

大赛璐 手性分析的近期进展



北京金欧亚科技发展有限公司

北京崇文区左安门内大街8号伟图大厦301室

PC: 100061

Tel : 010-67136152/67100708

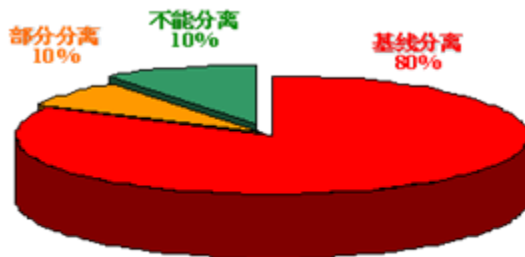
Fax : 010-67114016/67113925

[http: //www. jinouya. cn](http://www.jinouya.cn)

E-mail: [china. hp1c@163. com](mailto:china.hp1c@163.com)

手性色谱技术的研发动向

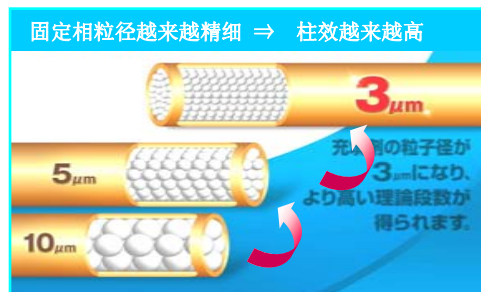
更加广泛



对10%的
责任和挑战

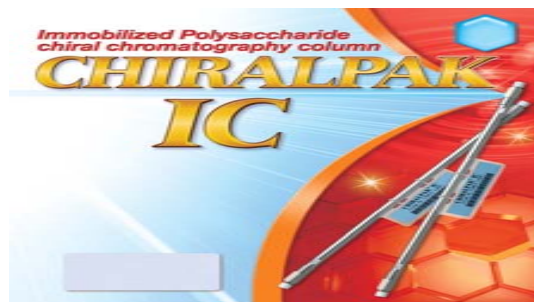
新型固定相
AY, OZ, AZ, IC

更加快速



3微米固定相
普通系列 ⇒ H系列 ⇒ 3系列

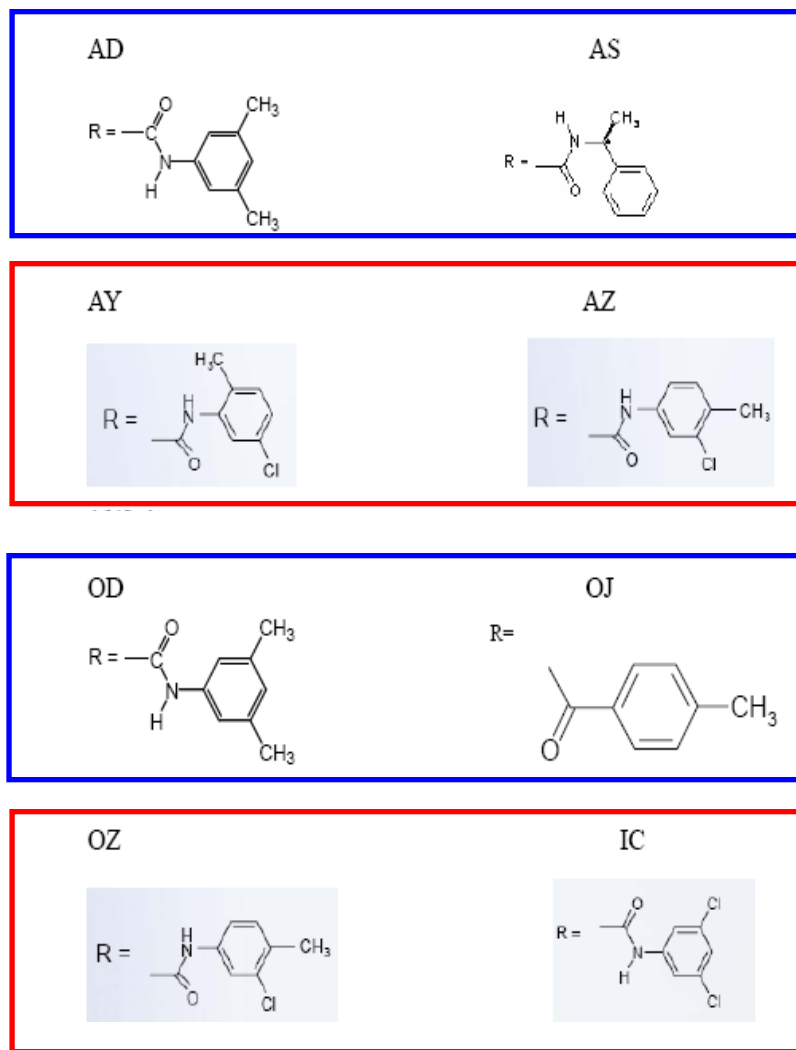
更加稳定



键合型固定相
IA, IB, IC

一、新型固定相的开发及应用

四大金刚

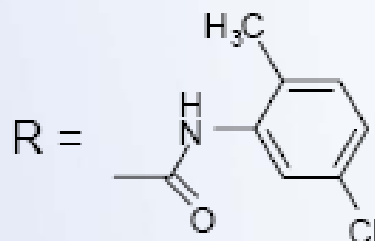
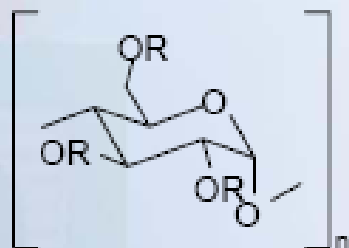


直链淀粉

多糖

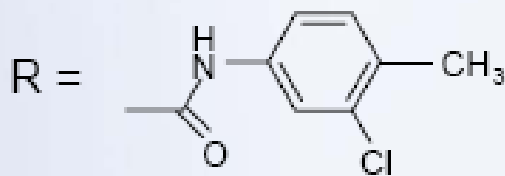
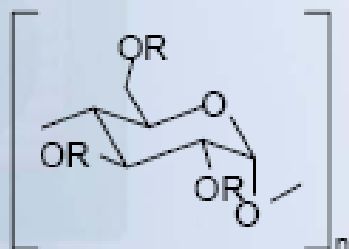
纤维素

一、新型固定相的开发及应用



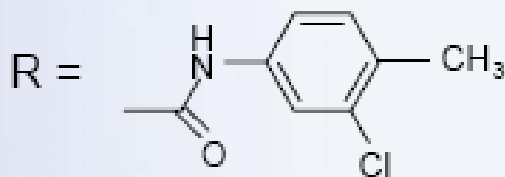
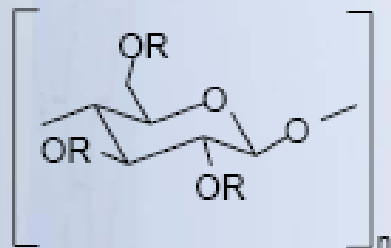
CHIRALPAK AY-H

Amylose tris-(5-chloro-2-methylphenylcarbamate)



CHIRALPAK AZ-H

Amylose tris-(3-chloro-4-methylphenylcarbamate)

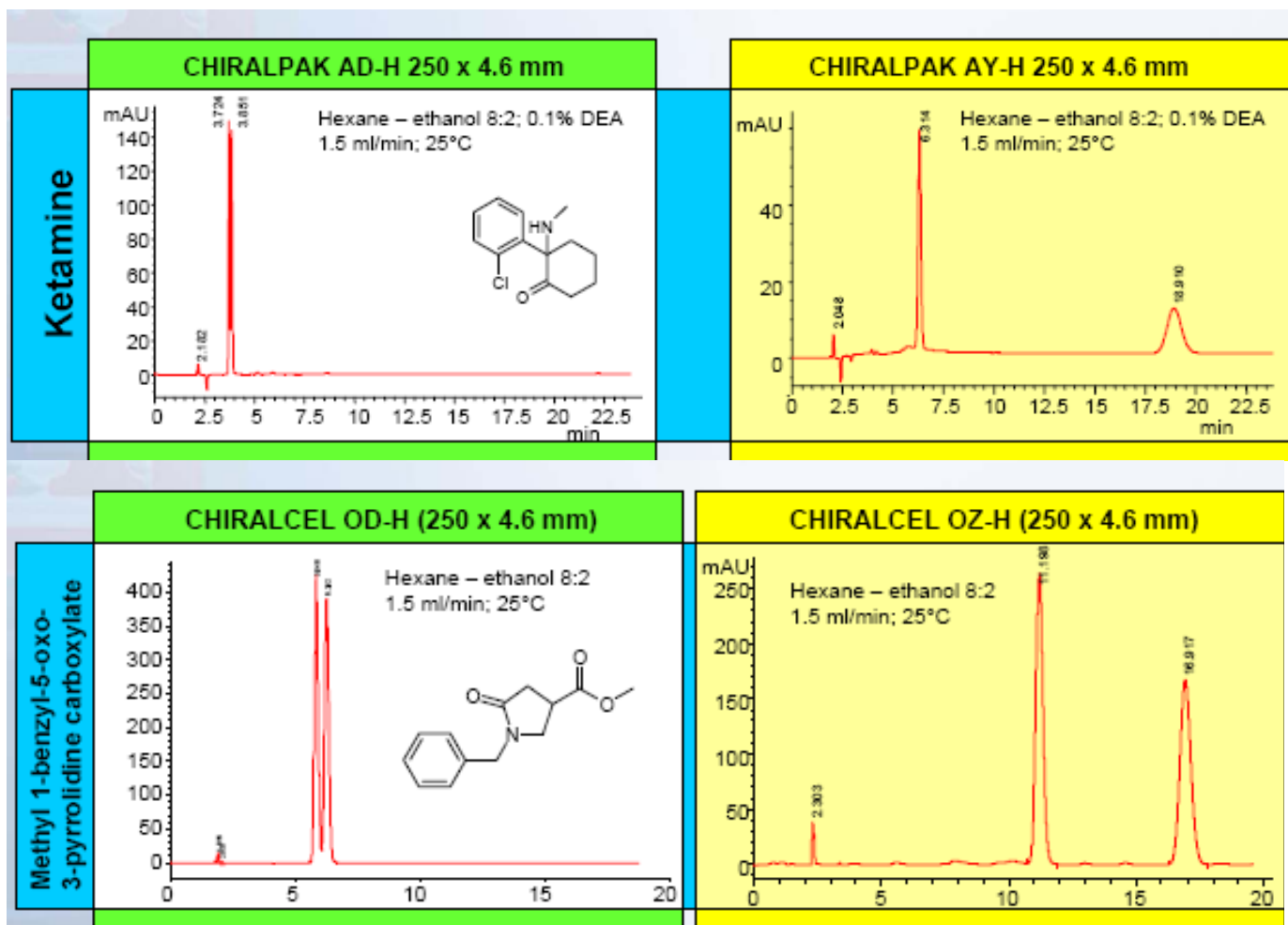


CHIRALCEL® OZ-H

Cellulose tris-(3-chloro-4-methylphenylcarbamate)

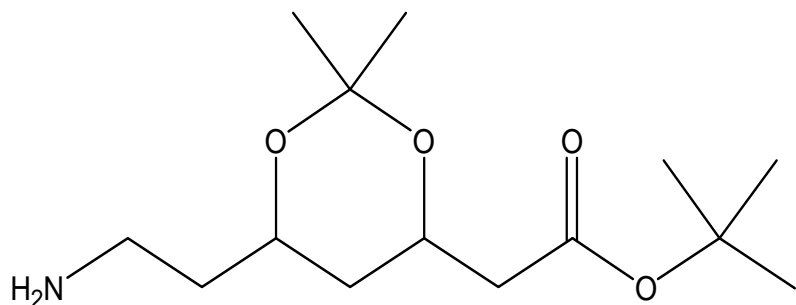
一、新型固定相的开发及应用

- 选择性差异

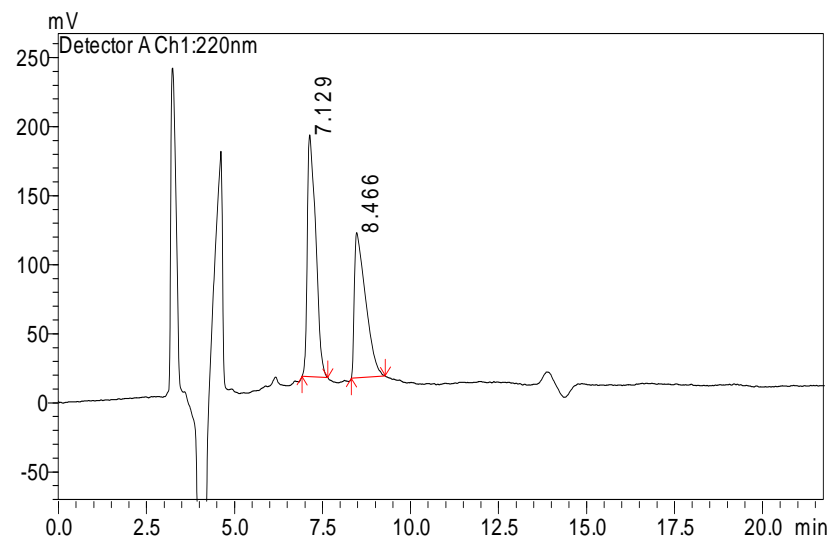


一、新型固定相的开发及应用

- 选择性优势



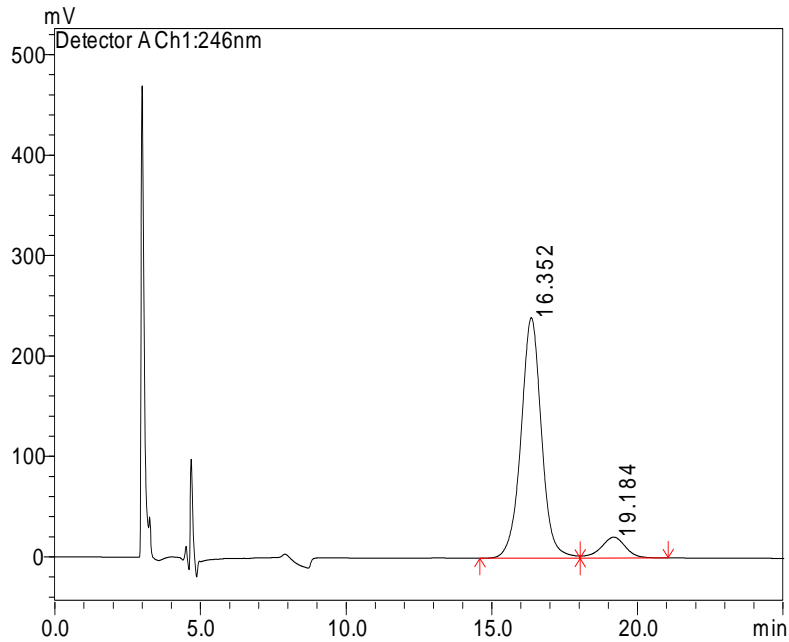
Hexane/EtOH/DEA =94/6/0.1 (v/v/v)



