Puerarin 검출
- 칩냉면 : Puerarin 불검출

■ 분석법

1. HPLC법

○ 전처리 방법

- 표준액 조제 : Puerarin  
→ 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 10 µg/mL)
- Ononin  
→ 일정량 취함 → 증류수 소량과 Formic acid 20%를 가함  
→ 100% 메탄올 가함 → 최종 농도(약 10 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Puerarin, Ononin

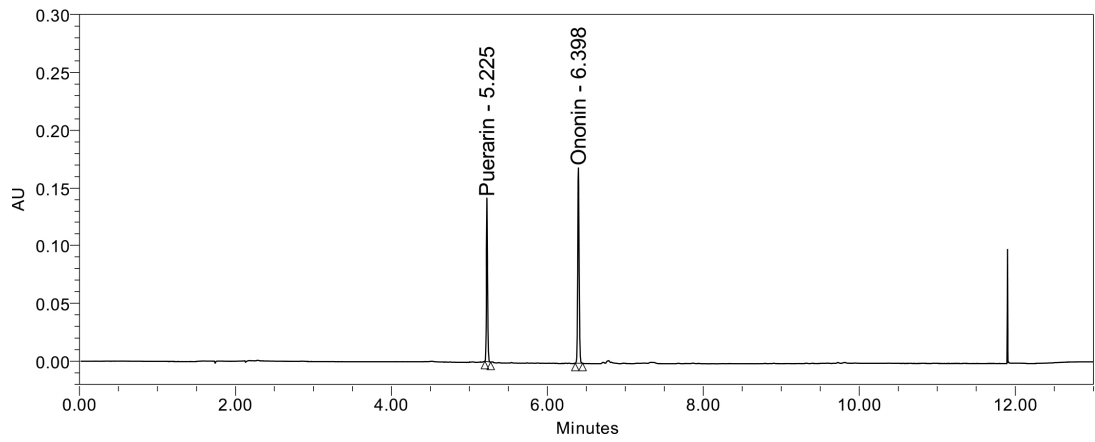
○ Analytical conditions of HPLC

- Instrument Waters ACQUITY UPLC
- Column Waters ACQUITY UPLC BEH C<sub>18</sub> (2.1 mm × 100 mm, 1.7 µm)
- Column Temp. 40°C
- Mobile Phase (A) 10 mM Ammonium acetate in Water  
(B) 100% Acetonitrile

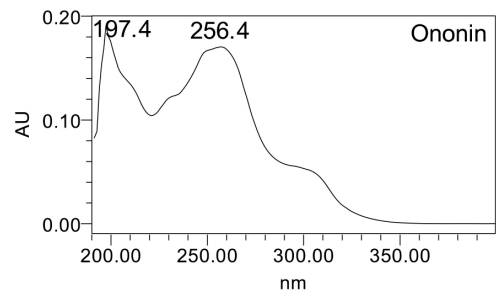
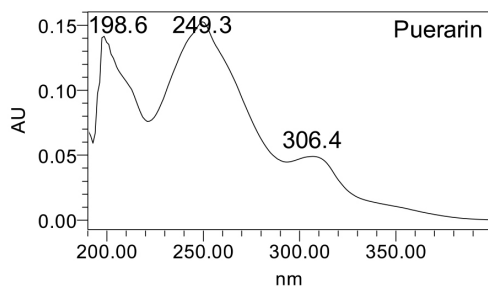
Time (min)	A (%)	B (%)
0.0	95.0	5.0
2.0	95.0	5.0
8.0	5.0	95.0
10.0	5.0	95.0
10.1	95.0	5.0
13.0	95.0	5.0

- Flow Rate 0.2 mL/min
- Inj. Volume 1 µL
- UV Detection 210 nm, 254 nm
- PDA Range 190~400 nm

### ○ Chromatogram



### ○ PDA Spectrum





## 2. LC-MS/MS법

## ○ Analytical conditions of HPLC

• Instrument	Shiseido SP3133																					
• Column	Capcell pak C18 MGII (2.0 mm × 100 mm, 3.0 μm)																					
• Column Temp.	40°C																					
• Mobile Phase	(A) 100% Water (B) 100% Acetonitrile																					
	<table border="1"> <thead> <tr> <th>Time (min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0.0</td> <td>90.0</td> <td>10.0</td> </tr> <tr> <td>2.0</td> <td>90.0</td> <td>10.0</td> </tr> <tr> <td>5.0</td> <td>60.0</td> <td>40.0</td> </tr> <tr> <td>8.0</td> <td>60.0</td> <td>40.0</td> </tr> <tr> <td>10.0</td> <td>90.0</td> <td>10.0</td> </tr> <tr> <td>12.0</td> <td>90.0</td> <td>10.0</td> </tr> </tbody> </table>	Time (min)	A (%)	B (%)	0.0	90.0	10.0	2.0	90.0	10.0	5.0	60.0	40.0	8.0	60.0	40.0	10.0	90.0	10.0	12.0	90.0	10.0
Time (min)	A (%)	B (%)																				
0.0	90.0	10.0																				
2.0	90.0	10.0																				
5.0	60.0	40.0																				
8.0	60.0	40.0																				
10.0	90.0	10.0																				
12.0	90.0	10.0																				
• Flow Rate	0.3 mL/min																					
• Inj. Volume	5 μL																					

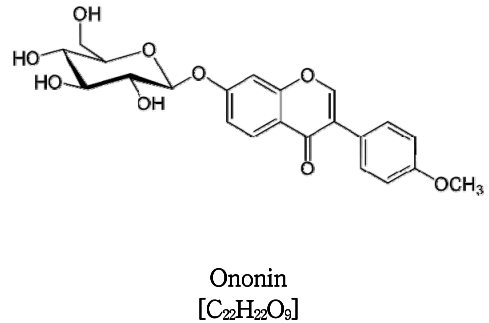
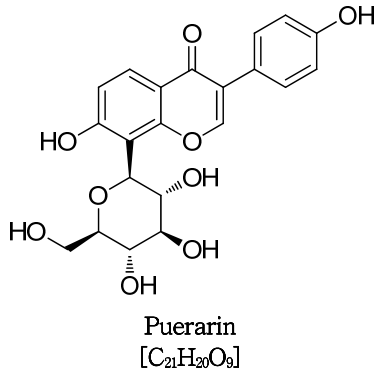
## ○ Analytical condition of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (+)
• Curtain Gas	30 psi
• Collision Gas	Medium
• Ion Voltage	5500 V
• Ion Source Gas 1	50 psi
• Ion Source Gas 2	50 psi
• Source Temp.	500°C

## ○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion (m/z)	DP (V)	Product Ion (m/z)	CE (V)	CXP (V)
Puerarin	+	417.10	120	297.0	37	15
				321.0	30	15
Ononin	+	431.13	120	269.1	40	20
				254.0	60	20
				213.1	60	20

## ■ 구조식



## ■ 참고문헌

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## III-19 코치닐추출색소(카르민산) 분석법

### 배 경

- 식품의 색깔을 돋보이게 하는 등의 시각적 자극을 통해 식욕을 증대시키고, 풍미를 인식시키는 데 도움을 주어 식품의 외형적 가치를 높이고자 첨가함
- 식품첨가물공전(2015. 11.)에 따르면 코치닐추출색소는 다류에서는 사용하지 않으나, 시판중인 딸기, 복분자, 오미자, 석류 등의 적황색 과실추출 분말 다류 일부에서 코치닐추출색소 색조의 주성분인 카르민산이 검출됨



### 특 성

- 중남미 자생 선인장(*Opuntia coccinellifera*, *Opuntia tura* 등)에 기생하는 연지벌레 암컷 분말을 물-알코올성 용액으로 추출한 뒤 알코올성분을 제거시켜 얻은 농축물로서 안트라퀴논계 화합물인 카르민산(Carminic acid)이 색소의 주성분이며 가공식품, 화장품, 직물, 의약품 등의 천연색소로 이용되고 있음
- 물, 에탄올, 에테르에 쉽게 녹고 벤젠, 클로로포름, 유지에는 녹지 않음
- pH 의존성이 매우 높아 Halochromism 현상을 나타냄
- 산성(pH 3 이하)에서는 등적색, pH 5-6에서는 적자색, pH 7 이상에서는 자색을 나타냄
- 코치닐추출색소가 각종 알레르기성 질환을 유발할 수 있음이 보고됨

### 분석사례

- 차뜨래 딸기라떼 : Carminic acid 검출
- 난새콤달콤한생맥차야 : Carminic acid 검출
- 복분자차, 석류차, 오미자차 : Carminic acid 검출

## ■ 분석법

### 1. HPLC법

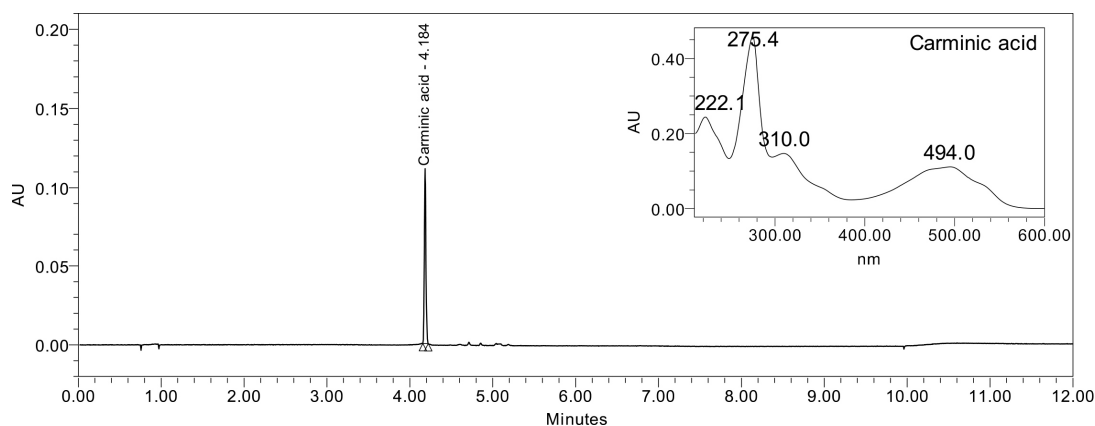
#### ○ 전처리 방법

- 표준액 조제 : Carminic acid
  - 약 20 mg 취함 → 50% 메탄올:10% 염산(4:1) 용액을 가함
  - 일정량 취함 → 50% 메탄올:10% 염산(4:1) 용액으로 희석
  - 최종 농도(약 1.0 mg/mL)
- 검액 조제 : 약 10 g 취함 → 50% 메탄올:10% HCl(4:1), *n*-Hexane 가함
  - 30분 진탕 → 원심분리 후 메탄올 층 취함

#### ○ Analytical condition of HPLC

• Instrument	Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)		
• Column Temp.	30℃		
• Mobile Phase	(A) 0.1% Trifluoroacetic acid in Water		
	(B) 0.1% Trifluoroacetic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	2.0	90	10
	6.0	50	50
	6.1	10	90
	9.0	10	90
	9.1	90	10
	12.0	90	10
• Flow Rate	0.3 mL/min		
• Inj. Volume	5.0 μL		
• UV Detection	495 nm		
• PDA Range	210~600 nm		

○ Chromatogram & PDA Spectrum



2. LC-MS/MS법

○ Analytical conditions of HPLC

• Instrument	Waters ACQUITY UPLC
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.7 μm)
• Column Temp.	40°C
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile

Time (min)	A (%)	B (%)
0.0	95	5
2.0	95	5
6.0	60	40
8.0	60	40
8.1	10	90
10.0	10	90
10.1	95	5
12.0	95	5