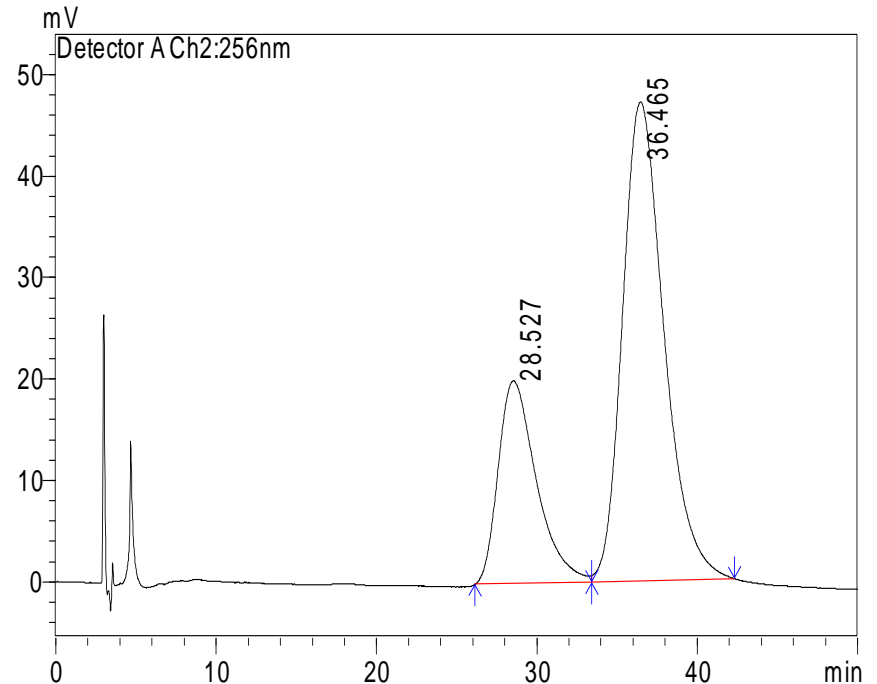
- 仅**AY-H**可以分

一、新型固定相的开发及应用

- 阿托伐他汀钙
- **AD-H**

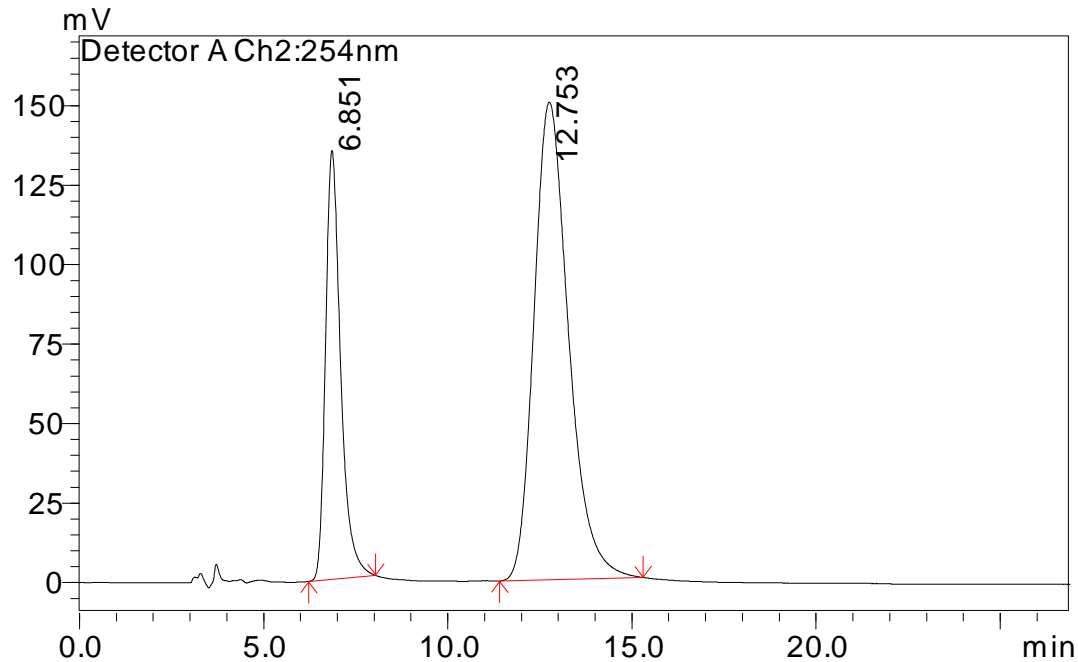


OD-H



一、新型固定相的开发及应用

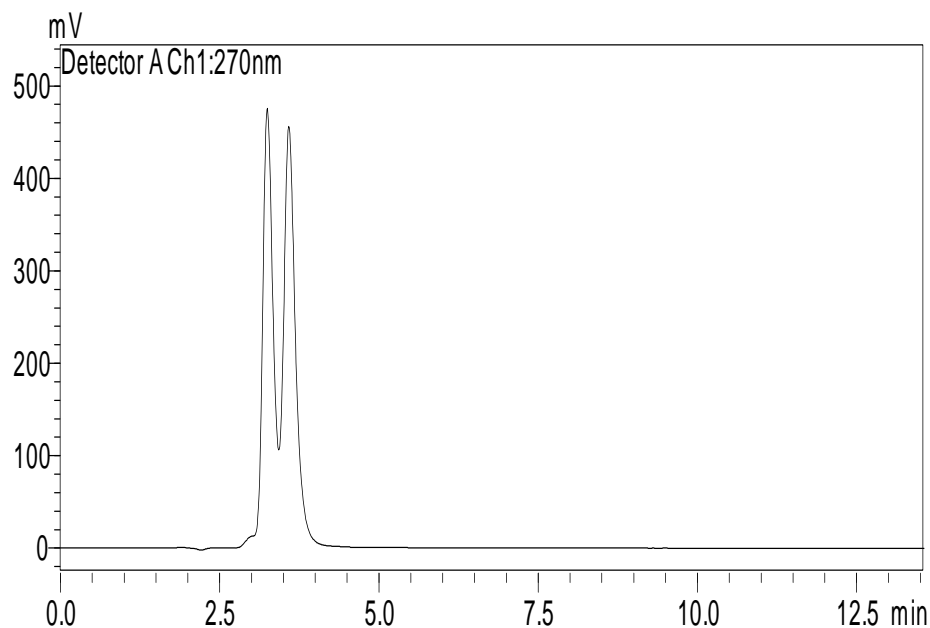
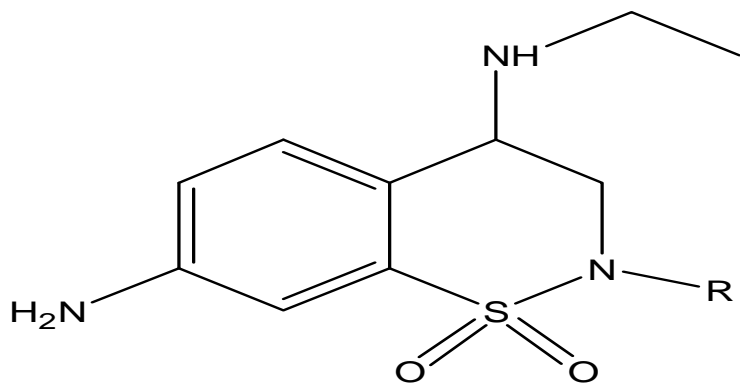
- 阿托伐他汀钙
- **OZ-H**



一、新型固定相的开发及应用

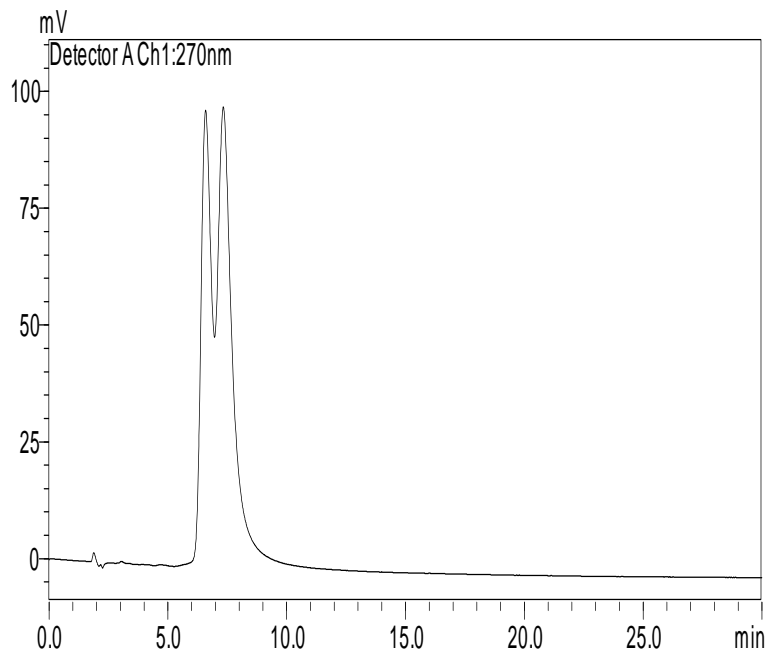
- H/I/DEA=70/30/0.1

- ADH

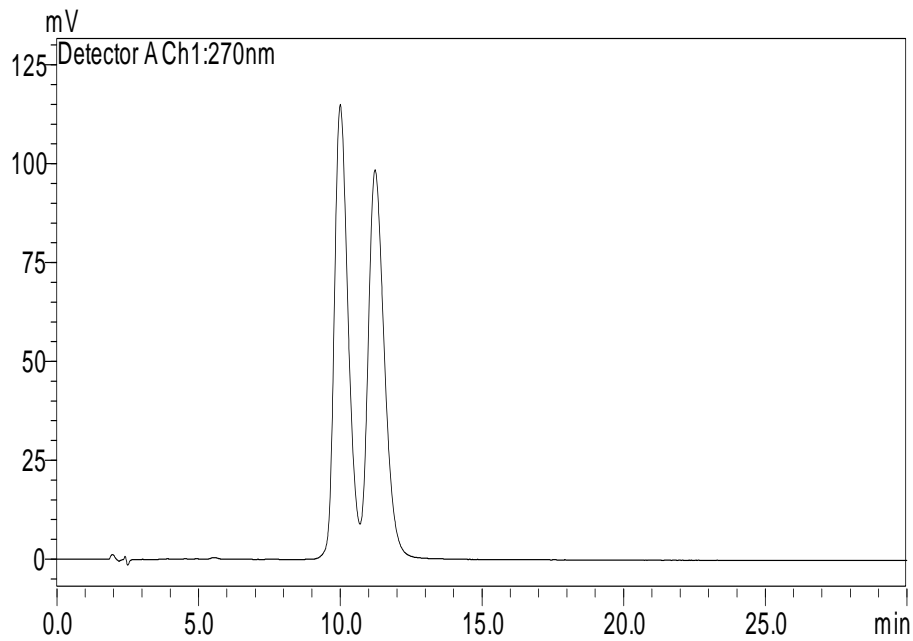


一、新型固定相的开发及应用

- OD-H

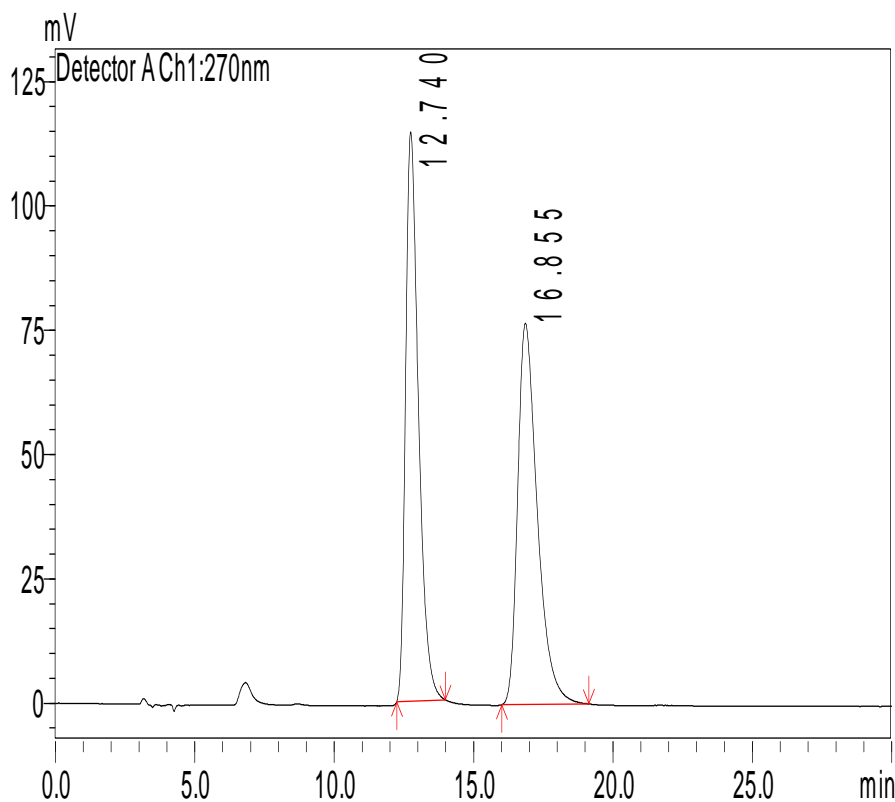


OJ-H

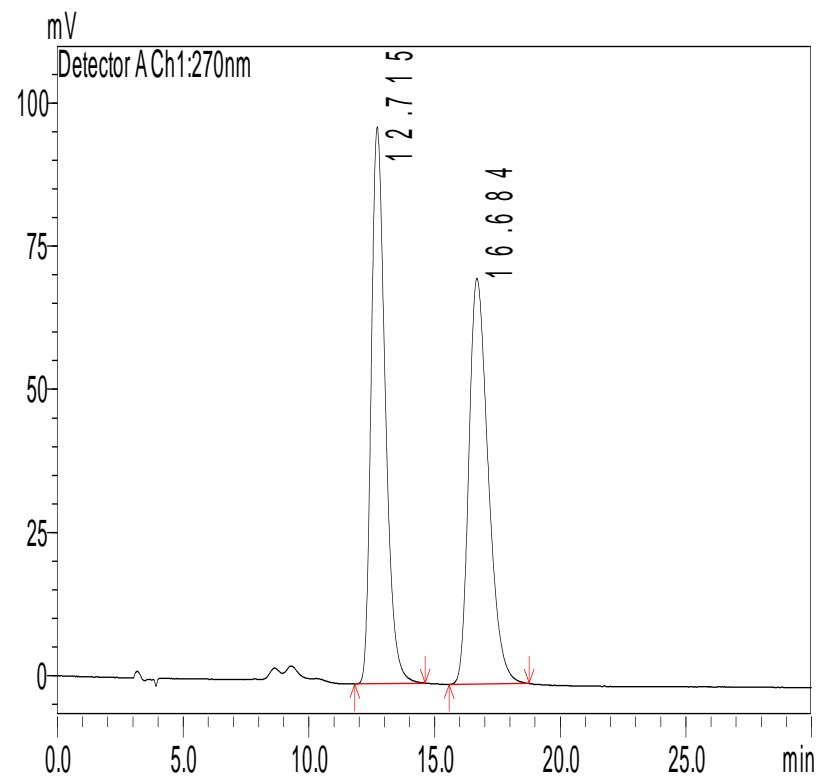


一、新型固定相的开发及应用

• AY-H



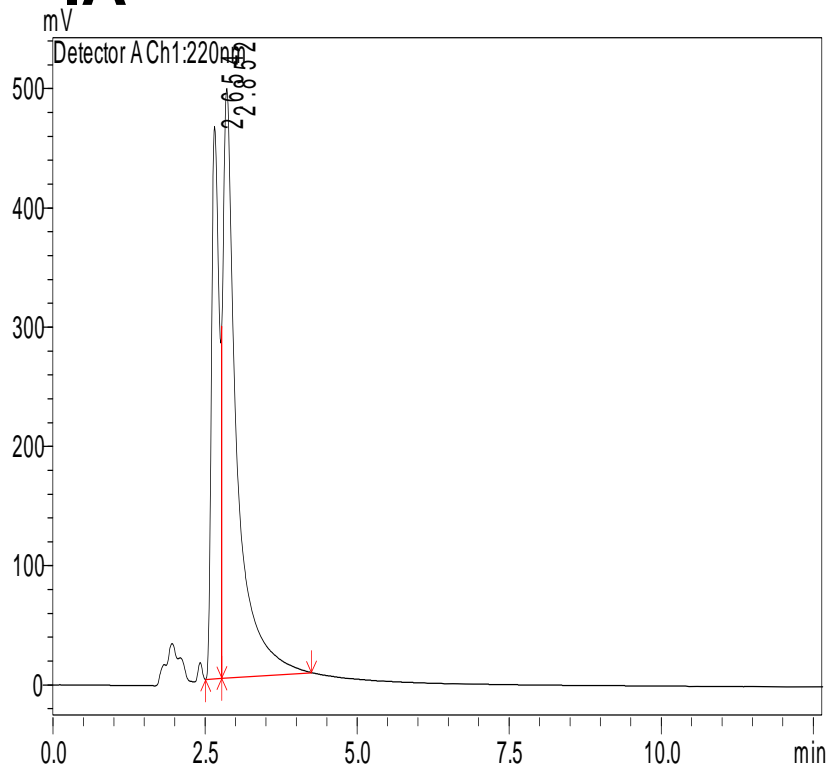
OZ-H



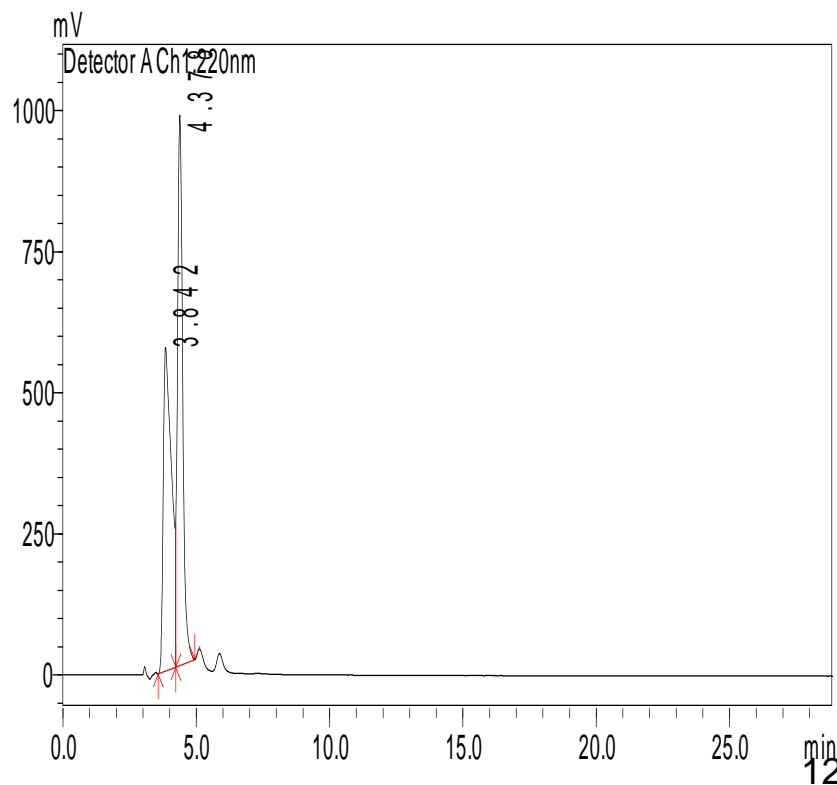
一、新型固定相的开发及应用

- Compound G 结构未知，含苯基、羟基、羧基、酰胺基
- Hexane / IPA / TFA=70/30/0.1

• IA

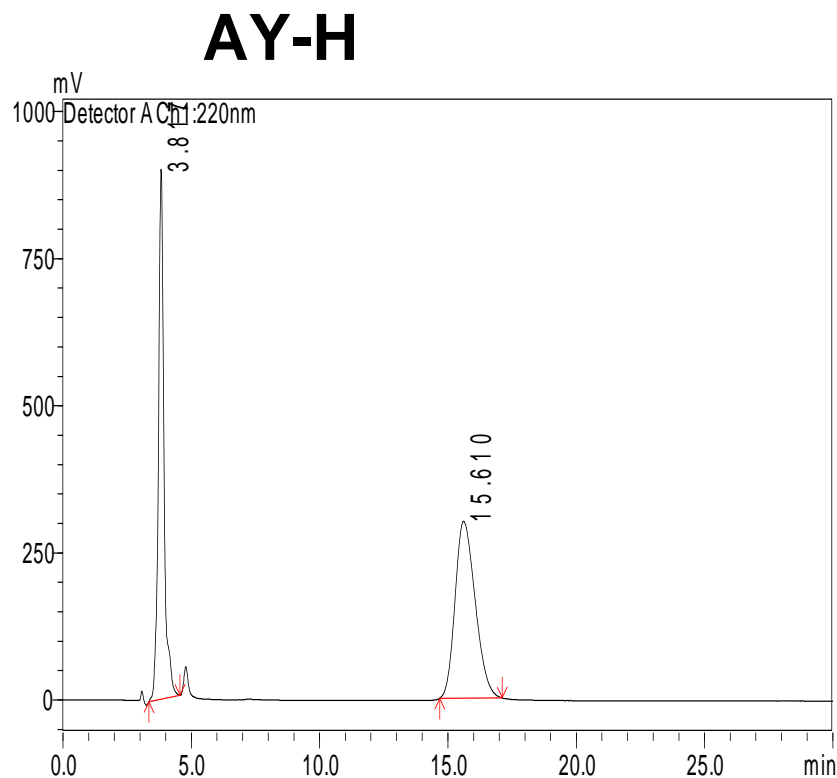
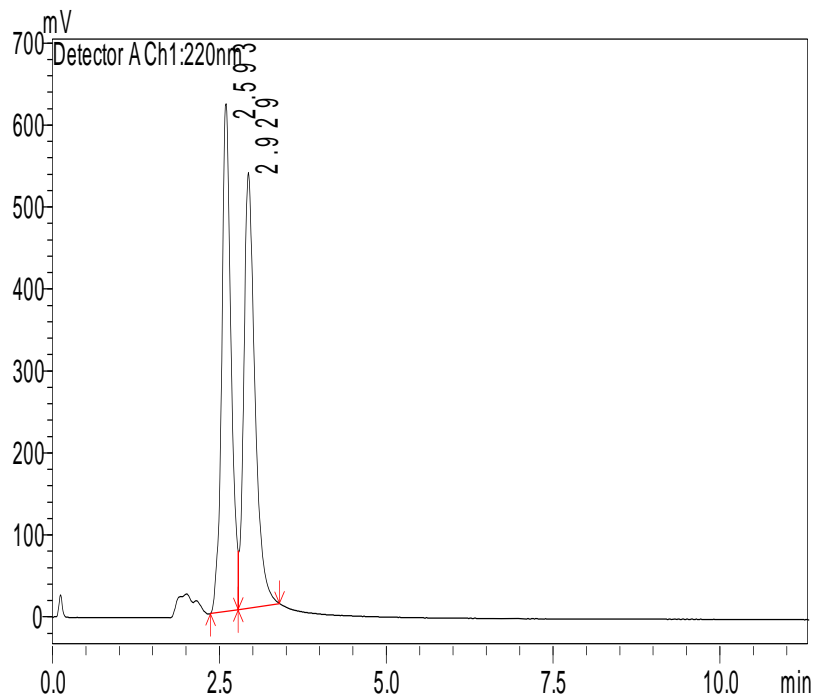


OZ-H



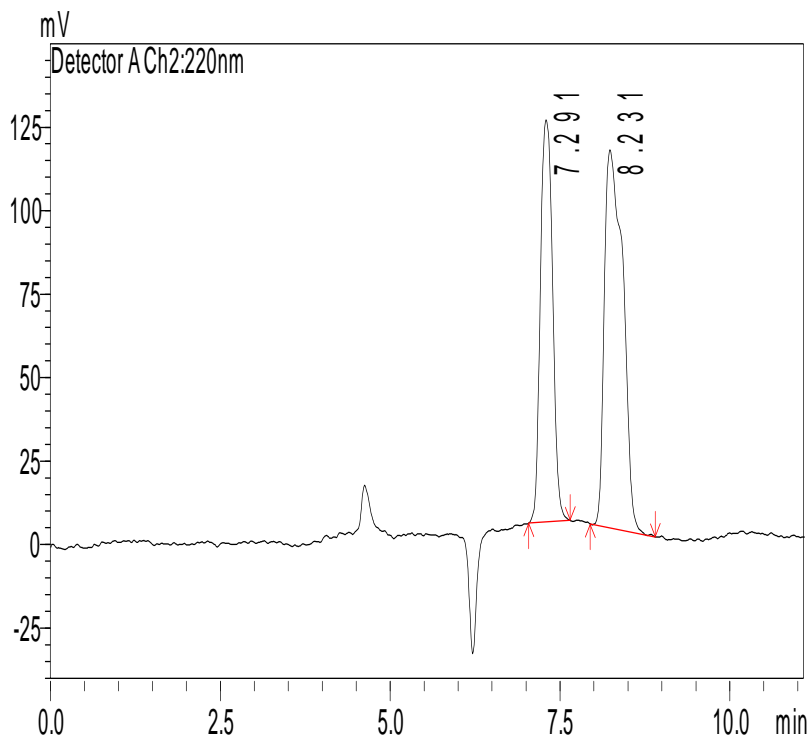
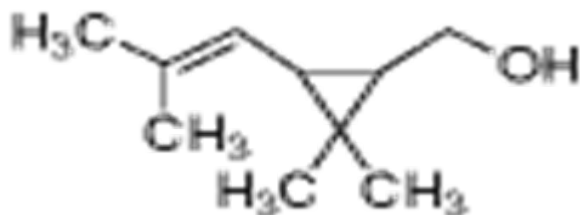
一、新型固定相的开发及应用

- **Compound G** 结构未知，含苯基、羟基、羧基、酰胺基
- **Hexane / IPA / TFA=70/30/0.1**
- **AD-H**