• Flow Rate	0.2 mL/min
• Inj. Volume	2 μL

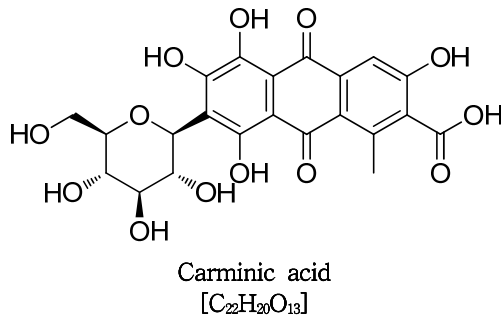
○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (-)
• Capillary Voltage	2.5 kV
• Desolvation Temp.	400°C
• Desolvation Gas Flow	600 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	50 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion (m/z)	CV (V)	Product ion (m/z)	CE (eV)
Carminic acid	-	491.12	35	326.90	24
				356.91	25
				446.93	20

■ 구조식



■ 참고문헌

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2. Kunkely H and Vogler A. Absorption and luminescence spectra of cochineal. *Inor Chem Commun.* 13, 1153-1155 (2011)

## III-20 통캣알리 성분 분석법

### 배 경

- 통캣알리는 말레이시아, 인도네시아 등 동남아 지역에서 자라는 식물로 남성 성기능 촉진에 효능이 있다고 알려지면서 인터넷을 통해 암암리에 판매됐으나, 우리나라를 비롯한 유럽, 미국, 일본 등 대부분 국가에서는 안전성 문제 때문에 식품 원료로 승인되지 않음
- 통캣알리 원 제품과 함께 함유 제품 또한 우리나라에 정식으로 수입 되지 않음



### 특 성

- 말레이시아 원주민들 사이에서 말라리아 예방제, 최음제, 당뇨병 치료제, 살균제, 해열제 등으로 사용되고 있고, 특히 성기능 개선을 위한 정력강장제로 많이 이용되고 있음
- 정확한 성분이나 효과, 효능 및 독성 평가가 이뤄지지 않은 상태에서 말레이시아를 비롯한 아시아 및 기타 국가에서 유통이 이뤄지고 있음
- 주요성분: 13,21-Dihydroeurycomanone, 14,15β-Dihydroxyklaineanone, Eurycomalactone, Eurycomanone, Longilactone

### 분석사례

- TONGKAT ALI : 통캣알리 성분 검출

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Eurycomalactone 등 5종  
→ 일정량 취함 → 100% 메탄올 가함 → 최종 농도(약 30~50 µg/mL)
- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 10 mL 정용 → 3시간 진탕  
→ 5분간 원심분리 → 상정액 취함

\* 표준액 : 13,21-Dihydroeurycomanone, 14,15β-Dihydroxyklaineanone, Eurycomalactone, Eurycomanone, Longilactone

#### ○ Analytical condition of HPLC

• Instrument	Shiseido SP LC
• Column	Agilent Pursuit Ultra XRs C18 (2 mm × 100 mm, 2.8 µm)
• Column Temp.	40°C
• Mobile Phase	(A) 0.1% Formic acid in Water (B) 0.1% Formic acid in Acetonitrile

Time (min)	A (%)	B (%)
0.0	95	5
2.0	95	5
8.0	0	100
10.0	0	100
10.1	95	5
12.0	95	5

• Flow Rate	0.25 mL/min
• Inj. Volume	2 µL

#### ○ Analytical conditions of LC-MS/MS

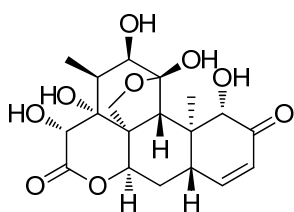
• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (+)
• Curtain Gas	30 psi
• Collision Gas	12
• Ion Voltage	5000 V
• Ion Source Gas 1	50 psi
• Ion Source Gas 2	50 psi
• Source Temp.	500°C



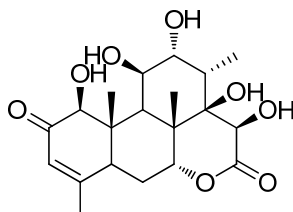
○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion ( <i>m/z</i> )	CV (V)	Product Ion ( <i>m/z</i> )	CE (V)	CXP (V)
13,21-Dihydroeurycomanone	+	411.2	70	393.2	25	13
				375.2	31	13
				345.1	35	13
14,15β-Dihydroxyklaineaneone	+	397.2	70	343.2	19	13
				361.2	19	13
				379.2	17	13
Eurycomalactone	+	349.1	130	331.1	25	13
				303.0	25	13
				313.1	27	13
Eurycomanone	+	409.2	76	391.1	21	16
				165.1	93	20
Longilactone	+	367.1	121	331.0	19	14
				313.1	23	12

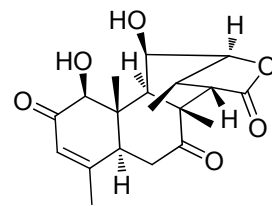
■ 구조식



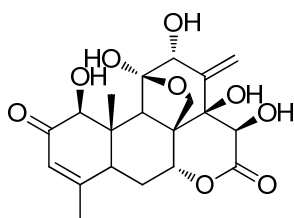
13,21-Dihydroeurycomanone  
[C<sub>19</sub>H<sub>24</sub>O<sub>8</sub>]



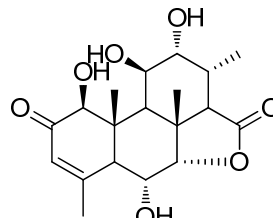
14,15β-Dihydroxyklaineaneone  
[C<sub>20</sub>H<sub>28</sub>O<sub>8</sub>]



Eurycomalactone  
[C<sub>19</sub>H<sub>24</sub>O<sub>6</sub>]



Eurycomanone  
[C<sub>20</sub>H<sub>24</sub>O<sub>9</sub>]



Longilactone  
[C<sub>19</sub>H<sub>26</sub>O<sub>7</sub>]

## ■ 참고문헌

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## III-21 푸에라리아 미리피카 성분 분석법

### 배 경

- 안전성이 미확보 되어 식품용으로 사용할 수 없는 원료인 태국췌(*Pueraria mirifica*)이 함유된 제품을 가슴 확대 효과가 있다고 광고하며 인터넷 블로그나 중고거래 인터넷을 통해 몰래 판매한 일당이 적발('14. 9.)
- *Pueraria mirifica*와 비슷한 isoflavone 화합물(에스트로젠 활성, 항산화 활성)을 함유하고 있는 유사 식물인 한국산 췌(*Pueraria thunbergiana*) 및 *Pueraria lobata*가 혼용될 가능성이 있으므로 성분 확보 또는 유전자 분석을 통해 시료의 동등성이나 분별에 필요한 방법의 확립 필요



### 특 성

- 태국췌는 에스트로젠(여성호르몬) 활성, 폐경기 여성의 골다공증 예방 및 치료에 효과가 있다고 보고되었고 가슴이 커질 수 있지만, 동물실험 결과 적혈구와 백혈구 감소 및 자궁비대 등의 부작용 확인됨
- 수입된 제품을 섭취한 소비자 중 상당수는 하혈을 하거나 생리가 멎지 않는 부작용 사례 보고됨
- 주요성분: Miroestrol, Isomiroestrol

### 분석사례

- 가슴발육제: Miroestrol, Isomiroestrol 검출

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Miroestrol → 일정량 취함 → 100% 메탄올 가함  
→ 최종 농도(약 20~100 µg/mL)
- Isomiroestrol → 일정량 취함 → 100% 메탄올 가함  
→ 최종 농도(약 10~50 µg/mL)

- 검액 조제 : 약 1 g 취함 → 70% 메탄올 가함 → 30분 진탕 → 50 mL 정용

\* 표준액 : Miroestrol, Isomiroestrol

#### ○ Analytical condition of HPLC

- Instrument Shiseido SP3133
- Column Waters XBridge C<sub>18</sub> (2.1 mm × 150 mm, 3.5 µm)
- Column Temp. 40°C
- Mobile Phase (A) 0.1% Formic acid in Water  
(B) 0.1% Formic acid in Acetonitrile

Time (min)	A (%)	B (%)
0.0	90	10
3.0	90	10
8.0	50	50
12.0	5	95
15.0	5	95
15.1	90	10
20.0	90	10

- Flow Rate 0.25 mL/min
- Inj. Volume 2 µL

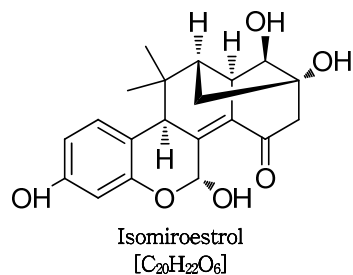
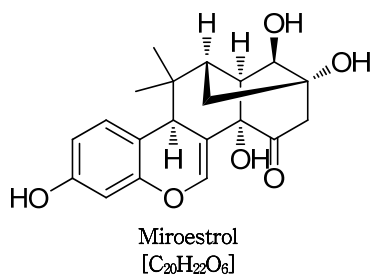
○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (-)
• Curtain Gas	30 psi
• Collision Gas	9 psi
• Ion Voltage	4500 V
• Ion Source Gas 1	50 psi
• Ion Source Gas 2	50 psi
• Source Temp.	450°C

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor ion ( <i>m/z</i> )	CV (V)	Product ion ( <i>m/z</i> )	CE (V)	CXP (V)
Miroestrol	-	357.1	150	188.9	44	19
				144.8	44	13
				108.9	40	13
				120.9	46	9
Isomiroestrol	-	357.1	120	108.9	38	7
				297.0	32	9
				120.8	40	9
				269.0	38	21

■ 구조식



## 2. 유전자 분석법

### ○ PCR을 위한 주형유전자의 준비

#### - 유전자추출키트(DNeasy Mini Kit) 이용하여 추출

(재현성 및 검출효율 등을 고려하여 QIAGEN DNA Mini Kits 또는 동등 이상의 제품 사용 가능)

• <b>검액 조제</b>	① 약 100 mg을 취함
	② 400 $\mu$ L의 Buffer AP1, 4 $\mu$ L의 RNase A를 가함 → Vortex Mixer를 사용하여 균질화 → 65°C incubator에 2시간 방치
	③ 130 $\mu$ L의 Buffer AP2 가함 → Vortex Mixer를 사용하여 균질화 → 5분간 ice에 방치
	④ 8분간 14,000 rpm에서 원심 분리 → 상층액을 취함 → IAshredder spin column에 넣고 2분간 14,000 rpm에서 원심 분리
	⑤ column을 통과한 액을 새로운 tube에 옮김 → 이의 1.5배의 Buffer AP3/E를 가하고 균질화
	⑥ 650 $\mu$ L를 취함 → DNeasy Mini spin column에 넣고 1분간 8,000 rpm에서 원심 분리 → 통과한 액을 버림
	⑦ ⑥ 반복
	⑧ Spin column을 새로운 2 mL collection tube에 넣음 → 500 $\mu$ L의 Buffer AW를 가함 → 1분간 8,000 rpm에서 원심 분리 → 통과한 액을 버림
	⑨ ⑧번 반복
	⑩ Column을 새로운 1.5 mL 또는 2 mL microcentrifuge tube에 옮김 → 60 $\mu$ L의 증류수 가함 → 15분간 실온에서 방치
	⑪ 1분간 8,000 rpm에서 원심 분리 → 통과된 액을 취함
• <b>농도 확인</b>	DNA 원액을 TE 완충액(pH 8.0) 또는 멸균증류수로 적절히 희석 → 분광광도계를 사용하여 260 nm에서 흡광도(Absorbance, A) 측정 → 그 값이 1일 때 DNA 농도가 50 ng/ $\mu$ L인 것으로 하여 계산

- **순도 확인** : 230, 260, 280 nm에서 흡광도를 각각 측정
  - $A_{260}/A_{280}$ 과  $A_{260}/A_{230}$ 이 1.7~2.0일 경우 PCR에 적합한 DNA로 판단
  - ※ 단, 가공식품의 경우 이러한 순도 적용이 어려운 경우가 있으므로 반드시 적용되는 것은 아님
  - ※  $A_{260}/A_{280}$ 이 낮아 단백질 유래 불순물의 혼입이 우려되는 경우
    - 단백질 분해효소(protease)로 처리한 후 DNA 회수
  - ※  $A_{260}/A_{230}$ 이 낮을 경우
    - 전분 분해효소(amylose)로 처리한 후 DNA를 회수하여 PCR에 사용