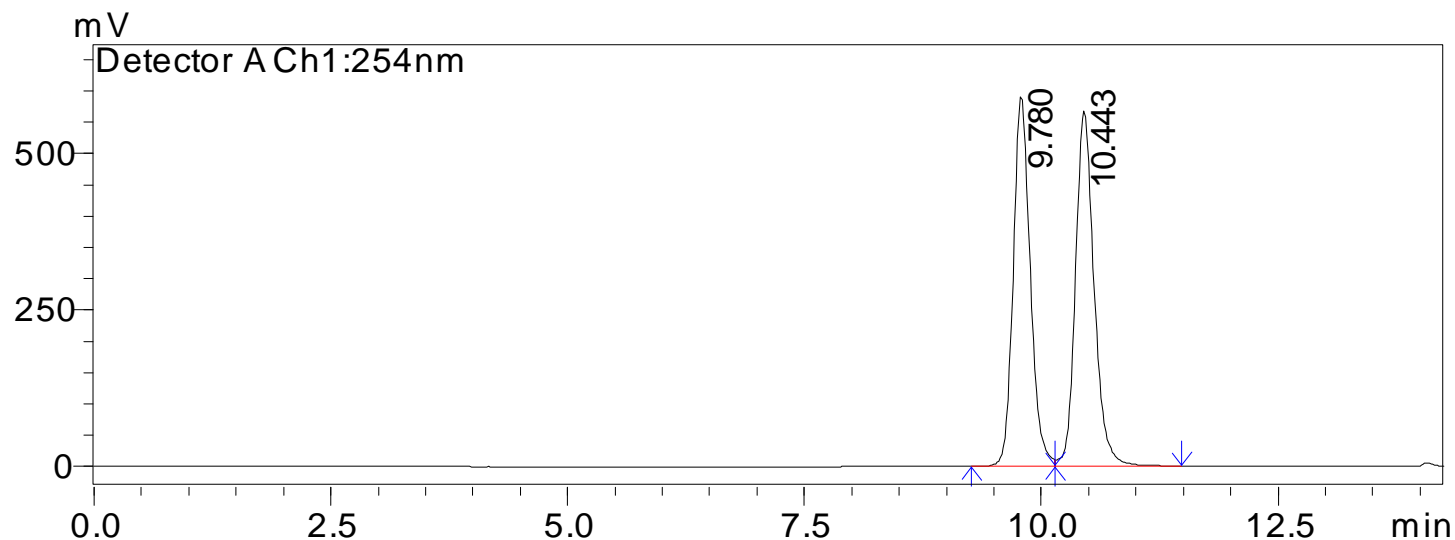
一、新型固定相的开发及应用

- 选择性优势
- **AY-H**
- **Hexane/IPA/DEA**
- **98/2/0.1**



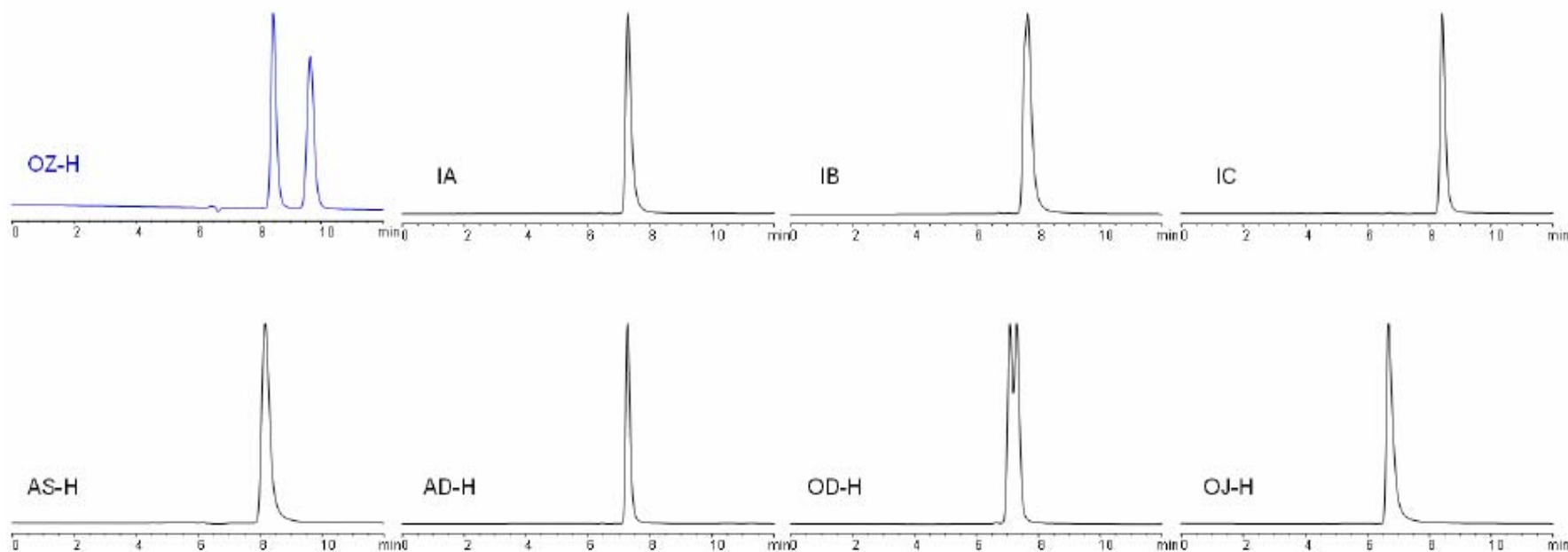
一、新型固定相的开发及应用

- 选择性优势
- 苯甲酸仲丁酯 Hexane/IPA=99/1 单峰
- **AY-H EtOH/MeOH=95/5 分离度1.8**



一、新型固定相的开发及应用

- 选择性优势
- 阿替洛尔 **EtOH/DEA=100/0.1**



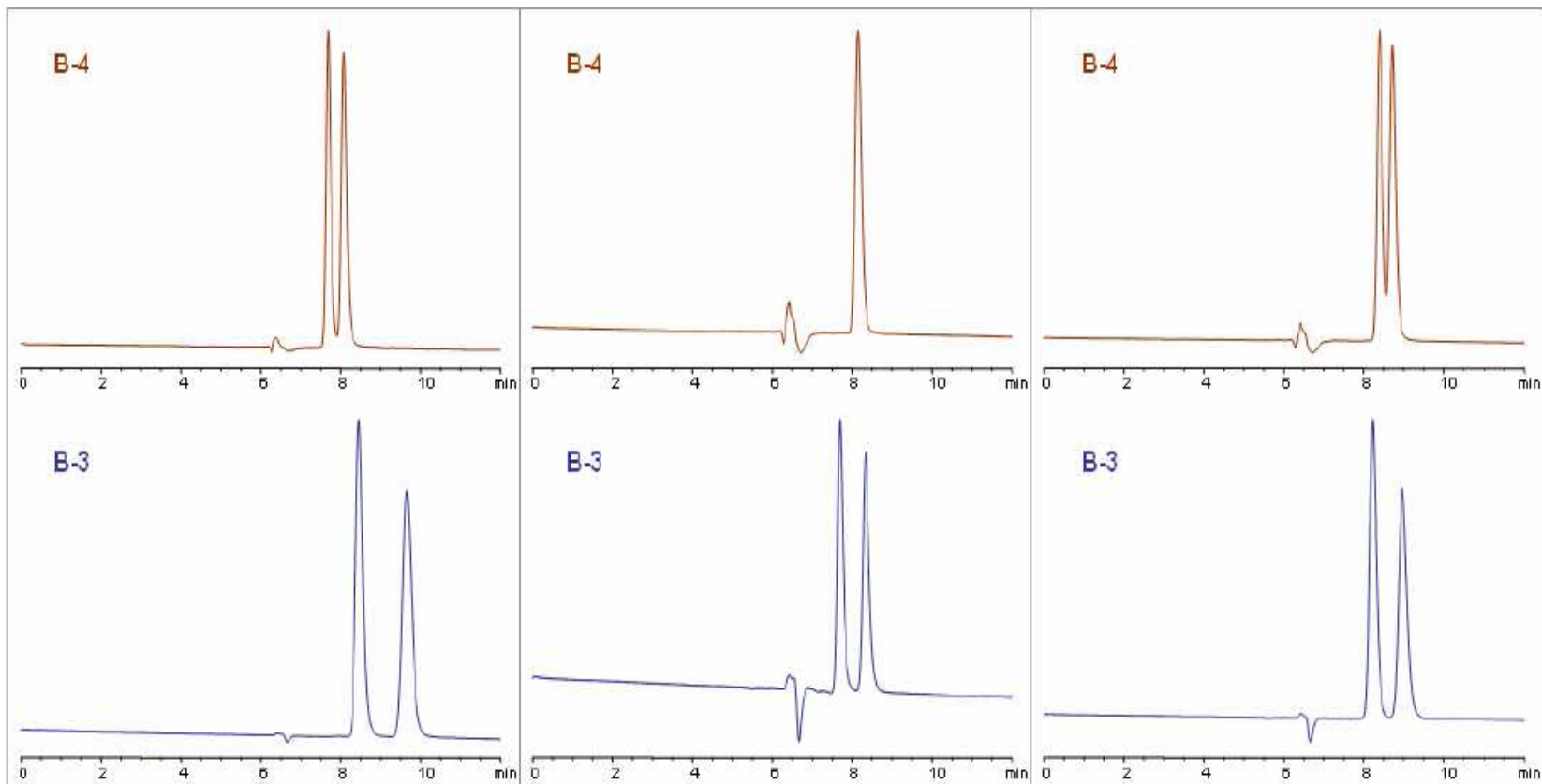
一、新型固定相的开发及应用

- **OZ-H** (B-3:EtOH/DEA=100/0.1; B-4:MeOH/DEA=100/0.1)

- 苕氟塞嗪

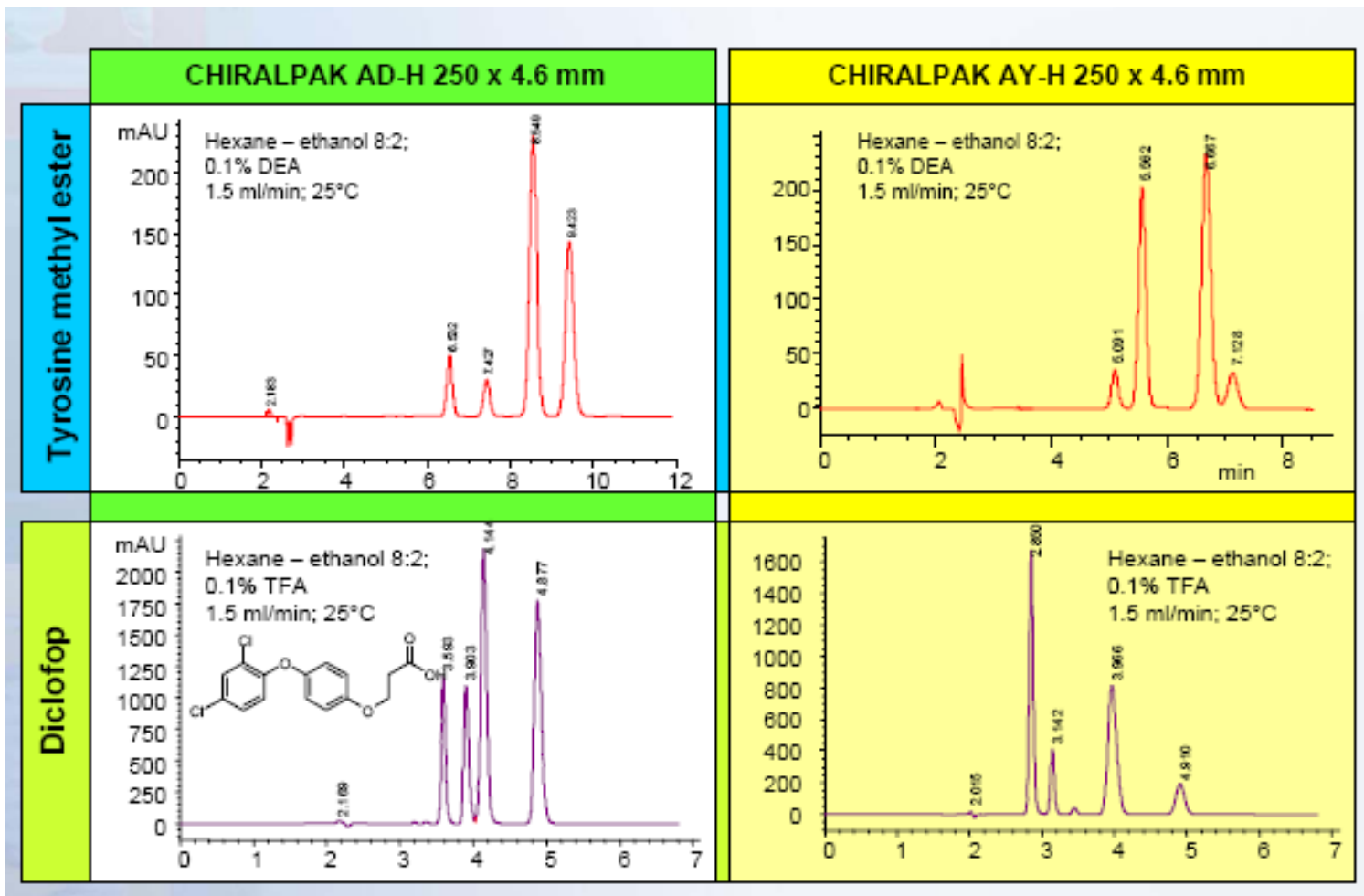
阿托品

达舒平



一、新型固定相的开发及应用

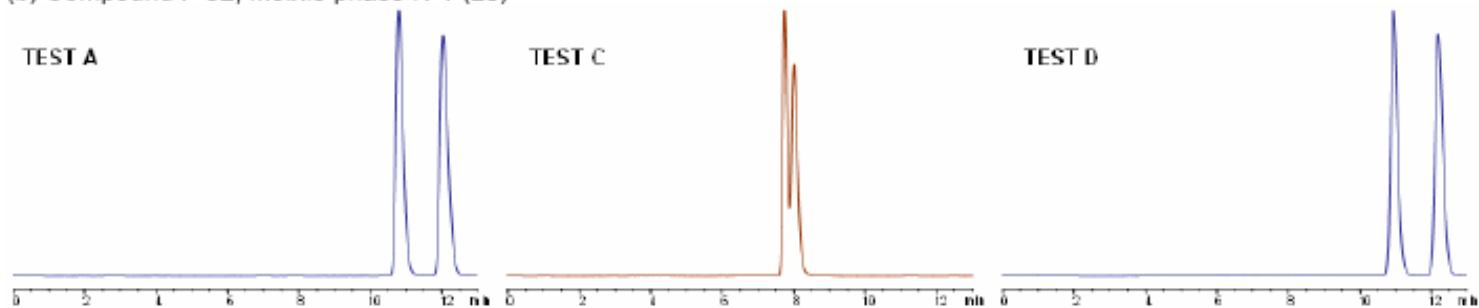
- 出峰顺序差异



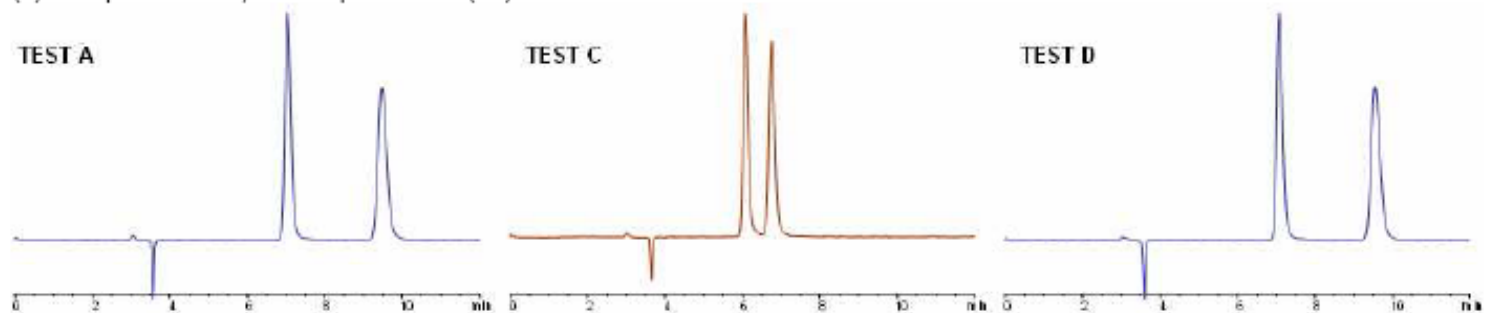
一、新型固定相的开发及应用

- **AY-H 特性（IPA损伤、ETOH修复）**

(b) Compound F-02, Mobile phase N-1 (20)

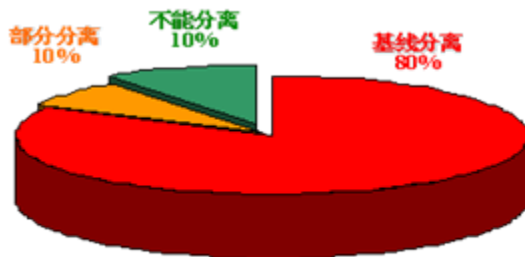


(c) Compound B-23; Mobile phase B-1 (20)



手性色谱技术的研发动向

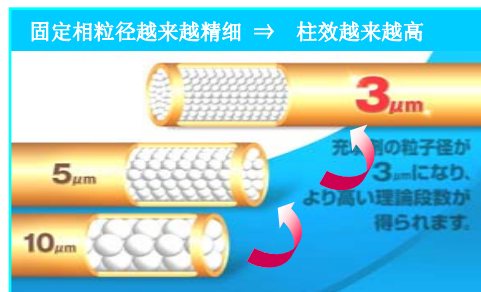
更加广泛



对10%的责任和挑战

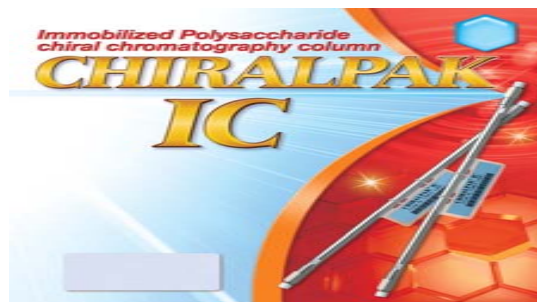
新型固定相
AY, OZ, AZ, IC

更加快速



3微米固定相
普通系列 ⇒ H系列 ⇒ 3系列

更加稳定



键合型固定相
IA, IB, IC

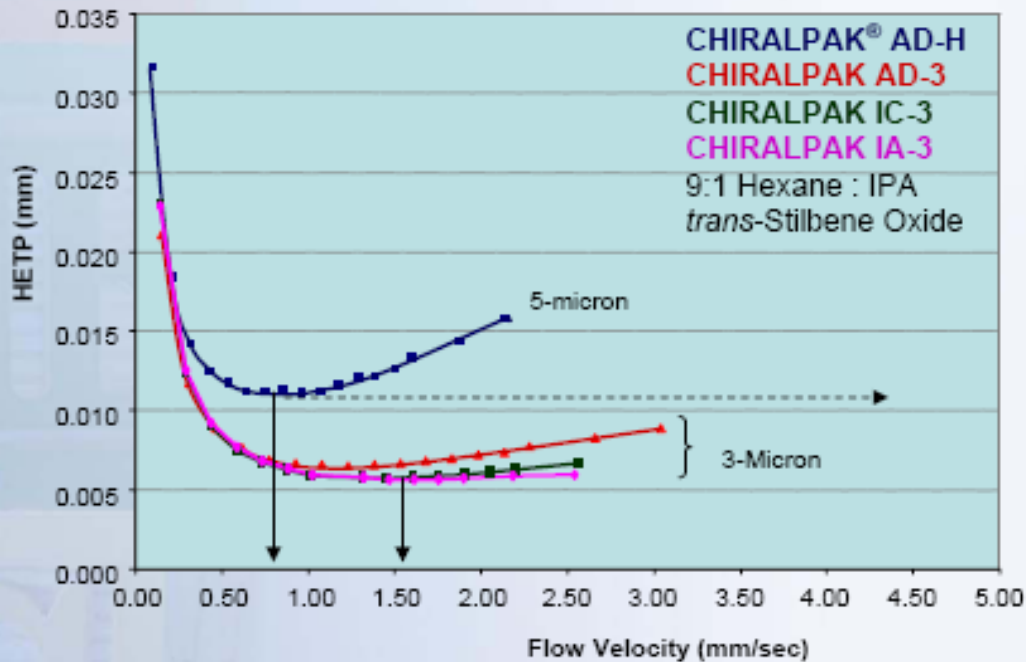
二、3微米固定相：快速分析、效率更高

- 柱效更高
- 流速更大
- 适用于快速分析
- 可承受柱压更高

二、3微米固定相：快速分析、效率更高

- 柱效更高

Van Deemter plot



- *Higher optimum flow rate with smaller particles leads to faster analyses and higher efficiency*
- *Smaller HETP allows shorter columns – and faster analyses*

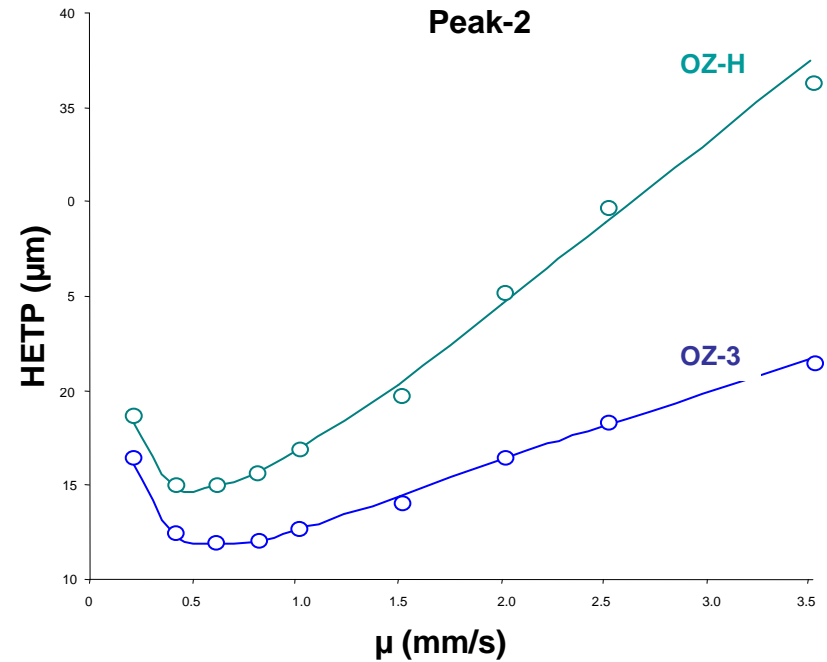
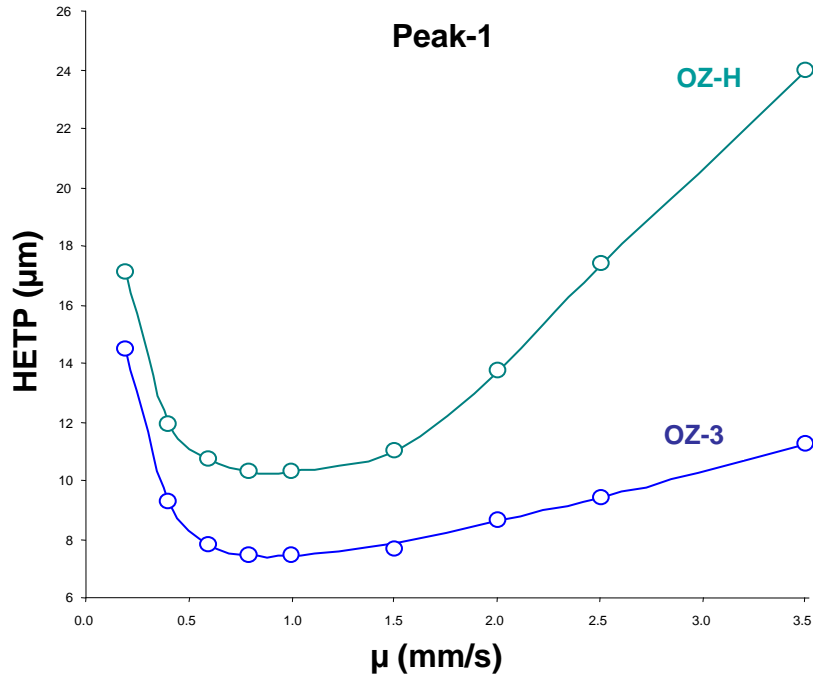
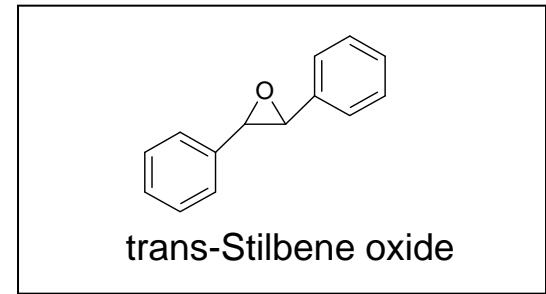
二、3微米固定相：快速分析、效率更高

- 柱效更高

MP: hexane/2-propanol 90/10

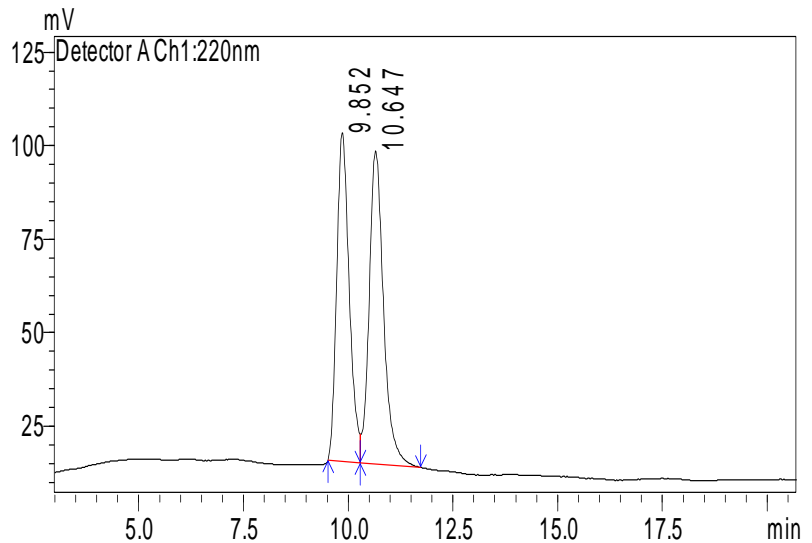
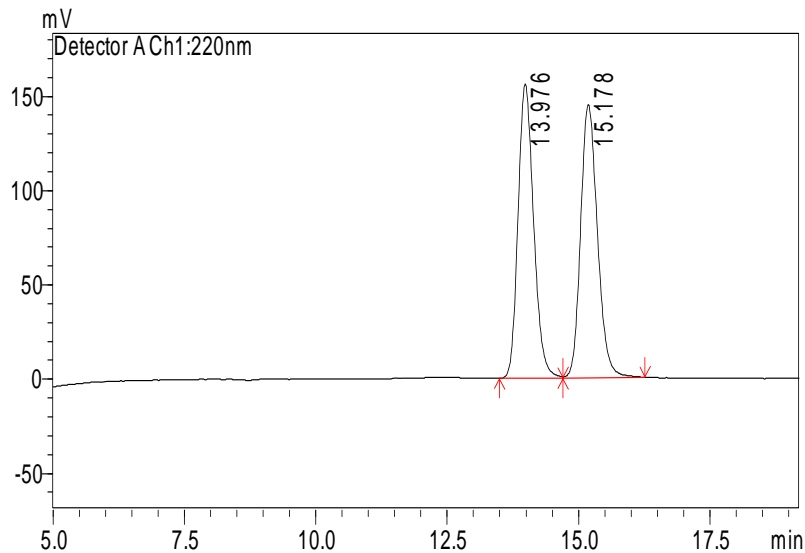
T= 25° C

Column size: 4.6x150mm



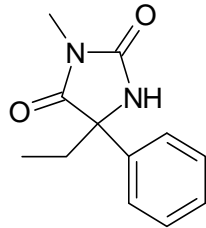
二、3微米固定相：快速分析、效率更高

- 柱效更高，分离度更大
- 化合物A Hexane/IPA/HAc=100/1/0.1 (v/v/v)
- **OD-3 (R=2.1)** **OD-H (R=1.3)**



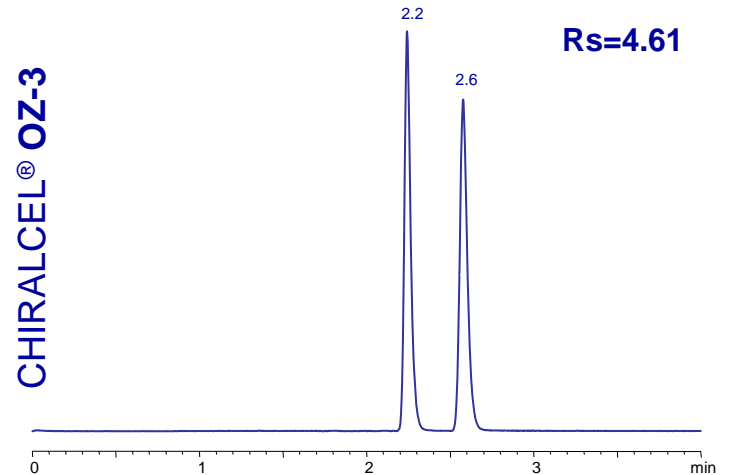
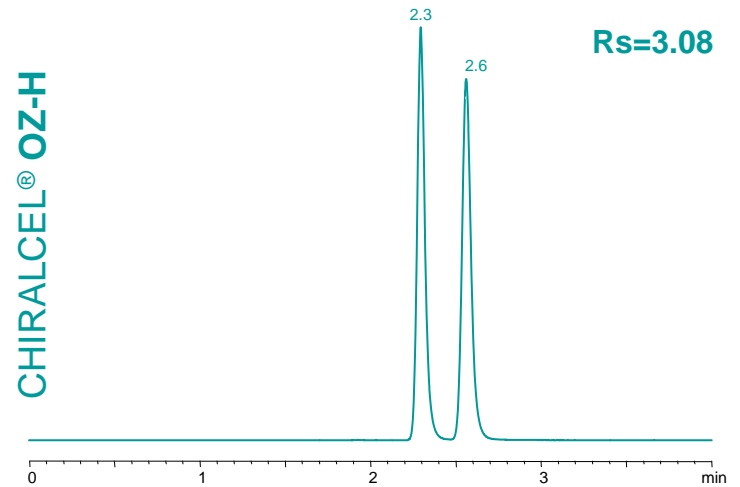
二、3微米固定相：快速分析、效率更高