○ PCR을 위한 프라이머 염기서열

구분	프라이머 명	염기서열(5'-3')	예상 크기 (bp)	비고
태국취	SFI12-Miri-F	TCT CAC ACG ACA CGT TCT G	216	ITS2
	SFI12-Miri-R	TCT CGT TGA GAG CGT CTC CCC GAA		

○ PCR 반응액 조제

성분	최종농도	Stock용액농도	1회용량	비고
완충액	1×	10×	2.5 $\mu$ L	
MgCl <sub>2</sub>	2.5 mM	25 mM	2.5 $\mu$ L	
dNTPs	200 $\mu$ M	2.5 mM	2 $\mu$ L	
프라이머(F)	10 pmole/tube	100 pmole/ $\mu$ L	1 $\mu$ L	
프라이머(R)	10 pmole/tube	100 pmole/ $\mu$ L	1 $\mu$ L	
주형DNA	25~50 ng 또는 5 $\mu$ L	-	3 $\mu$ L	
Taq	2.5 U/tube	5 U/ $\mu$ L	0.5 $\mu$ L	
증류수	-	-	12.5 $\mu$ L	
전체량	-	-	25 $\mu$ L	

○ PCR 반응조건

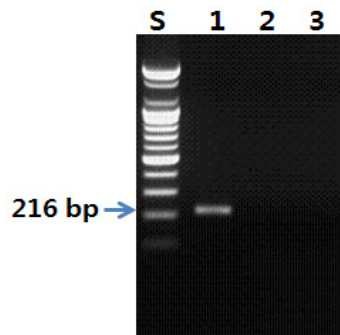
구분	온도	시간	반복 수	비고
초기변성(Initial denaturation)	95℃	5분	1	
변성(Denaturation)	95℃	30초		
결합(Annealing)	65℃	30초	30	
신장(Extension)	72℃	30초		
최종신장(Elongation)	72℃	5분	1	
보존	4℃	-	-	

○ 결과 확인

- 결과 확인 : PCR 반응 후 최종산물의 확인은 반응액 5  $\mu$ L를 취함  
 → 1.5% SeaKEM LE agarose로 100 V, 30분간 전기영동  
 → UV투영기를 이용하여 확인

○ 유전자 증폭산물의 결과 판정

- PCR 산물 확인: 종 특이 프라이머(Species-specific primer)를 사용한 PCR 결과 산물의 생성유무 및 크기를 확인한 후, PCR 산물에 대하여 염기서열을 결정하고 유전자 DB를 이용하여 종 동정을 수행

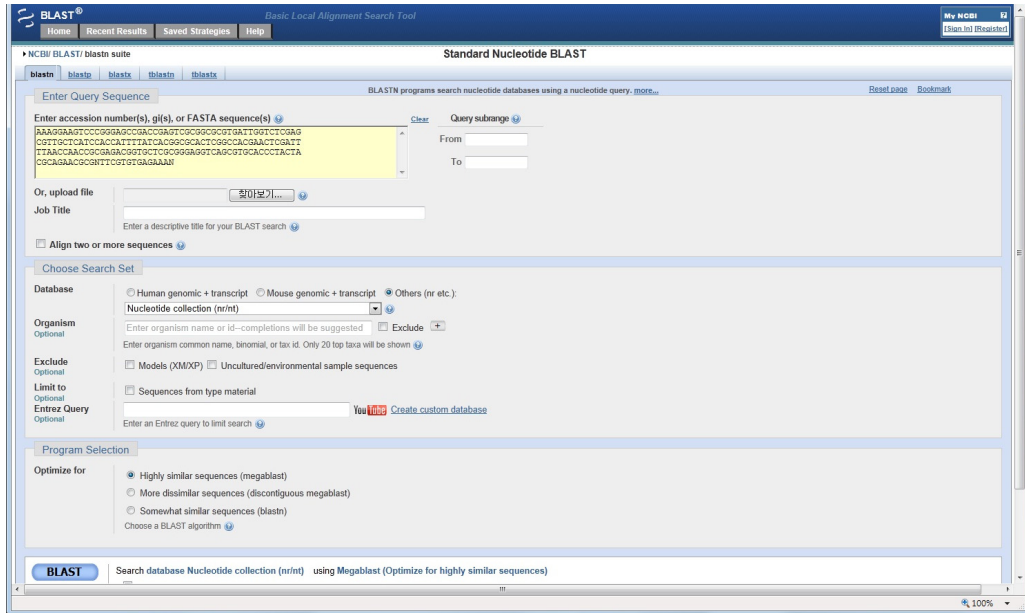


태국참 프라이머를 이용한 PCR 결과  
 Lane 1 ; 태국참(*Pueraria mirifica*), lane 2 ; 국산참(*Pueraria lobata*), lane 3 ; 태국참(*Butea superba*)

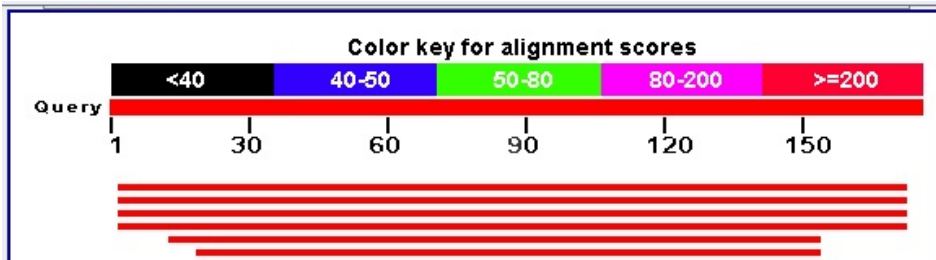
- 염기서열 분석: 일반 프라이머(universal primer)를 사용한 경우 PCR 산물은 염기서열을 결정하고 NCBI([www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) 등 유전자 DB를 사용하여 최종 동정을 실시



① Blast 등의 프로그램을 이용하여 염기서열 입력



② 입력된 자료는 DB내의 염기서열 자료와 비교



③ 염기서열을 분석하여 가장 근접한 종과의 일치도를 나타냄

Descriptions

Sequences producing significant alignments:

Select All None Selected 0

Alignments Download GenBank Graphics Distance tree of results

Description	Max score	Total score	Query cover	E value	Ident	Accession
<input type="checkbox"/> <i>Pueraria candollei</i> var. <i>merficia</i> isolate Ref-2 internal transcribed spacer 1, partial sequence, 5.8S ribosomal RNA gene, complete sequence, and internal transcribed spaco	272	272	97%	8e-70	95%	KC817872.1
<input type="checkbox"/> <i>Pueraria candollei</i> var. <i>merficia</i> isolate Ref-1 internal transcribed spacer 1, partial sequence, 5.8S ribosomal RNA gene, complete sequence, and internal transcribed spaco	272	272	97%	8e-70	95%	KC817871.1
<input type="checkbox"/> <i>Dianthus barbatus</i> var. <i>merficia</i> 5.8S ribosomal RNA gene, partial sequence, internal transcribed spacer 2, complete sequence, and 5.8S ribosomal RNA gene, partial seq	267	267	97%	8e-69	95%	J088463.1

## ■ 참고문헌

1. Ji Hyun Lee, Jung Yeon Kim, So-Hyun Cho, Ji Hye Jeong, Sooyeul Cho, Hyoung Joon Park, and Sun Young Baek. Determination of Miroestrol and Isomiroestrol From *Pueraria mirifica*(White Kwao Krua) in Dietary Supplements by LC-MS-MS and LC-Q-Orbitrap/MS. *Journal of Chromatographic Science*, 2017, Vol. 55, No. 3, 214-221
2. Satoko Shimokawa, Takuya Kumamoto, Tsutomu Ishikawa, Miho Takashi, Yoshihiro Higuchi, Chaiyo Chaichantipyuth and Sunee Chansakaow. Quantitative analysis of miroestrol and kwakhurin for standardisation of Thai miracle herb 'Kwao Keur' (*Pueraria mirifica*) and establishment of simple isolation procedure for highly estrogenic miroestrol and deoxymiroestrol. *Nat Prod Res*, 27(4 - 5), 371 - 378 (2013)
3. Sunee Chansakaow, Tsutomu Ishikawa, Hiroko Seki, Keiko Sekine (née Yoshizawa), Mineaki Okada, and Chaiyo Chaichantipyuth. Identification of Deoxymiroestrol as the Actual Rejuvenating Principle of "Kwao Keur", *Pueraria mirifica*. The Known Miroestrol May Be an Artifact. *J Nat Prod*. 63(2), 173-175 (2010)
4. Yong-Chjun Park, Sang-Wook Jin, Mi-Ra Kim, Kyu-Heon Kim, Jae-Hwang Lee, Tae-Yong Cho, Hwa-Jung Lee, Sang-Jae Lee, and Sang-Bae Han. Detection Method for Identification of *Pueraria mirifica* (Thai kudzu) in Processed Foods. *J Fd Hyg Safety*. 27(4), 466-472 (2012)

## III-22 < 프탈레이트(6종) 분석법

### ■ 배 경

- PVC 수액용기 ‘환경호르몬’에 무방비('05. 5.)
- PVC 의료용품 이용환자, 환경호르몬 일반인의 8배('07. 5.)
- 발암물질 프탈레이트 함유 수액세트 제조 금지('15. 6.)
- 환경호르몬 프탈레이트, 어린이 지능·주의력 떨어뜨려('17. 4.)
- 美시판 가루치즈 마카로니서 환경호르몬 프탈레이트 검출('17. 7.)



### ■ 특 성

- 프탈레이트는 딱딱한 플라스틱을 부드럽게 만들어주는 플라스틱 가소제로 화장품, 장난감, 세제 등 각종 PVC 제품 및 향수의 용매, 가정용 바닥재 등 광범위한 용도로 쓰임
- 환경호르몬의 일종인 프탈레이트는 인체 내분비계 교란을 가져옴
- DEHP, DBP, BBP 등 3종의 프탈레이트계 가소제가 발암성과 변이독성, 재생독성이 있는 물질임
- 프탈레이트류(DEHP, DBP, BBP)는 화장품 중 배합금지 성분임.

### ■ 분석 사례

- 수액세트 : DEHP 1.40 mg/g 검출

## ■ 분석법

### 1. GC/MS 법

#### ○ 전처리 방법

<ul style="list-style-type: none"> <li>표준액 조제 : Dibutyl phthalate 등 6종*</li> </ul>
(의료기기류) : → 각각 일정량 취함 → 아세토니트릴:테트라하이드로퓨란(2:1) 가함 → 혼합액 0.5 mL과 내부표준용액*** 0.5 mL 혼합 → 최종농도(약 5 µg/mL)
(화장품 등) : → 각각 일정량 취함 → 헥산:아세톤(8:2) 가함 → 일정량 취함 → 내부표준용액 4 mL 가함 → 헥산:아세톤(8:2)으로 10 mL 정용 → 최종농도(약 25 µg/mL)
<ul style="list-style-type: none"> <li>검액 조제</li> </ul>
(의료기기류) : 약 50 mg 유리 삼각플라스크에 취함 → 테트라하이드로퓨란 5 mL 가함 → 30분간 진탕 → 아세토니트릴 10 mL 가함 → 혼합 후 10분 방치 후 필터 → 혼합액 0.5 mL과 내부표준용액 0.5 mL 혼합
(화장품 등) : 약 1 g 유리 삼각플라스크에 취함 → 헥산:아세톤(8:2) 10 mL 가함 → 30분간 진탕 후 원심분리(2,400 rpm, 10분) → 상등액 5 mL을 취함 → 내부표준용액 4 mL 가함 → 헥산:아세톤(8:2)으로 10 mL 정용

\* 전처리 방법에 이용된 모든 초자 기구는 glass 이용

\*\* 표준액 : Dibutyl phthalate(DBP), Benzyl butyl phthalate(BBP), Bis (2-ethylhexyl) adipate(DEHA), Bis (2-ethylhexyl) phthalate(DEHP), Di-n-octyl phthalate(DNOP), Dioctyl terephthalate(DOTP)

\*\*\* 내부표준용액 : Benzyl benzoate(BB)  
 의료기기류 → 아세토니트릴:테트라하이드로퓨란(2:1)에 녹임 → 최종농도(약 1 mg/mL)  
 화장품 등 → 헥산:아세톤(8:2)에 녹임 → 최종농도(약 1 mg/mL)

#### ○ Analytical conditions of GC

• Instrument	Agilent, 7890A
• Column	Agilent DB-5MS (30 m × 0.25 mm, 0.25 µm)
• Oven Temp.	150°C(3 min) → 10°C/min → 300°C(12 min)
• Inj. Temp.	300°C
• Transfer Line	280°C
• Inj. Mode	Splitless mode (purge to split vent 50 mL/min, 1.5 min)
• Carrier Gas	He, 1 mL/min
• Inj. Volume	1 µL

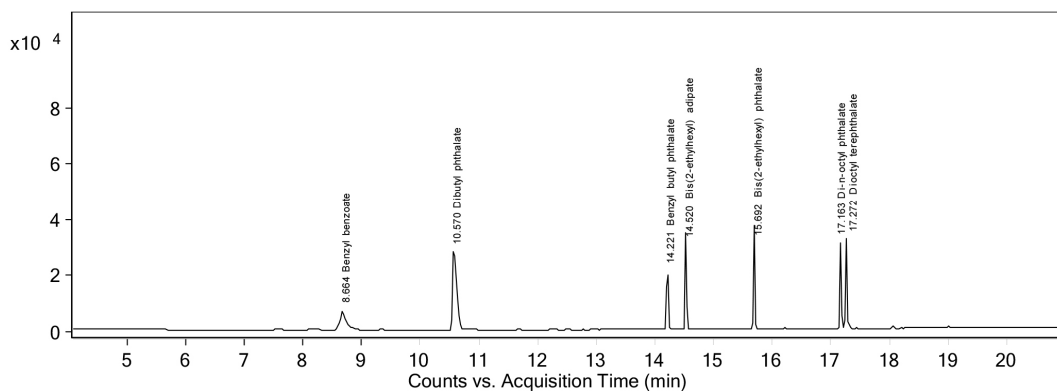
○ Analytical condition of GC-MS : SIM and Scan

• Instrument	Agilent, GC/MSD, 5975C
• Ionization Mode	EI
• Ionization Energy	70 eV
• Source Temp.	230°C
• Quad Temp.	150°C
• Mass Mode	SIM and Scan
• Scan Range	50~500 amu
• SIM Dwell Time	100 ms

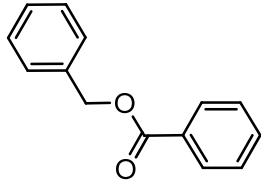
- SIM ions

Compound	Ion ( <i>m/z</i> )		
Benzyl benzoate(I.S)	105	212.1	194.1
Dibutyl phthalate	149.1	223	205
Benzyl butyl phthalate	149.1	91	206
Bis (2-ethylhexyl) adipate	129.1	112	147
Bis (2-ethylhexyl) phthalate	149.1	167	279
Di-n-octyl phthalate	149.1	279	261
Diethyl terephthalate	261		

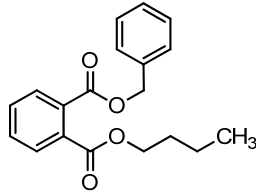
○ Chromatogram



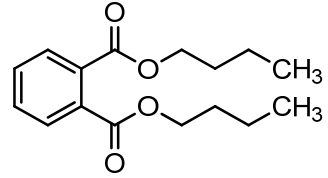
## ■ 구조식



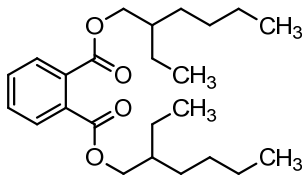
Benzyl benzoate  
[C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>]



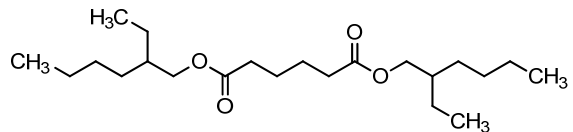
Benzyl butyl phthalate  
[C<sub>19</sub>H<sub>20</sub>O<sub>4</sub>]



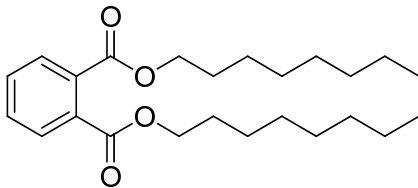
Dibutyl phthalate  
[C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>]



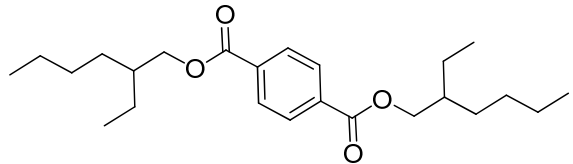
Bis(2-ethylhexyl) phthalate  
[C<sub>24</sub>H<sub>38</sub>O<sub>4</sub>]



Bis(2-ethylhexyl) adipate  
[C<sub>22</sub>H<sub>42</sub>O<sub>4</sub>]



Di-n-octyl phthalate  
[C<sub>24</sub>H<sub>38</sub>O<sub>4</sub>]



Dioctyl terephthalate  
[C<sub>24</sub>H<sub>38</sub>O<sub>4</sub>]

## ■ 참고문헌

1. 고분자 재료 중의 프탈레이트계 가소제 정량 방법, 산업표준심의회 (2015)
2. 화장품 원료지정에 관한 규정 전부 개정고시, 식품의약품안전처 고시 제2013 - 2호 (2013)
3. Amayreh Mousa, Chanbasha Basheer, Abdul Rahman Al-Arfaj, Determination of phthalate esters in bottled water using dispersive liquid - liquid microextraction coupled with GC - MS, J . Sep. Sci., 36, 2003-2009 (2013)

## Ⅲ-23 < 화장품 중 스테로이드류(43종) 분석법

### ■ 배 경

- 주름완화, 여드름 예방 효과가 탁월한 화장품에서 스테로이드 성분 대거 검출('13. 9.)
- 스테로이드 성분이 포함된 아토피크림을 생약성분의 천연아토피 크림이라고 허위·과대 광고하여 판매한 판매업자 적발('15. 6.)



### ■ 특 성

- 스테로이드
  - 스테로이드 핵인 cyclopentanoperhydrophenanthrene을 갖는 화합물군의 총칭
  - 당질 코르티코이드류는 코르티손, 코르티솔, 코르티코스테론 등이 포함된 부신피질에서 합성분비되는 스테로이드 호르몬
  - 지금까지 개발된 물질 중 가장 강력한 항염증제로 아토피나 건선습진과 같은 피부질환 등 여러 가지 질병치료제로 쓰임
  - 피부에 장기 도포할 경우 모낭염, 혈관확장, 피부 괴사 등 부작용이 나타날 수 있음

### ■ 분석 사례

- 아토피 크림: Betamethasone dipropionate 835  $\mu\text{g/g}$  검출
- 화장품: Betamethasone 29.2~331  $\mu\text{g/g}$  검출  
 Clobetasol propionate 66.0~119  $\mu\text{g/g}$  검출  
 Triamcinolone acetonide 15.2~28.6  $\mu\text{g/g}$  검출

## ■ 분석법

### 1. LC-MS/MS법

#### ○ 전처리 방법

- 표준액 조제 : Prednisolone 등 43종\*
  - 각각 일정량 취함 → 내부표준물질 250  $\mu$ L 가함
  - 100% 메탄올 가함 → 최종 농도(약 1  $\mu$ g/mL)
- 검액 조제 : 약 1 g 취함 → 내부표준물질 250  $\mu$ L 가함
  - 0.1% 포름산 1 mL 가함 → 100% 메탄올 가함 → 30분 진탕
  - 10 mL 정용 → 원심분리(2,500 rpm, 10분) → 상층액 4 mL 취함
  - 0.1% 포름산 80% 메탄올 가함 → 20 mL 정용

\* 표준액 : Prednisolone, Hydrocortisone, Betamethasone, Dexamethasone, Prednisone 21-acetate, Cortisone 21-acetate, Prednisolone 21-acetate, Hydrocortisone 21-acetate, Hydrocortisone 17-acetate, Beclomethasone, Budesonide, Betamethasone 21-acetate, Dexamethasone 21-acetate, Triamcinolone acetonide, Methylprednisolone, Hydrocortisone 17-valerate, Hydrocortisone 21-valerate, Beclomethasone 21-acetate, Beclomethasone 21-propionate, Beclomethasone 17-propionate, Clobetasol 17-propionate, Betamethasone 17-valerate, Betamethasone 21-valerate, Triamcinolone diacetate, Dexamethasone 21-hemisuccinate, Fluticasone propionate, Betamethasone 21-hemisuccinate, Betamethasone 17,21-dipropionate, Prednisone, 6 $\alpha$ -Methylprednisolone, Beclomethasone 21-hemisuccinate, Beclomethasone 17,21-dipropionate, Amcinonide, Fludrocortisone acetate, Fluticasone furoate, Clobetasone butyrate, Flucinolone acetonide, Dichlorisone acetate, 6 $\alpha$ -Methylprednisolone aceponate, Flurandrenolide, Hydrocortisone 17-butyrate, Hydrocortisone 21-hemisuccinate, Mometasone furoate

\* 내부 표준액 : Triamcinolone-6-d<sub>1</sub> acetonide-d<sub>8</sub> (100% 메탄올에 녹임, 최종농도 200  $\mu$ g/mL)

#### ○ Analytical conditions of HPLC

• Instrument	UPLC Waters ACQUITY UPLC		
• Column	Waters ACQUITY UPLC BEH C <sub>18</sub> (2.1 mm × 100 mm, 1.8 $\mu$ m)		
• Column Temp.	35°C		
• Mobile Phase	A: 0.1% Formic acid in Water B: 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	80	20
	3.0	80	20
	13.0	40	60
	17.0	0	100
	22.0	0	100
	22.1	80	20
	25.0	80	20
• Flow Rate	0.25 mL/min		
• Inj. Volume	3 $\mu$ L		



○ Analytical conditions of LC-MS/MS

• Instrument	Waters Xevo TQ
• Ionization Mode	ESI (+)
• Capillary Voltage	2.7 kV
• Desolvation Temp.	500°C
• Desolvation Gas Flow	400 L/Hr (N <sub>2</sub> )
• Cone Gas Flow	60 L/Hr (N <sub>2</sub> )

○ Analyte MS/MS transition

Compound	Ion mode	Precursor ion (m/z)	CV (v)	Product Ion (m/z)	CE (eV)
Prednisone	+	359.40	20	146.90	20
				170.92	25
				265.03	15
Prednisolone	+	361.44	15	307.07	10
				325.09	10
				343.09	10
Hydrocortisone	+	363.45	25	120.85	25
				309.07	15
				327.07	15
6α-Methylprednisolone	+	375.46	15	321.10	13
				339.10	10
				357.10	10
Betamethasone	+	393.46	20	279.05	20
				355.10	10
				373.08	10
Dexamethasone	+	393.20	15	237.00	15
				355.11	10
				373.12	10
Prednisone 21-acetate	+	401.45	18	313.05	15
				341.05	10
				383.06	10
Prednisolone 21-acetate	+	403.48	15	307.04	15
				325.10	10
				385.10	10