- 柱效更高
- 相同保留时间，分离度更大



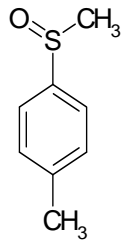
Mephénytoin

ACN 1.0ml/min, 25° C
UV 230nm
4.6x150mm



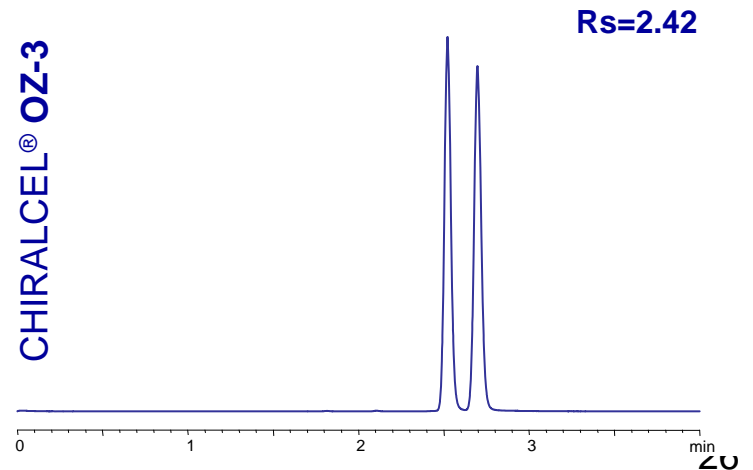
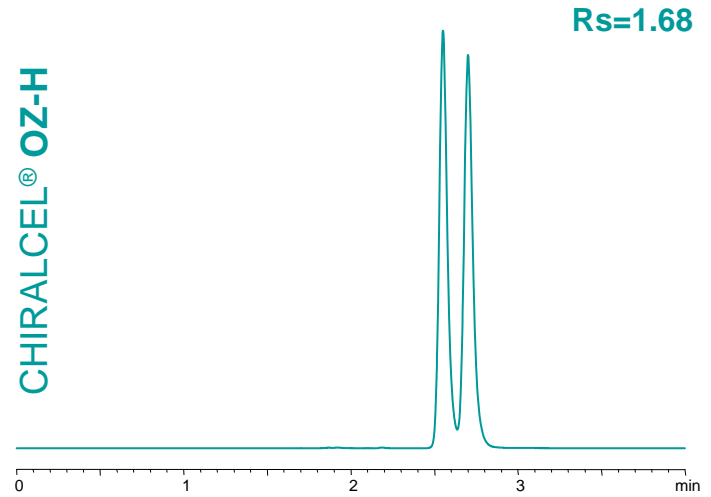
二、3微米固定相：快速分析、效率更高

- 柱效更高，分离度更大



Methyl p-tolyl sulfonate

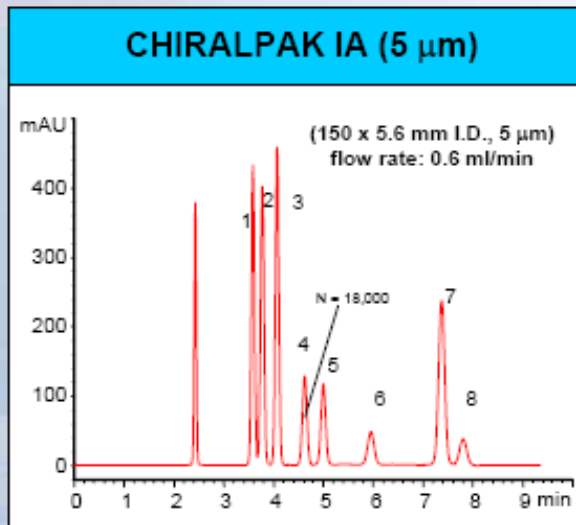
MeOH 1.0ml/min
25° C, 254nm
4.6x150mm



二、3微米固定相：快速分析、效率更高

- 流速更大

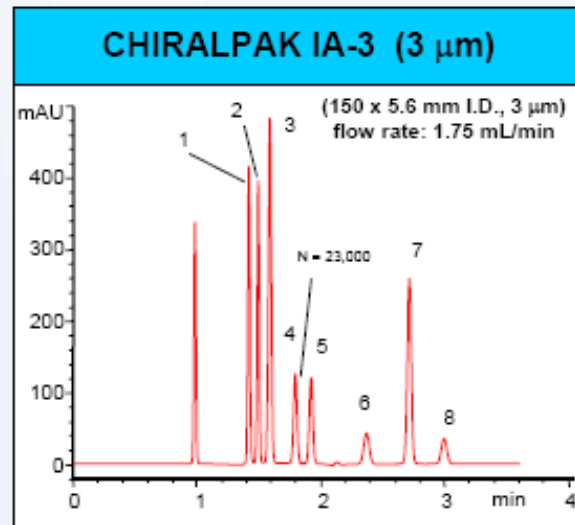
Increase in speed from 5 to 3 microns



Mecoprop methyl ester: 1,2

trans-Stilbene oxide: 3,7

Benzoin ethyl ether: 4,5 Ruelene: 6,8



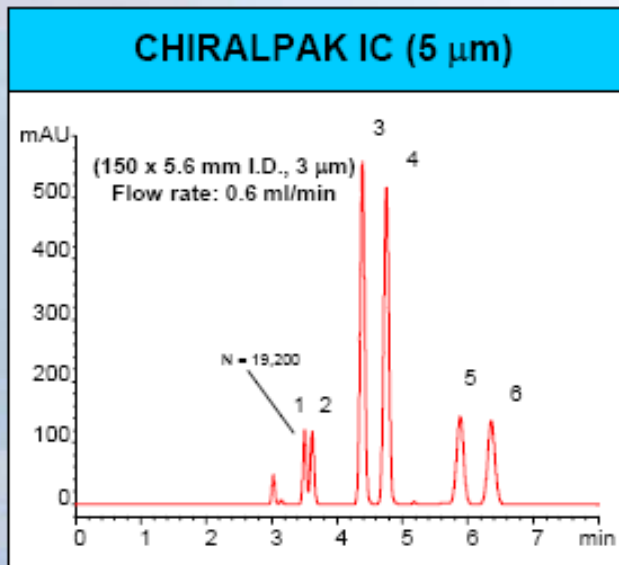
~ 3-fold decrease in analysis time

Hexane-Isopropanol 90:10 (v/v) UV 210 nm, 25° C

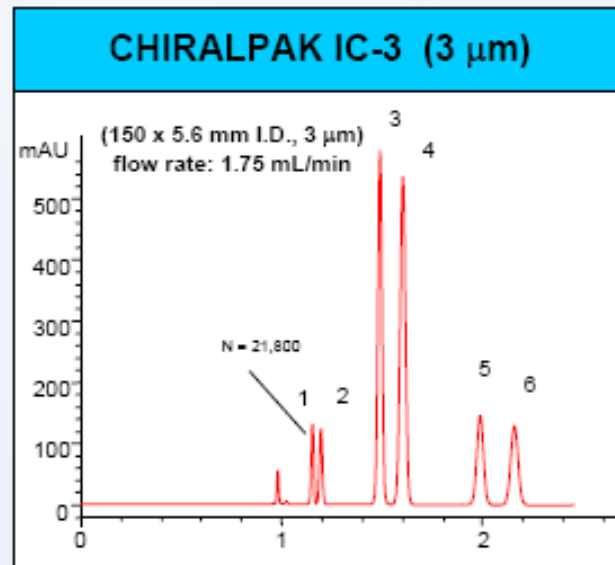
二、3微米固定相：快速分析、效率更高

- 流速更大

Increase in speed from 5 to 3 microns



1-Phenyl-2,2,2-trifluoroethanol: 1,2
Tetrahydronaphthol: 3,4
Mecoprop methyl ester: 5,6

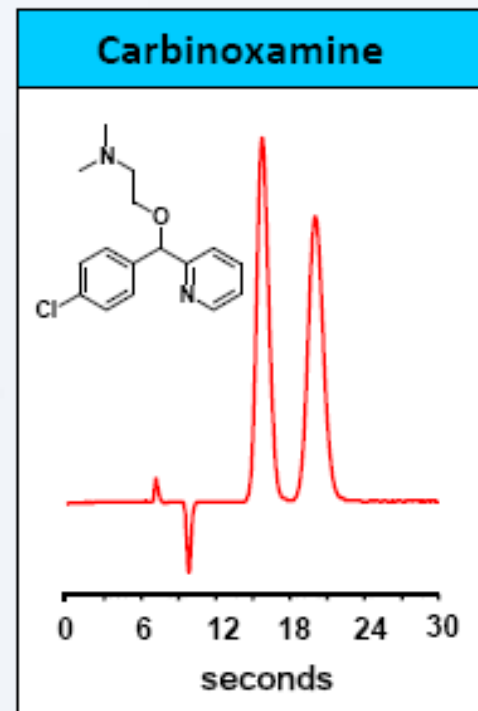
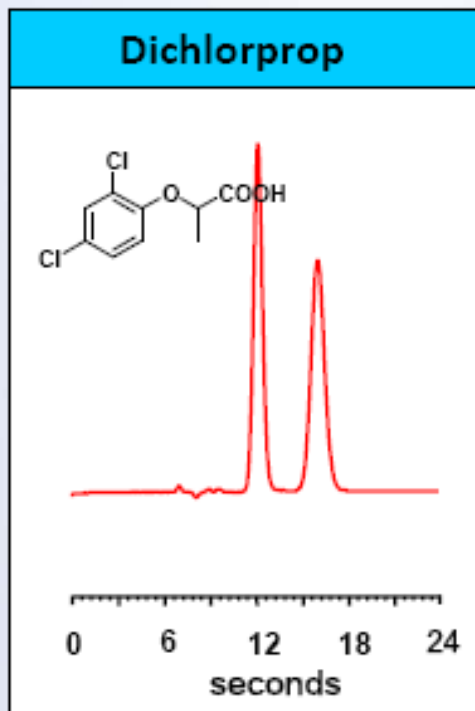
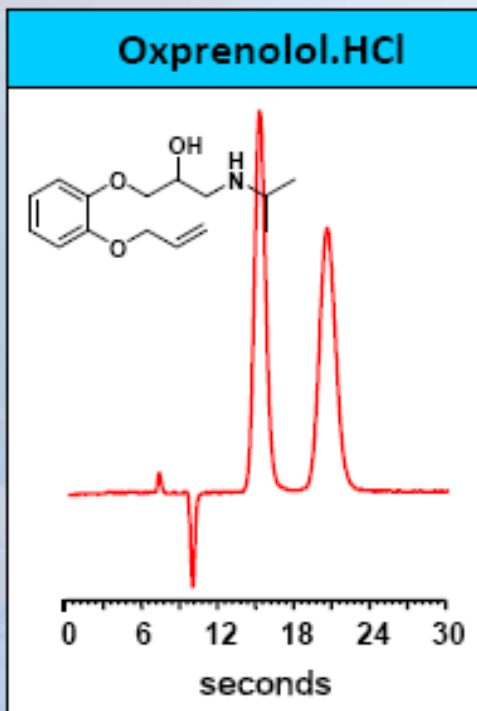


~ 3-fold decrease in analysis time

Hexane-Isopropanol 90:10 (v/v) UV 210 nm, 25° C

二、3微米固定相：快速分析、效率更高

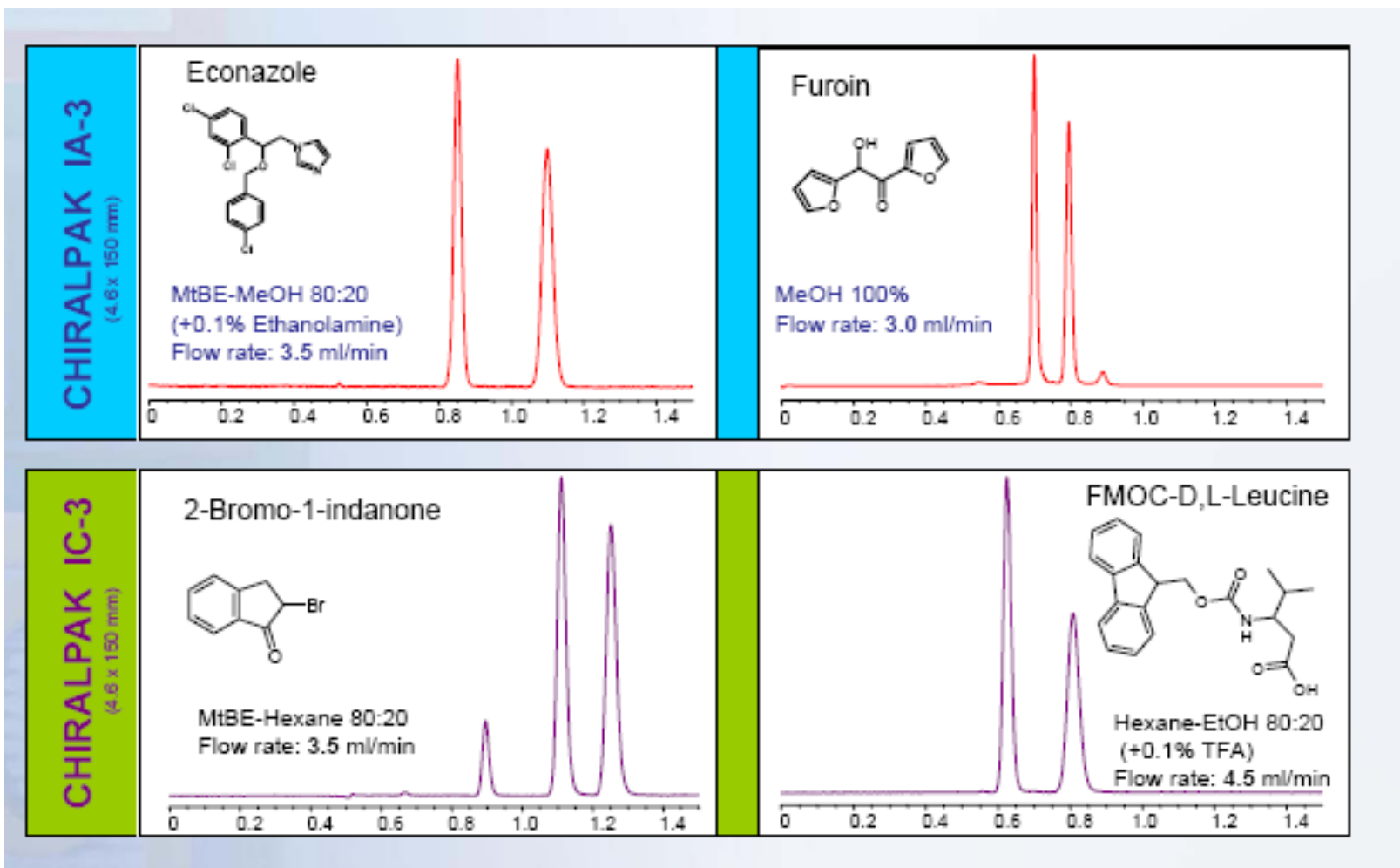
- 快速分析



CHIRALPAK® AD-3 (50 x 4.6 mm I.D.); for oxprenolol and carbinoxamine: n-hexane/2-propanol/diethylamine 90/10/0.1 (v/v/v); for dichlorprop: n-hexane/2-propanol/trifluoroacetic acid 90/10/0.1 (v/v/v); flow rate: 5.0 mL/min; UV-detection: 235 nm; temperature: 25°C.