Compound	Ion mode	Precursor ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Cortisone 21-acetate	+	403.48	30	162.90	25
				325.10	20
				343.10	20
Hydrocortisone 21-acetate	+	405.50	25	241.00	20
				309.10	15
				327.05	15
Hydrocortisone 17-acetate	+	405.50	25	309.10	15
				327.05	15
				345.10	15
Beclomethasone	+	409.43	20	279.05	20
				373.10	10
				391.05	10
Fludrocortisone acetate	+	423.46	25	239.00	25
				325.10	20
				343.05	20
Budesonide	+	431.50	20	323.05	16
				395.10	10
				413.10	10
Hydrocortisone 17-butyrate	+	433.50	25	309.05	20
				327.10	15
				345.10	15
Betamethasone 21-acetate	+	435.45	15	237.00	20
				279.10	15
				397.10	10
Dexamethasone 21-acetate	+	435.45	15	237.00	20
				309.05	15
				397.10	10
Triamcinolone acetonide	+	435.45	20	339.10	15
				397.10	15
				415.10	15
Flurandrenolide	+	437.50	30	225.00	25
				341.10	20
				361.10	20

III-23. 화장품 중 스테로이드류(43종) 분석법

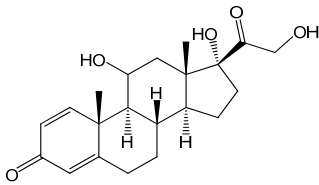
Compound	Ion mode	Precursor ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Triamcinolone-6-d <sub>1</sub> acetone-d <sub>6</sub> (I.S)	+	442.30	15	340.17	15
				404.30	15
				422.25	15
Hydrocortisone 21-valerate	+	447.50	25	309.10	20
				327.10	20
				345.10	20
Hydrocortisone 17-valerate	+	447.50	25	120.85	25
				309.10	20
				345.10	15
Beclomethasone 21-acetate	+	451.45	20	319.05	15
				397.10	10
				433.10	10
Fluocinolone acetonide	+	453.45	20	337.05	15
				413.10	10
				433.10	10
Dichlorisone acetate	+	455.09	15	237.00	20
				305.05	15
				419.05	10
Hydrocortisone 21-hemisuccinate	+	463.50	25	309.05	15
				327.05	15
				445.10	10
Beclomethasone 21-propionate	+	465.45	15	319.05	20
				411.10	10
				447.10	10
Beclomethasone 17-propionate	+	465.45	15	337.10	15
				355.10	10
				447.10	10
Clobetasol 17-propionate	+	467.45	15	355.10	15
				373.05	10
				447.10	10
6 $\alpha$ -Methylprednisolone aceponate	+	473.52	15	303.10	15
				381.10	10
				455.10	10

Compound	Ion mode	Precursor ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Betamethasone 21-valerate	+	477.52	15	279.07	15
				355.10	10
				457.15	10
Betamethasone 17-valerate	+	477.52	15	279.07	15
				355.10	10
				457.15	10
Clobetasone butyrate	+	479.45	25	279.07	15
				343.10	15
				371.05	15
Triamcinolone diacetate	+	479.45	15	399.10	15
				441.10	10
				459.10	10
Dexamethasone 21-hemisuccinate	+	493.50	15	319.05	15
				337.05	15
				455.10	10
Betamethasone 21-hemisuccinate	+	493.50	15	319.05	15
				455.10	10
				475.15	10
Diflorasone diacetate	+	495.50	20	279.05	15
				317.05	15
				335.05	15
Fluticasone propionare	+	501.45	15	275.05	25
				293.05	15
				313.05	15
Amcinonide	+	503.52	15	339.05	15
				399.10	10
				483.15	10
Betamethasone 17,21-dipropionate	+	505.54	15	355.10	15
				411.15	10
				485.15	10
Beclomethasone 21-hemisuccinate	+	509.45	15	319.10	15
				437.10	10
				491.10	10

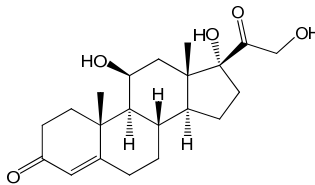
Compound	Ion mode	Precursor ion (m/z)	CV (V)	Product Ion (m/z)	CE (eV)
Mometasone furoate	+	521.42	15	279.10	20
				355.05	15
				503.05	10
Beclomethasone 17,21-dipropionate	+	521.42	15	319.10	15
				429.10	10
				503.15	10
Fluticasone furoate	+	539.45	15	204.90	20
				265.00	20
				275.00	20

- I.S: Internal Standard

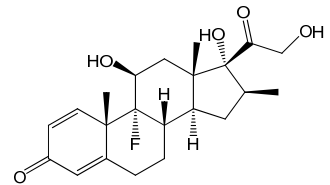
## ■ 구조식



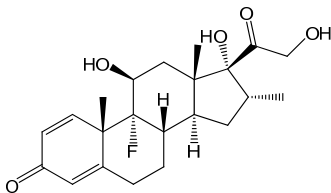
Prednisolone  
[C<sub>21</sub>H<sub>28</sub>O<sub>5</sub>]



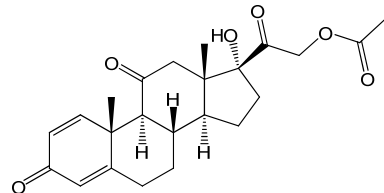
Hydrocortisone  
[C<sub>21</sub>H<sub>30</sub>O<sub>5</sub>]



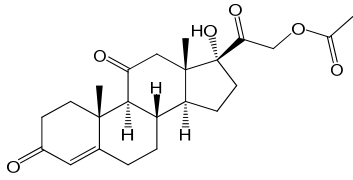
Betamethasone  
[C<sub>22</sub>H<sub>28</sub>FO<sub>5</sub>]



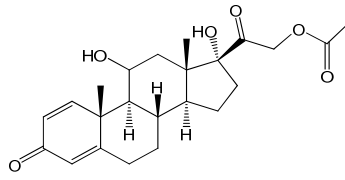
Dexamethasone  
[C<sub>22</sub>H<sub>28</sub>FO<sub>5</sub>]



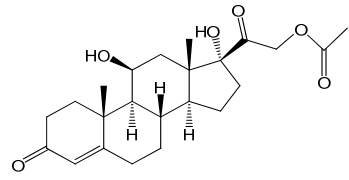
Prednisone-21-acetate  
[C<sub>23</sub>H<sub>28</sub>O<sub>6</sub>]



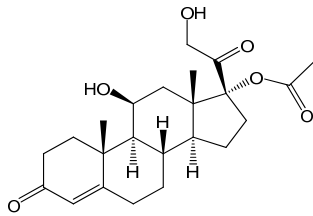
Cortisone-21-acetate  
[C<sub>23</sub>H<sub>30</sub>O<sub>6</sub>]



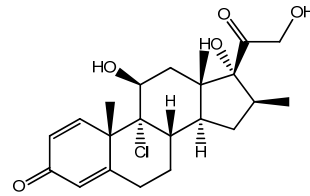
Prednisolone-21-acetate  
[C<sub>23</sub>H<sub>30</sub>O<sub>6</sub>]



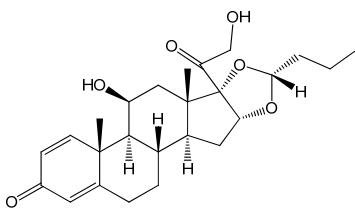
Hydrocortisone-21-acetate  
[C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>]



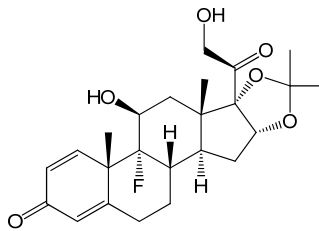
Hydrocortisone-17-acetate  
[C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>]



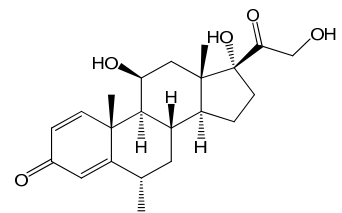
Beclomethasone  
[C<sub>22</sub>H<sub>29</sub>ClO<sub>5</sub>]



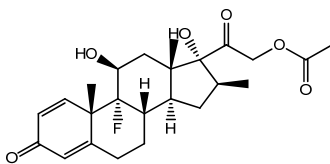
Budesonide  
[C<sub>25</sub>H<sub>34</sub>O<sub>6</sub>]



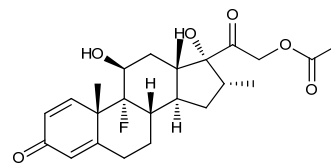
Triamcinolone acetonide  
[C<sub>24</sub>H<sub>31</sub>F<sub>2</sub>O<sub>6</sub>]



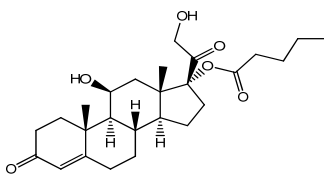
6α-Methylprednisolone  
[C<sub>22</sub>H<sub>30</sub>O<sub>5</sub>]



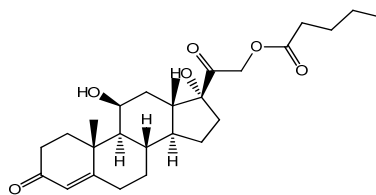
Betamethasone 21-acetate  
[C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>]



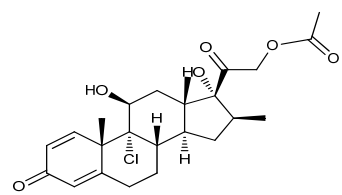
Dexamethasone 21-acetate  
[C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>]



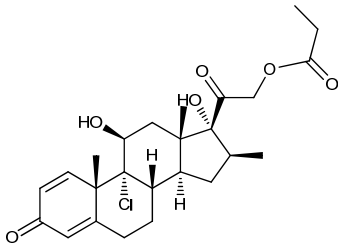
Hydrocortisone 17-valerate  
[C<sub>26</sub>H<sub>38</sub>O<sub>6</sub>]



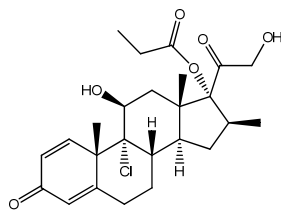
Hydrocortisone 21-valerate  
[C<sub>26</sub>H<sub>38</sub>O<sub>6</sub>]



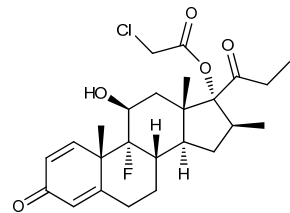
Beclomethasone 21-acetate  
[C<sub>24</sub>H<sub>31</sub>ClO<sub>6</sub>]



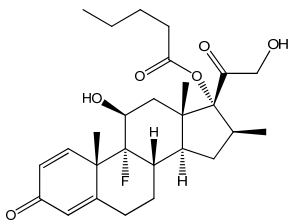
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[C<sub>25</sub>H<sub>33</sub>ClO<sub>6</sub>]



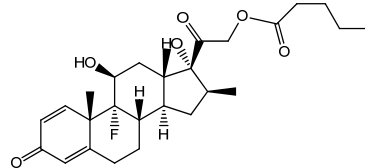
Beclomethasone 17-propionate  
[C<sub>25</sub>H<sub>33</sub>ClO<sub>6</sub>]



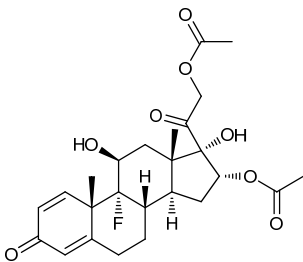
Clobetasol 17-propionate  
[C<sub>25</sub>H<sub>32</sub>ClFO<sub>5</sub>]