二、3微米固定相：快速分析、效率更高

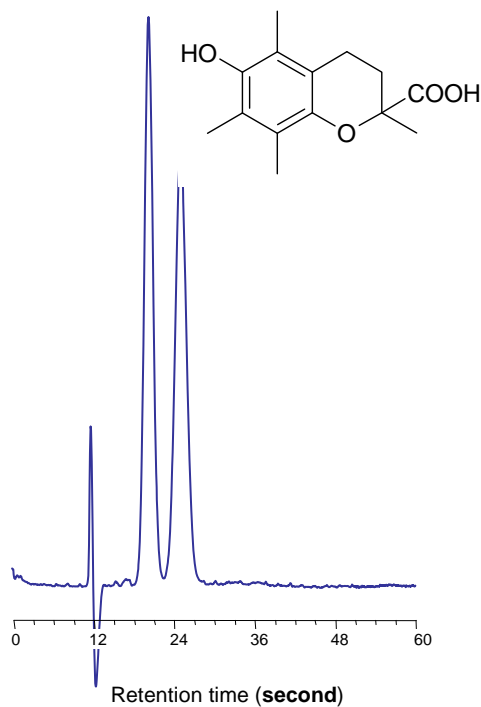
- 快速分析



二、3微米固定相：快速分析、效率更高

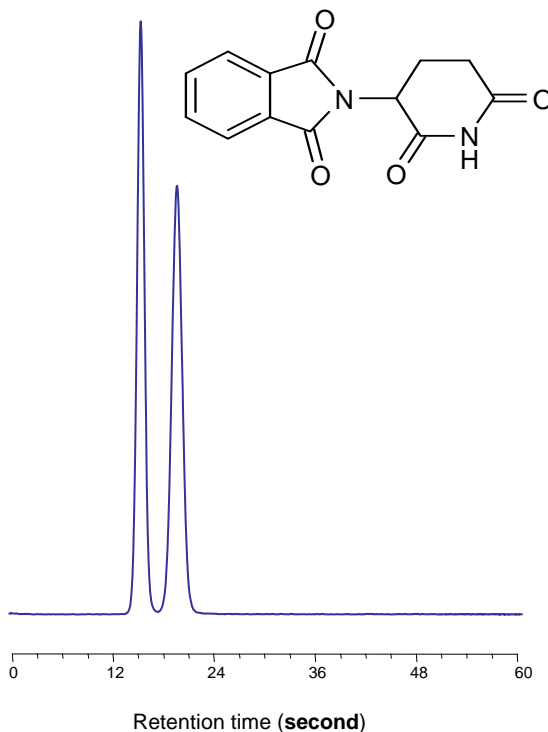
- 快速分析(OZ-3)

6-Hydroxy-2,5,7,8-tetramethyl
Chromane-2-carboxylic acid



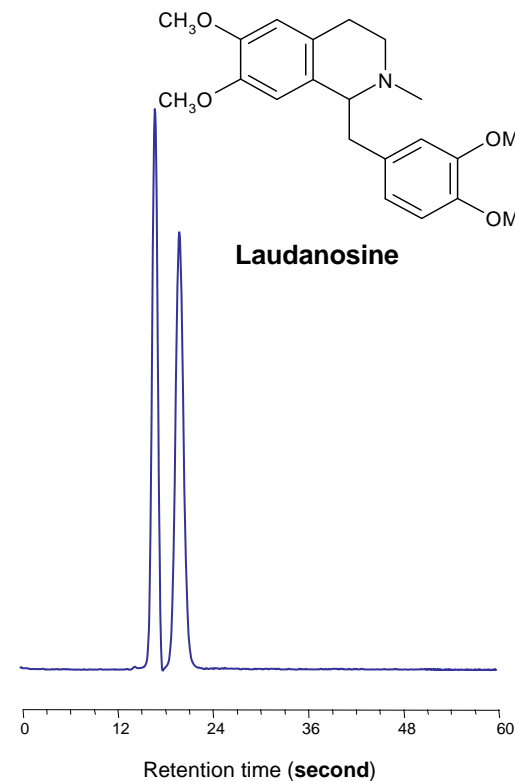
Hexane-EtOH 90:10 (+0.1% TFA)
Flow rate: 3.0 ml/min

Thalidomide



ACN
Flow rate: 4.0 ml/min

Laudanosine



ACN (+0.1% DEA)
Flow rate: 3.0 ml/min

二、3微米固定相：快速分析、效率更高

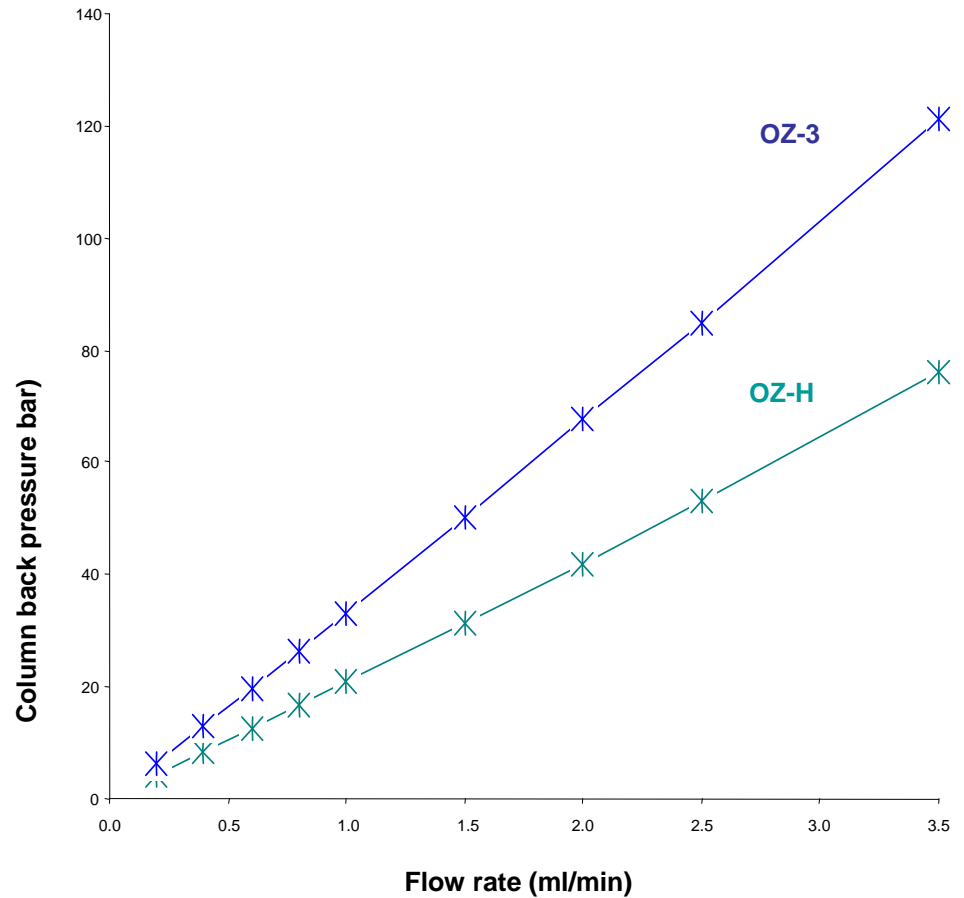
- 可承受柱压更高

Pressure ratio **OZ-3/OZ-H: 1.58**

Hexane-2-propanol 90:10

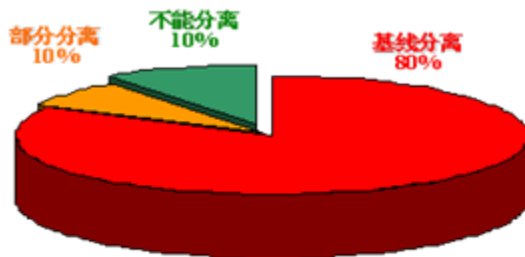
T= 25° C

Column size: 4.6x150mm



手性色谱技术的研发动向

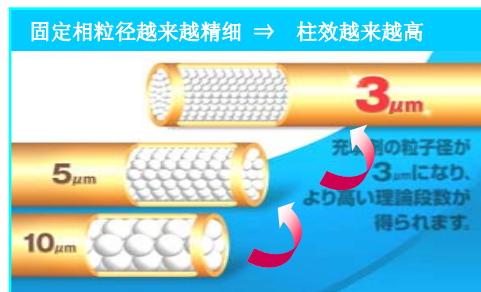
更加广泛



对10%的责任和挑战

新型固定相
AY, OZ, AZ, IC

更加快速



3微米固定相
普通系列 ⇒ H系列 ⇒ 3系列

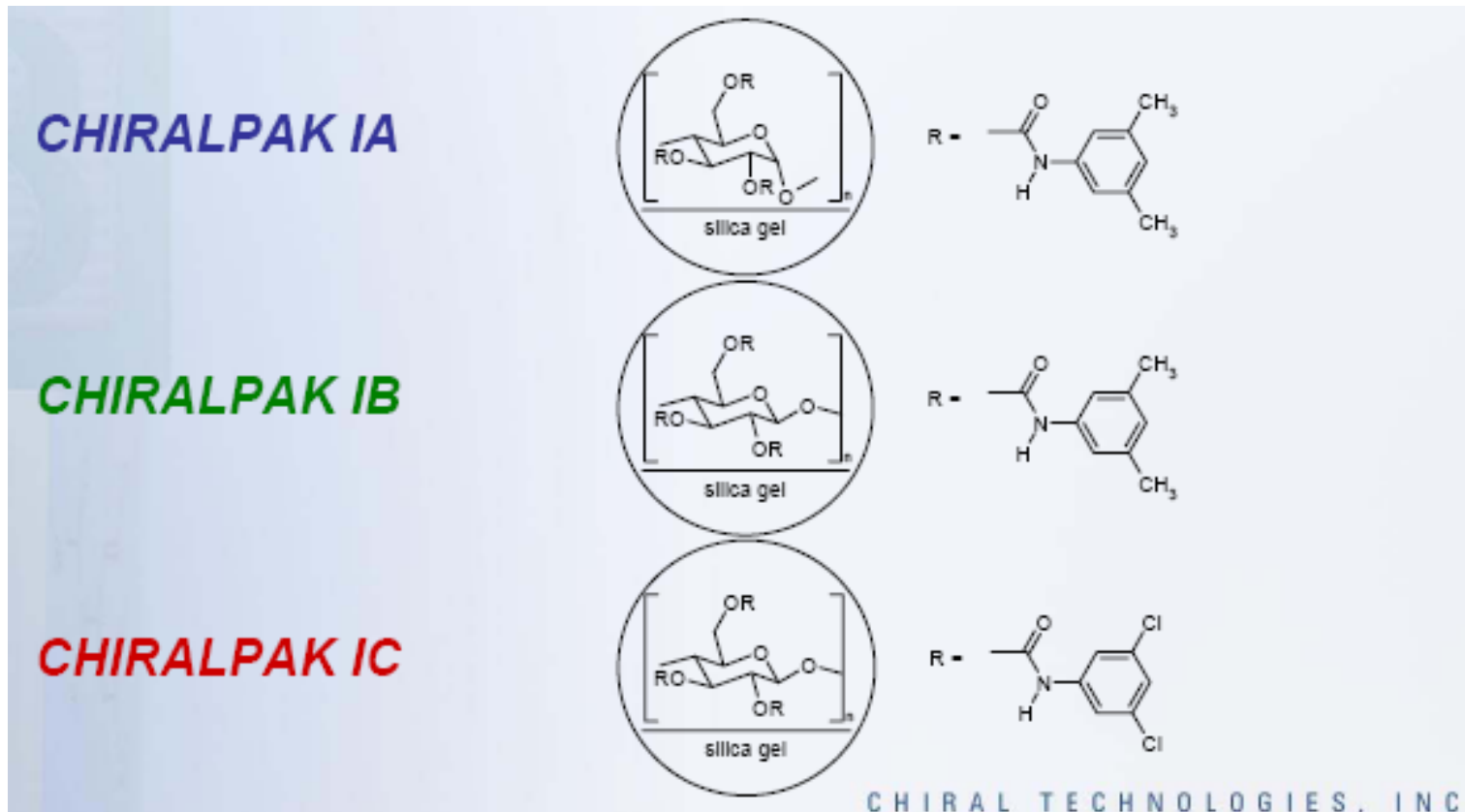
更加稳定



键合型固定相
IA, IB, IC

三、键合型固定相：更稳定

- **IA:**直链淀粉-三（3，5二甲苯基氨基甲酸酯）
- **IB:**纤维素-三（3，5二甲苯基氨基甲酸酯）
- **IC:**纤维素-三（3，5-二氯苯基氨基甲酸酯）