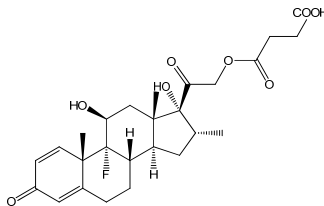
Betamethasone 17-valerate  
[C<sub>27</sub>H<sub>37</sub>FO<sub>6</sub>]



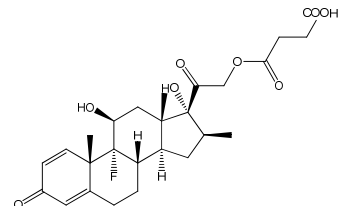
Betamethasone 21-valerate  
[C<sub>27</sub>H<sub>37</sub>FO<sub>6</sub>]



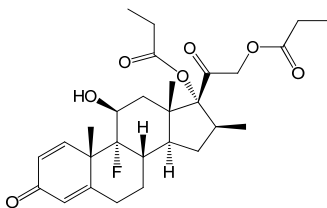
Triamcinolone diacetate  
[C<sub>25</sub>H<sub>31</sub>FO<sub>8</sub>]



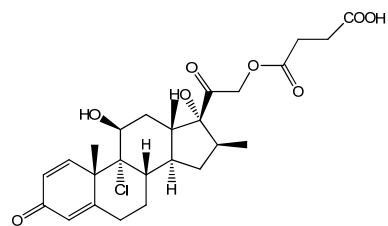
Dexamethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>FO<sub>8</sub>]



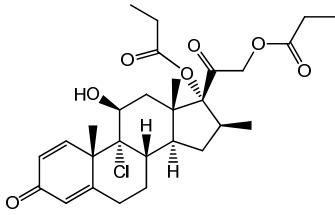
Betamethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>FO<sub>8</sub>]



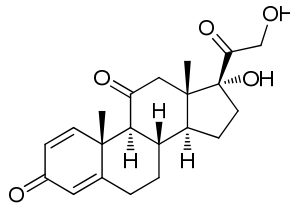
Betamethasone 17,21-dipropionate  
[C<sub>28</sub>H<sub>37</sub>FO<sub>7</sub>]



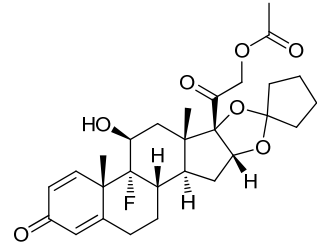
Beclomethasone 21-hemisuccinate  
[C<sub>26</sub>H<sub>33</sub>ClO<sub>8</sub>]



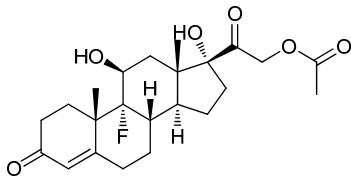
Beclomethasone 17,21-dipropionate  
[C<sub>28</sub>H<sub>37</sub>ClO<sub>7</sub>]



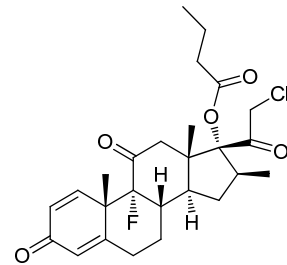
Prednisone  
[C<sub>21</sub>H<sub>26</sub>O<sub>5</sub>]



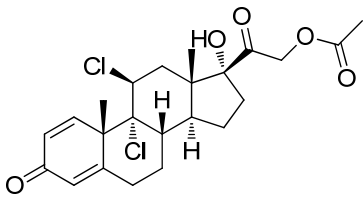
Amcinonide  
[C<sub>28</sub>H<sub>35</sub>FO<sub>7</sub>]



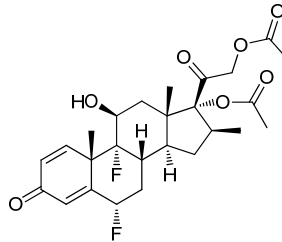
Fludrocortisone acetate  
[C<sub>23</sub>H<sub>31</sub>FO<sub>6</sub>]



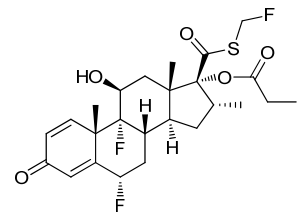
Clobetasone butyrate  
[C<sub>26</sub>H<sub>32</sub>ClFO<sub>5</sub>]



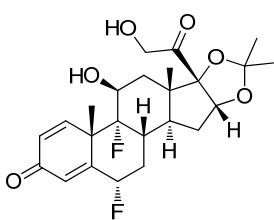
Dichlorisone acetate  
[C<sub>23</sub>H<sub>28</sub>Cl<sub>2</sub>O<sub>5</sub>]



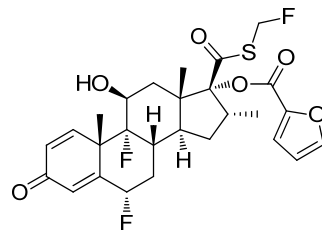
Diflorasone diacetate  
[C<sub>26</sub>H<sub>32</sub>F<sub>2</sub>O<sub>7</sub>]



Fluticasone propionate  
[C<sub>25</sub>H<sub>31</sub>F<sub>3</sub>O<sub>5</sub>S]

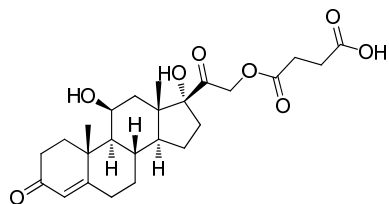


Fluocinolone acetonide  
[C<sub>24</sub>H<sub>30</sub>F<sub>2</sub>O<sub>6</sub>]

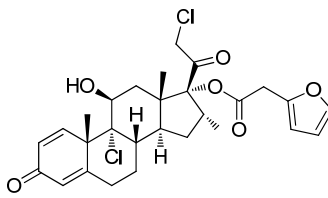


Fluticasone furoate  
[C<sub>27</sub>H<sub>29</sub>F<sub>3</sub>O<sub>6</sub>S]

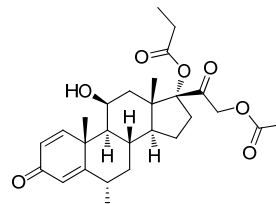




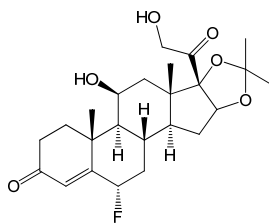
Hydrocortisone-21-hemisuccinate  
[C<sub>25</sub>H<sub>34</sub>O<sub>8</sub>]



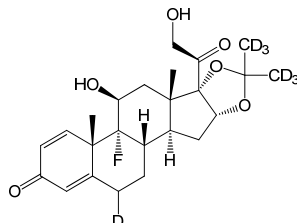
Mometasone furoate  
[C<sub>28</sub>H<sub>32</sub>O<sub>6</sub>Cl<sub>2</sub>]



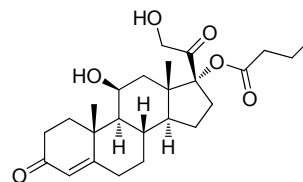
6α-Methylprednisolone aceponate  
[C<sub>27</sub>H<sub>36</sub>O<sub>7</sub>]



Flurandrenolide  
[C<sub>24</sub>H<sub>33</sub>FO<sub>6</sub>]



Triamcinolone-6-d<sub>1</sub>  
acetonide-d<sub>6</sub>(I.S)  
[C<sub>24</sub>H<sub>24</sub>D<sub>7</sub>FO<sub>6</sub>]



Hydrocortisone-17-butylrate  
[C<sub>25</sub>H<sub>36</sub>O<sub>6</sub>]

## ■ 참고문헌

1. Nam Sook Kim, Geum Joo Yoo, Ji Hyun Lee, Hyong-Joom Park, Sooyeul Cho, Dong Woo Shin, Younglim Kim and Sun Young Baek. Determination of 43 prohibited glucocorticoids in cosmetic products using a simultaneous LC-MS/MS method. *Analytical Methods*. DOI:10.1039/c6ay03065c
2. Jessica Fiori, Vincenza Andrisano. LC-MS method for the simultaneous determination of six glucocorticoids in pharmaceutical formulations and counterfeit cosmetic products. *J Phar. Bio Anal* 91, 185-192 (2014)
3. So Hyun Cho, Hyoung Joon Park, Ji Hyun Lee, Hyung Joo Kim, Soo yeul Cho, Chang-Yong Yoon, Woo Seong Kim. Monitoring of 35 illegally added steroid compounds in foods and dietary supplements. *Food Additives & Contaminants: Part A* 31(9), 1470-1475 (2014)
4. Cai Sheng Wu, Ying Jin, Jin-Lan Zhang, Yan Ren, Zhi-Xin Jia. Simultaneous determination of seven prohibited substances in cosmetic products by liquid chromatography-tandem mass spectrometry. *Chinese Chemical Letters* 24,509-511 (2013)

## III-24 HEDP성분 분석법

### ■ 배경

- 보일러 청관제가 함유된 스팀을 식품에 직접 접촉하는 방법으로 당류를 제조한 업체에 대한 민원이 접수된 사례 있음
- 재발방지를 위해 청관제와 유사한 용도로 사용되는 수처리제에 대한 사용기준설정해야 할 실정이며, 이에 대한 분석법을 확립하여 지속적인 안전관리가 필요
- 미국 연방규정집(CFR)에서는 등재된 물질의 경우 식품 기계·기구의 유행 목적으로 사용할 수 있도록 규정함



### ■ 특성

- 금속이온 봉쇄제, 킬레이트제로 광물성 이온들을 제거하여 내용물의 안정화를 기여하는 물질로서는 염모제의 산화제, 청관제 등에 주로 사용
- 치석예방과 항균작용에 탁월한 치약과 화장품에 첨가될 뿐만 아니라 골다공증증, 골 파제트병 등의 뼈조직에 치명적인 증상을 막는 의약품으로도 사용.

■ 분석법

1. LC-MS/MS법

○ 전처리 방법

- 
- 표준액 조제 : HEDP 20 mg 취함 → 물 20 mL 가함 → 이액 중 1 mL 취함  
→ 물 50 mL 가함 → 이액 중 25 mL 취함  
→ <유도체화 전처리 방법>에 따름
  - 검액 조제 : 약 1 g 취함 → 물을 가해 1,000배 희석 → 이액 중 3 mL 취함  
→ 물 1 mL 가함 → 이액 중 25  $\mu$ L 취함  
→ <유도체화 전처리 방법>에 따름
    - ① Acetic acid 1 mL 가함
    - ② Trimethyl orthoacetate(TMOA) 4 mL 가함
    - ③ 진탕(10초)
    - ④ 100°C, 30분(Heating block)
    - ⑤ Cooling(얼음물 5분)
    - ⑥ 상온 5분 방치
  - <유도체화 전처리 방법>
    - ⑦ Formic acid 1 mL 가함
    - ⑧ Water 3 mL 가함
    - ⑨ Methyl tert-butyl ether(MTBE) 8 mL 가함
    - ⑩ 진탕(10초)
    - ⑪ 원심분리(32,000 rpm, 5분)
    - ⑫ 유기층 취함
    - ⑬ ⑧ ~ ⑫ 2회 반복
    - ⑭ 감압농축
    - ⑮ 50% MeOH를 1 mL로 녹임
- 

\* HEDP [Etidronic acid, 1-hydroxyethylidene-1,1-diphosphonic acid]

○ Analytical condition of HPLC

• Instrument	Shiseido SP		
• Column	Shiseido MG II C <sub>18</sub> (2.0 mm × 100 mm, 3.0 μm)		
• Column Temp.	50℃		
• Mobile Phase	(A) 5 mM Ammonium acetate buffer(pH 3.8) (B) 0.1% Formic acid in Acetonitrile		
	<b>Time (min)</b>	<b>A (%)</b>	<b>B (%)</b>
	0.0	90	10
	2.0	90	10
	6.0	80	20
	6.1	0	100
	8.0	0	100
	8.1	90	10
	10.0	90	10
• Flow Rate	0.3 mL/min		
• Inj. Volume	1 μL		

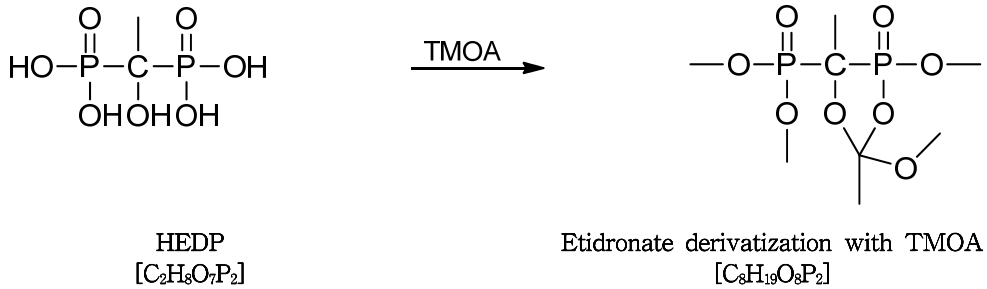
○ Analytical conditions of LC-MS/MS

• Instrument	AB SCIEX Triple Quad 5500
• Ionization Mode	ESI (+)
• Curtain Gas	30 psi
• Collision Gas	8 psi
• Ion Voltage	5500 V
• Ion Source Gas 1	70 psi
• Ion Source Gas 2	20 psi
• Source Temp.	550℃

○ Analyte MS/MS transition

Compound	Ion Mode	Precursor Ion (m/z)	CV (V)	Product Ion (m/z)	CE (V)	CXP (V)
HEDP	+	305.2	55	137.1	35	45
				152.9	35	45

■ 구조식



\* TMOA [Trimethyl orthoacetate], Etidronate [A salt of etidronic acid]

■ 참고문헌

1. Mahmoud Hasan, Gitta Schumacher, Anne Seekamp, Tobias Teadken, Werner Siegmund, Stefan Oswald. Journal of Pharmaceutical and Biomedical Analysis. 314-347(2014)
2. Isabela Tarcomnicu, Luigi Silvedrstro, Simona Rizea Savu, Adriana Gherase, Constanta Dulea. Journal of Chromatography A. 1160 (2007) 21-33



**고지혈증치료제 ..... 9**

- 1 Pitavastatin calcium
- 2 Benfluorex
- 3 D-Thyroxine
- 4 Cerivastatin sodium salt hydrate
- 5 Triparanol
- 6 Rosuvastatin calcium
- 7 Lomitapide
- 8 Clofibric acid
- 9 Bezafibrate
- 10 Ezetimibe
- 11 Etofibrate
- 12 Ciprofibrate
- 13 Atorvastatin calcium salt trihydrate
- 14 Fenofibric acid
- 15 Lapaquistat acetate
- 16 Gemfibrozil
- 17 Fenofibrate
- 18 Anacetrapib
- 19 Pravastatin sodium salt hydrate
- 20 Fluvastatin sodium
- 21 Mevastatin
- 22 Lovastatin
- 23 Simvastatin
- 24 Lovastatin hydroxy acid sodium salt
- 25 simvastatin hydroxy acid ammonium salt

**등취 ..... 21**

- 26 Aristolochic acid A
- 27 Aristolochic acid B
- 28 Aristolochic acid C
- 29 Aristolochic acid D

**만병초 ..... 25**

- 30 Grayanotoxin I
- 31 Grayanotoxin III
- 32 Rhodiolide

**부테아 스테르바 ..... 29**

- 33 Butesuperin A
- 34 Butesuperin B

**알러지질환 항히스타민제 ..... 36**

- 35 Dimenhydrinate
- 36 Desloratadine
- 37 Chlorpheniramine maleate
- 38 Brompheniramine maleate
- 39 Triprolidine hydrochloride
- 40 Astemizole
- 41 Ketotifen fumarate salt
- 42 Epinastine hydrochloride
- 43 Olopatadine hydrochloride
- 44 Diphenhydramine hydrochloride
- 45 Acrivastine
- 46 Promethazine hydrochloride
- 47 Azelastine hydrochloride
- 48 Cyproheptadine hydrochloride sesquihydrate
- 49 Hydroxyzine hydrochloride
- 50 Fexofenadine hydrochloride
- 51 Loratadine
- 52 Cetirizine hydrochloride
- 53 Levocetirizine dihydrochloride
- 54 Clemastine fumarate salt
- 55 Terfenadine
- 56 Ebastine
- 57 Azatadine
- 58 Dimetindene
- 59 Tripelennamine
- 60 Rupatadine
- 61 Carbinoxamine
- 62 Dexbropeniramine
- 63 Mizolastine
- 64 Cyclizine
- 65 Diphenylpyramine
- 66 Pimethixene
- 67 Oxatomide
- 68 Mequitazine
- 69 Thiethylperazine
- 70 Deptropine

**화장품(립스틱류) 중 타르색소 ..... 56**

- 71 Pyranine conc
- 72 Tartrazine

**화장품(립스틱류) 중 타르색소 ..... 56**

- 73 Amaranth
- 74 Indigo carmine
- 75 New cocchine
- 76 Naphthol yellow S
- 77 Sunset yellow FCF
- 78 Fast acid magenta
- 79 Allura red AC
- 80 Uranine
- 81 Ponceau SX
- 82 Brilliant blue FCF
- 83 Eosine YS
- 84 Orange II
- 85 Alizurool purple
- 86 Tetrabromofluorescein
- 87 Tetrachlorotetrabromofluorescein
- 88 Quinoline yellow SS
- 89 Alizurine purple SS
- 90 Sudan III
- 91 Quinizarine green SS

**국소마취관련성분 ..... 67**

- 92 Menthol
- 93 2-Phenoxyethanol
- 94 Eugenol
- 95 Ethyl 3-aminobenzoate methanesulfonate
- 96 Benzocaine
- 97 Tiletamine hydrochloride
- 98 Prilocaine hydrochloride
- 99 Lidocaine
- 100 Procaine hydrochloride
- 101 Mepivacaine hydrochloride
- 102 Ropivacaine
- 103 Tetracaine hydrochloride
- 104 Bupivacaine hydrochloride
- 105 Proparacaine hydrochloride

**단백동화스테로이드 ..... 72**

- 106 1-Androstenedione
- 107 19-Norandrostenedione

**단백동화스테로이드 ..... 72**

- 108 Bolasterone
- 109 Boldenone
- 110 Boldione
- 111 Calusterone
- 112 Clostebol
- 113 Fluoxymesterone
- 114 Metenolone
- 115 Methylnortestosterone
- 116 Mibolerone
- 117 Nandrolone
- 118 Norbolethone
- 119 Norclostebol
- 120 Norethandrolone
- 121 Oral-turinabol(M)
- 122 Nandrolone(M1)
- 123 Nandrolone(M2)
- 124 Methandienone(M)
- 125 Boldenone(M)
- 126 Danazol(M)
- 127 Formebolone(M)
- 128 Nandrolone decanoate
- 129 Testosterone
- 130 Testosterone-17-valerate
- 131 Testosterone-17-propionate
- 132 Methandrostenolone
- 133 Drostanolone propionate

**마약류 ..... 80**

- 134 Dihydrocodeine bitartrate
- 135 Ephedrine hydrochloride
- 136 Amphetamine
- 137 Phendimetrazine tartrate
- 138 Phentermine hydrochloride
- 139  $\alpha$ -Pyrrolidinopentiothiophenone
- 140 Methylphenidate hydrochloride
- 141 5-Meo-Dipt hydrochloride
- 142 Mazindol
- 143 Bromazepam
- 144 Fentanyl citrate
- 145 Flurazepam hydrochloride



마약류 ..... 80

- 146 AM2233
- 147 Estazolam
- 148 Lorazepam
- 149 Methaqualone
- 150 Flunitrazepam
- 151 Clobazam
- 152 Diazepam
- 153 Codeine phosphate hydrate
- 154 MDMA hydrochloride
- 155 Ketamine hydrochloride
- 156 Cocaine hydrochloride
- 157 2C-I hydrochloride
- 158 Pentazocine
- 159 Fenfluramine hydrochloride
- 160 Modafinil
- 161 Sufentanyl citrate
- 162 Triazolam
- 163 Temazepam
- 164 Alprazolam
- 165 AM2201
- 166 A-834735
- 167 JWH250
- 168 JWH073
- 169 XLR11
- 170 JWH018
- 171 JWH081
- 172 JWH122
- 173 JWH019
- 174 Tetrahydrocannabinol
- 175 APINAC

발기부전치료제와 그 유사성분 ..... 97

- 176 Acetylvardenafil
- 177 Hydroxyvardenafil
- 178 N-Desethylacetildenafil
- 179 Hydroxyhongdenafil
- 180 Hongdenafil
- 181 Lodenafilcarbonate
- 182 Sildenafil Imputrity A
- 183 Aminotadalafil

발기부전치료제와 그 유사성분 ..... 97

- 184 epi-Aminotadalafil
- 185 Benzylsildenafil
- 186 Mutaprodenafil
- 187 Mirodenafil
- 188 Thiosildenafil
- 189 Dimethylthiosildenafil
- 190 Propoxyphenylthiohomosildenafil
- 191 cis-Cyclopentyltadalafil
- 192 Nitrodenafil
- 193 Norneosildenafil
- 194 Vardenafil hydrochloride
- 195 Carbodenafil
- 196 Dimethylacetildenafil
- 197 Avanafil
- 198 Sildenafil citrate salt
- 199 Homosildenafil
- 200 Dimethylsildenafil
- 201 Udenafil
- 202 Cyclopentynafil
- 203 Dioxohongdenafil
- 204 Tadalafil
- 205 Xanthoanthrafil
- 206 Pseudovardenafil
- 207 Propoxyphenylthiohydroxyhomosildenafil
- 208 Gendenafil
- 209 Chloropretadalafil
- 210 Thioquinapiperifil
- 211 Desmethylcarbodenafil
- 212 Norneovardenafil
- 213 Piperidinohongdenafil
- 214 Methylhydroxyhomosildenafil
- 215 Hydroxythiovardenafil
- 216 Desulfovardenafil
- 217 Cinnamylidenafil
- 218 trans-Tadalafil
- 219 Hydroxythiohomosildenafil
- 220 Dithiodesmethylcarbodenafil
- 221 Propoxyphenylthioaildenafil
- 222 Dithiopropylcarbodenafil
- 223 Chlorodenafil

**발기부전치료제와 그 유사성분 ..... 97**

- 224 Octylnortadalafil
- 225 Yohimbine
- 226 Pyrazole N-desmethylsildenafil
- 227 Demethylhongdenafil
- 228 Oxohongdenafil
- 229 Icariin
- 230 Hydroxyhomosildenafil
- 231 Acetaminotadalafil
- 232 Demethyltadalafil
- 233 Diethylaminopretadalafil
- 234 2-Hydroxypropylnortadalafil
- 235 Acetil acid
- 236 Thiohomosildenafil
- 237 Propoxyphenylthiosildenafil
- 238 Hydroxychlorodenafil
- 239 N-butyltadalafil
- 240 trans-Cyclopentyltadalafil
- 241 Imidazosagatriazinone
- 242 Dichlorodenafil
- 243 Desmethylpiperazinylsildenafil
- 244 N-Desethylvardenafil
- 245 Papaverine hydrochloride
- 246 Tadalafil impurity A
- 247 Descarbonsildenafil
- 248 N-Desmethylsildenafil
- 249 Apixaban
- 250 Propoxyphenylsildenafil
- 251 Sildenafil coupled
- 252 Dapoxetine hydrochloride
- 253 Tadalafil impurity C
- 254 Homotadalafil
- 255 Isopropylnortadalafil
- 256 Bisprenortadalafil
- 257 5-Chloroimidazosagatriazinone

**체중감량성분\_비만치료관련성분 .. 129**

- 258 Atenolol
- 135 Ephedrine hydrochloride
- 259 β-Methylphenethylamine
- 137 Phendimetrazine tartrate

- 260 Diethylpropion hydrochloride
- 138 Phentermine hydrochloride
- 261 Clenbuterol
- 262 Phenobarbital
- 263 Bupropion hydrochloride
- 264 Propranolol hydrochloride
- 265 Bisacodyl
- 266 Liothyronine
- 267 Phenolphthalein
- 268 Didesmethylsibutramine
- 269 Flouxetine hydrochloride
- 270 Sibutramine hydrochloride
- 271 Chlorosipentramine
- 272 Rimonabant
- 273 Orlistat
- 274 2-Phenethylamine hydrochloride
- 275 Pseudoephedrine hydrochloride
- 276 Captopril
- 277 Sennoside B
- 278 Sennoside A
- 279 Lorcaserine hydrochloride
- 142 Mazindol
- 159 Fenfluramine hydrochloride
- 160 Modafinil
- 280 Phenytoin sodium
- 281 Paroxetine hydrochloride
- 282 Levothyroxine
- 283 Desmethylsibutramine hydrochloride salt
- 284 Sertraline hydrochloride
- 285 Benzylsibutramine hydrochloride
- 286 Chlorosibutramine

**수면유도제 ..... 143**

- 287 Zolpidem
- 262 Phenobarbital
- 288 Midazolam
- 289 Flurazepam
- 44 Diphenhydramine hydrochloride
- 290 Pentobarbital
- 291 Hexobarbital
- 147 Estazolam

**수면유도제 ..... 143**

- 150 Flunitrazepam
- 148 Lorazepam
- 162 Triazolam
- 163 Temazepam
- 164 Alprazolam
- 292 Clonazepam
- 293 Clemastine

**진통관련성분 ..... 151**

- 294 Acetaminophen
- 295 4-Dimethylaminoantipyrine
- 296 Phenacetin
- 297 Carbamazepine
- 298 Sulindac
- 299 Ketorolac
- 300 Naproxen sodium
- 301 Flurbiprofen
- 302 Indomethacin
- 303 Ibuprofen
- 304 Meclofenamate sodium
- 305 4-Aminoantipyrine
- 306 Dipyron
- 307 Aspirin
- 308 Piroxicam
- 309 4-Isopropylantipyrine
- 310 Ketoprofen
- 311 Meloxicam
- 312 Fenoprofen calcium
- 313 Diclofenac sodium
- 314 Celecoxib
- 315 Mefenamic acid

**갱년기치료관련성분 ..... 162**

- 316 Estrone
- 317  $\beta$ -Estradiol
- 318  $\beta$ -Estradiol 17-valerate
- 319 17 $\alpha$ -Ethinylestradiol
- 320 Estropipate
- 321  $\beta$ -Estradiol 17-cypionate

**갱년기치료관련성분 ..... 162**

- 322 Norethisterone acetate
- 323 Medroxyprogesterone acetate
- 324 Raloxifene hydrochloride

**고혈압치료관련성분 ..... 166**

- 325 Cartelol hydrochloride
- 326 Nadolol
- 327 Pindolol
- 328 Terazosin hydrochloride
- 329 Prazosin hydrochloride
- 330 Celiprolol
- 264 Propranolol hydrochloride
- 331 Doxazosin mesylate
- 332 Telmisartan
- 333 Olmesartan medoxomil
- 334 Losartan potassium
- 335 ( $\pm$ )-Penbutolol hydrochloride
- 336 Nifedipine
- 337 Lercanidipine hydrochloride
- 338 Isradipine
- 339 Nisoldipine
- 340 Candesartan cilexetil
- 258 Atenolol
- 341 Clonidine hydrochloride
- 342 Minoxidil
- 343 Acebutolol hydrochloride
- 344 ( $\pm$ )-Metoprolol (+)-tartrate salt
- 345 Phentolamine mesylate
- 346 Betaxolol hydrochloride
- 347 Diltiazem hydrochloride
- 348 Benazepril hydrochloride
- 349 Carvedilol
- 350 Irbesartan
- 351 Amlodipine besylate
- 352 Verapamil hydrochloride
- 353 Valsartan
- 354 Nitrendipine
- 355 Nilvadipine
- 356 Felodipine

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- 358 Buformin hydrochloride
- 359 Vildagliptin
- 360 Phenformin hydrochloride
- 361 Alogliptin
- 362 Rosiglitazone
- 363 Sitagliptin phosphate monohydrate
- 364 Pioglitazone hydrochloride
- 365 Carbutamide
- 366 Glymidine
- 367 Empagliflozin
- 368 Chlorpropamide
- 369 Repaglinide
- 370 Ipragliflozin
- 371 Glipizide
- 372 Tolbutamide
- 373 Tolazamide
- 374 Gliclazide
- 375 Canagliflozin
- 376 Mitiglinide Calcium
- 377 Glibornuride
- 378 Glibenclamide
- 379 Nateglinide
- 380 Glimepiride
- 381 Troglitazone
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- 384 Gastrodin

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- 386 Methylisoithiazolinone(MIT)

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- 387 Sulpiride
- 388 Metoclopramide hydrochloride
- 389 Domperidone

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- 390 Chlopromazine hydrochloride
- 323 Medroxyprogesterone acetate

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- 391 Triaminodil
- 342 Minoxidil
- 392 Bimatoprost
- 393 Alimemazine tartrate
- 394 Diphenylcyclopropenone
- 395 Alfatradiol
- 396 Finasteride
- 397 Methyltestosterone
- 398 Spironolactone
- 399 Flutamide
- 400 Cyproterone acetate
- 401 Dutasteride
- 131 Testosterone 17-propionate

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- 402 Aconitine
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- 406 Phosphatidylethanolamine
- 407 Phosphatidylserine
- 408 Phosphatidylcholine
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- 411 Campesterol
- 412 Stigmasterol
- 413  $\beta$ -sitosterol

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- 416 Betamethasone
- 417 Dexamethasone
- 418 Prednisone 21-acetate
- 419 Cortisone 21-acetate
- 420 Prednisolone-21-acetate
- 421 Hydrocortisone 21-acetate
- 422 Hydrocortisone 17-acetate
- 423 Beclomethasone
- 424 Budesonide
- 425 Betamethasone 21-acetate
- 426 Dexamethasone 21-acetate
- 427 Triamcinolone acetonide
- 428 6 $\alpha$ -Methylprednisolone
- 429 Hydrocortisone 17-valerate
- 430 Hydrocortisone 21-valerate
- 431 Beclomethasone 21-acetate
- 432 Beclomethasone-21-propionate
- 433 Beclomethasone 17-propionate
- 434 Clobetasol 17-propionate
- 435 Betamethasone 17-valerate
- 436 Betamethasone 21-valerate
- 437 Triamcinolone diacetate
- 438 Dexamethasone 21-hemisuccinate
- 439 Betamethasone 21-hemisuccinate
- 440 Betamethasone 17,21-dipropionate
- 441 Beclomethasone 21-hemisuccinate
- 442 Beclomethasone 17,21-dipropionate
- 443 Medroxyprogesterone 17-acetate
- 322 Norethisterone acetate
- 129 Testosterone
- 131 Testosterone 17-propionate
- 130 Testosterone 17-valerate
- 444 Megesterol acetate
- 445 11 $\alpha$ -OH-progesterone-hemisuccinate
- 446 6 $\alpha$ -Methylprednisolone aceponate
- 447 D(-)-norgestrel
- 448 Fluticasone furoate
- 449 Norethisterone
- 450 Prednisone

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- 451 Stanozolol C-3
- 452 Clobetasone butyrate
- 453 Dichlorisone diacetate
- 454 Diflorasone diacetate
- 455 Fluocinolone acetonide
- 456 Flurandrenolide
- 457 Hydrocortisone butyrate
- 458 Hydrocortisone 21-hemisuccinate
- 459 Mometasone furoate
- 460 Amcinonide
- 461 Fludrocortisone acetate
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- 463 Tetracycline hydrochloride
- 464 Dapsone
- 465 Clindamycin hydrochloride
- 466 6-Hydroxy-1,3-benzoxathiol-2-one
- 467 Nadifloxacin
- 303 Ibuprofen
- 468 Benzoyl peroxide
- 469 Triclosan
- 470 Bithionol
- 471 Isotretinoin
- 472 Adapalene

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- 475 Methazolamide
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- 481 Indapamide
- 482 Bendroflumethiazide
- 483 Xipamide
- 484 Bumetanide

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- 486 Chlorothiazide
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- 488 Triamterene
- 489 Trichlormethiazide
- 490 Furosemide
- 491 Eplerenone
- 492 Cyclothiazide
- 493 Azosemide
- 494 Piretanide
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- 501 14,15β-Dihydroxyklaineanone
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- 503 Eurycomanone
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- 507 Dibutyl phthalate(DBP)
- 508 Benzyl butyl phthalate(BBP)
- 509 Bis (2-ethylhexyl) adipate(DEHA)
- 510 Bis (2-ethylhexyl) phthalate(DEHP)
- 511 Di-n-octyl phthalate(DNOP)

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- 417 Dexamethasone
- 418 Prednisone 21-acetate
- 419 Cortisone 21-acetate
- 420 Prednisolone 21-acetate
- 421 Hydrocortisone 21-acetate
- 422 Hydrocortisone 17-acetate
- 423 Beclomethasone
- 424 Budesonide
- 425 Betamethasone 21-acetate
- 426 Dexamethasone 21-acetate
- 427 Triamcinolone acetonide
- 428 6a-Methylprednisolone
- 513 Methylprednisolone
- 429 Hydrocortisone 17-valerate
- 430 Hydrocortisone 21-valerate
- 431 Beclomethasone 21-acetate
- 432 Beclomethasone 21-propionate
- 433 Beclomethasone 17-propionate
- 434 Clobetasol 17-propionate
- 435 Betamethasone 17-valerate
- 436 Betamethasone 21-valerate
- 437 Triamcinolone diacetate
- 438 Dexamethasone 21-hemisuccinate
- 439 Betamethasone 21-hemisuccinate
- 440 Betamethasone 17,21-dipropionate
- 441 Beclomethasone 21-hemisuccinate
- 442 Beclomethasone 17,21-dipropionate
- 446 6a-Methylprednisolone aceponate
- 448 Fluticasone furoate
- 450 Prednisone
- 452 Clobetasone butyrate
- 455 Fluocinolone acetonide
- 456 Flurandrenolide
- 458 Hydrocortisone 21-hemisuccinate

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- 461 Fludrocortisone acetate
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11	2-Phenethylamine hydrochloride	130
12	2-Phenoxyethanol	68
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15	4-Isopropylantipyrine	152
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27	Acetildenafil	98
28	Acetylwardenafil	98
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30	Acrivastine	37
31	Adapalene	248
32	Aildenafil	98
33	Alfatradiol	212
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연번	논문명	학술지명	권(호)
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2	Isolation and structural identification of a novel minoxidil analogue in illegal dietary supplement: triaminodil	Food additives & contaminants part A	ISSN :1944-0057
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발행인	이선희
편집위원장	박혜경, 이주현
편집위원	강호일, 우영택, 박성관, 박성수, 신동우, 박형준, 허 석, 황태익, 조정화, 김준형, 김남숙, 이지현, 노은영, 이진희, 정지혜, 박한나, 강기행, 박옥림, 민아영, 문선희, 김지희, 신은진, 허혜진, 이창희, 이동구, 정애란, 백지현, 장명환, 박수진
문의처	충청북도 청주시 흥덕구 오송읍 오송생명2로 187 식품의약품안전평가원 첨단분석팀
전화	043)719-5301~25
팩스	043)719-5300

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식품의약품안전처

식품의약품안전평가원