三、键合型固定相：更稳定

- 流动相范围增大，成功分离把握增加

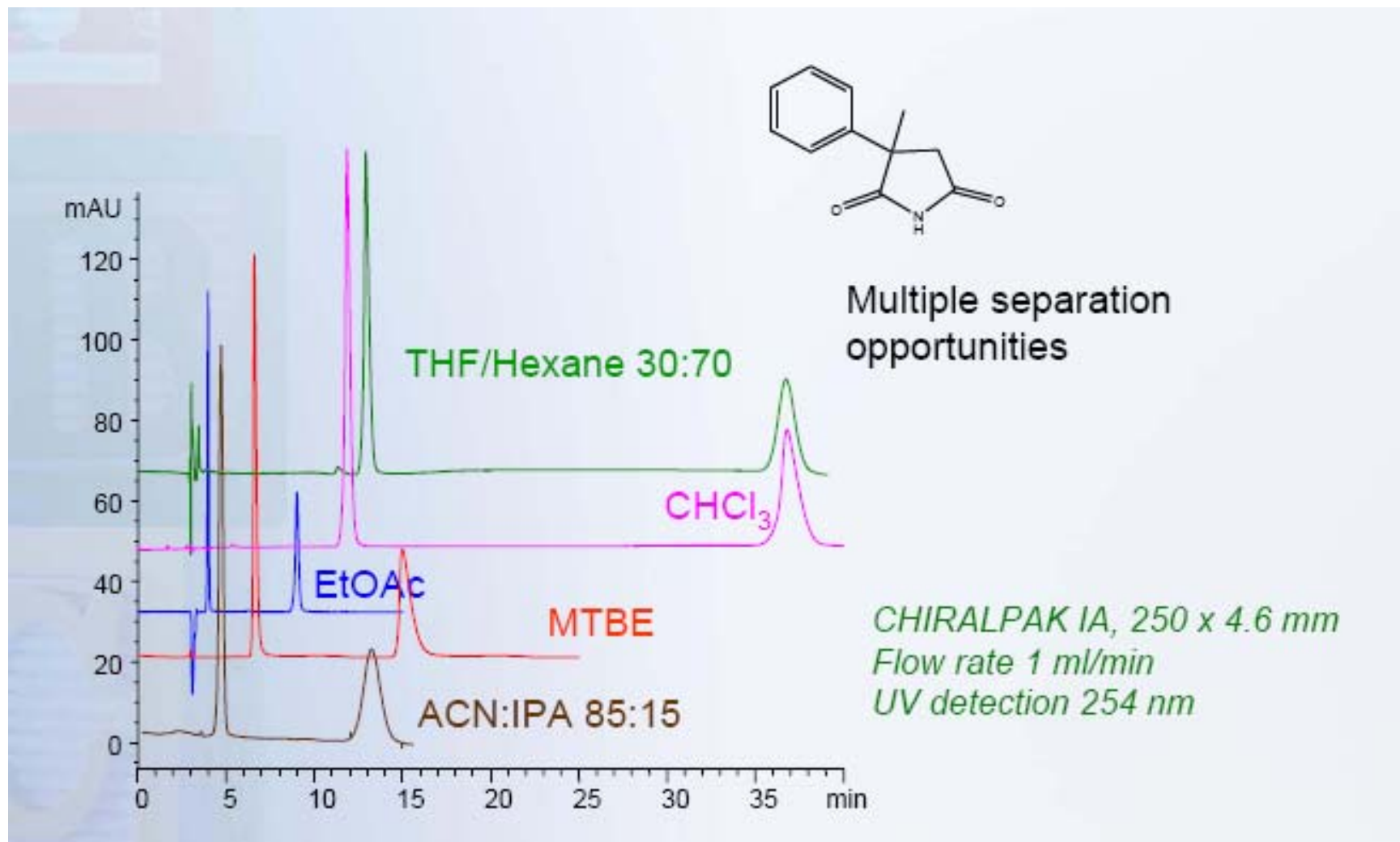
普通流动相：正己烷、异丙醇、乙醇

特殊流动相：乙酸乙酯、二氯甲烷、四氢呋喃、甲基叔丁基醚等

反相流动相：水、乙腈、甲醇

- 改善溶解度，提高制备效率
- **IC**新型固定相
- 可修复再生

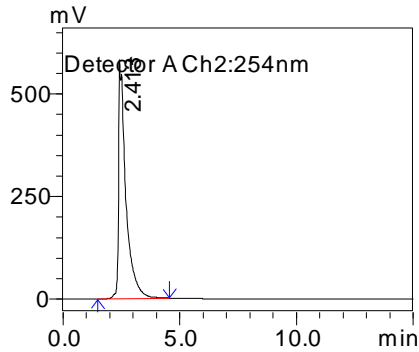
三、键合型固定相：更稳定



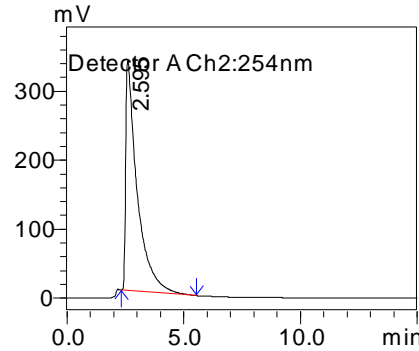
三、键合型固定相：更稳定

Analysis condition :H90I10

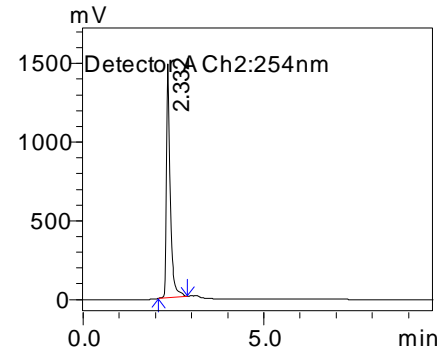
AD



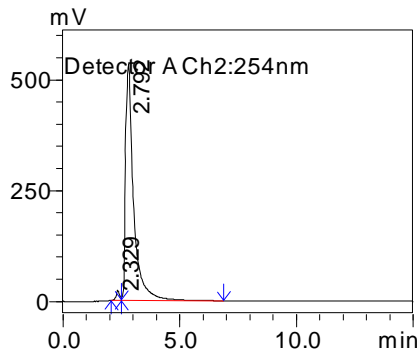
AS



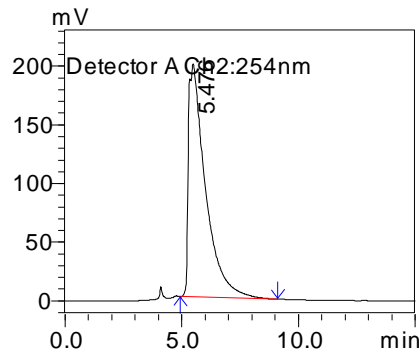
OD



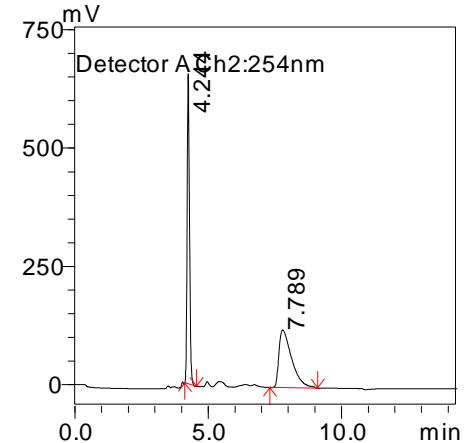
IA



IC



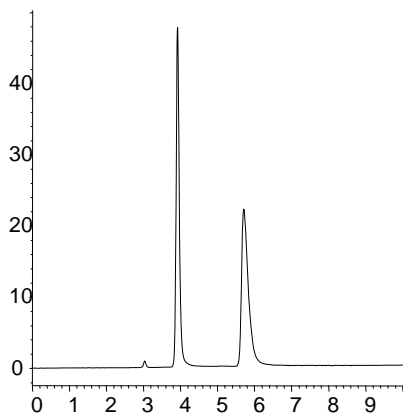
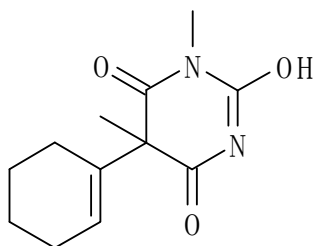
IC: H95THF5



CHIRALPAK® IA 分离实例

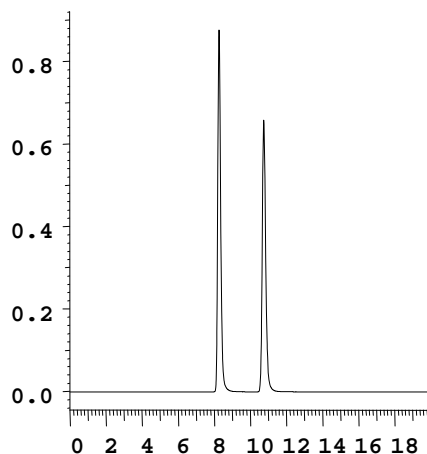
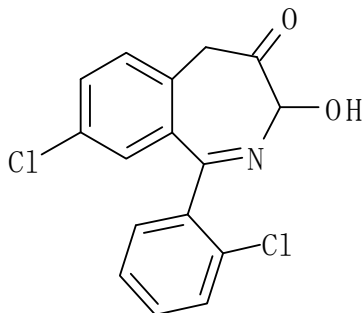
---中性样品---

Hexobarbital



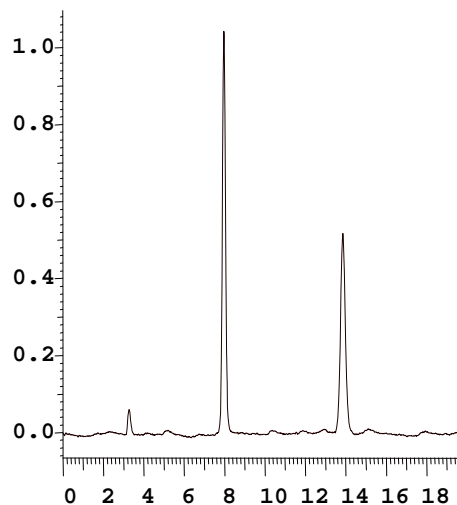
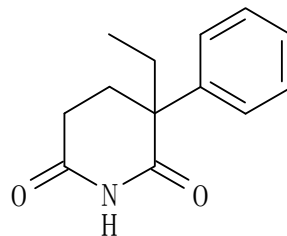
甲基叔丁基醚
=100
 $k_1' = 0.31, \alpha = 2.94$

Lorazepam



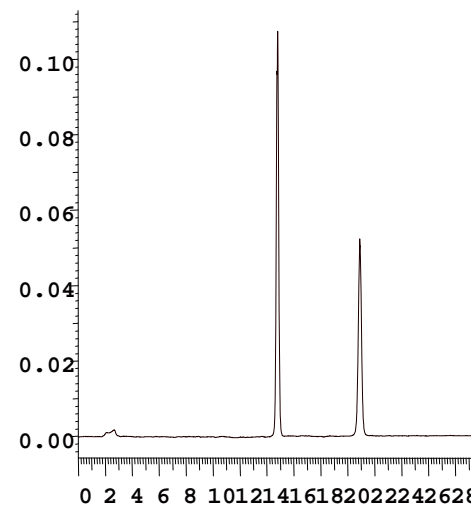
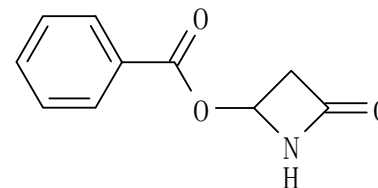
正己烷/丙酮
=60/40
 $k_1' = 1.75, \alpha = 1.47$

Glutethimide



正己烷/1,4-二氧环乙烷
=70/30
 $k_1' = 1.65, \alpha = 2.19$

4-Benzoyloxy-2-azetidinone

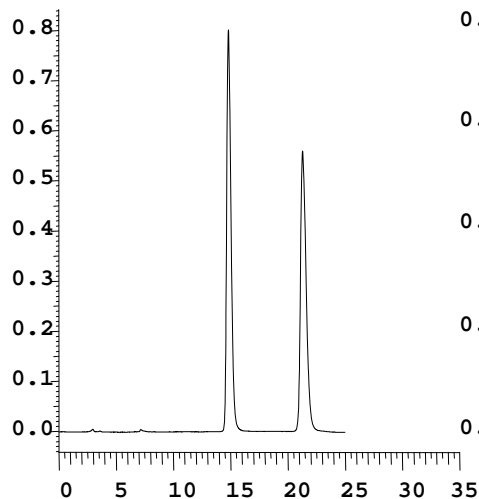
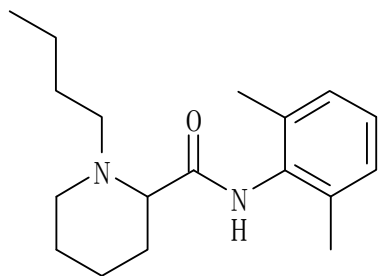


正己烷/二氯甲烷
=25/75
 $k_1' = 3.93, \alpha = 1.52$

CHIRALPAK® IA分离实例

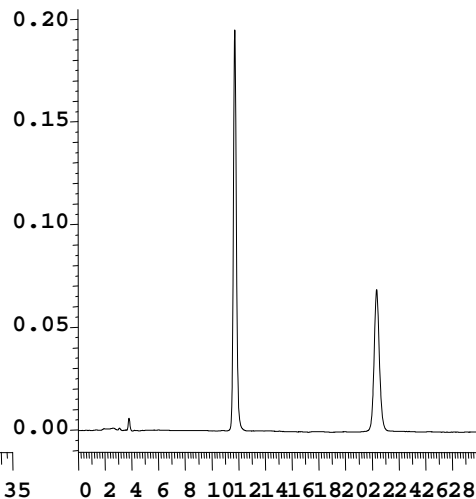
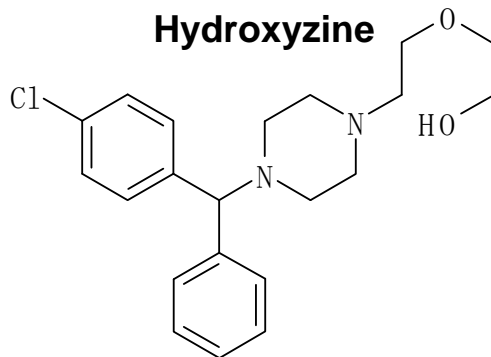
---碱性样品---

Bupivacaine



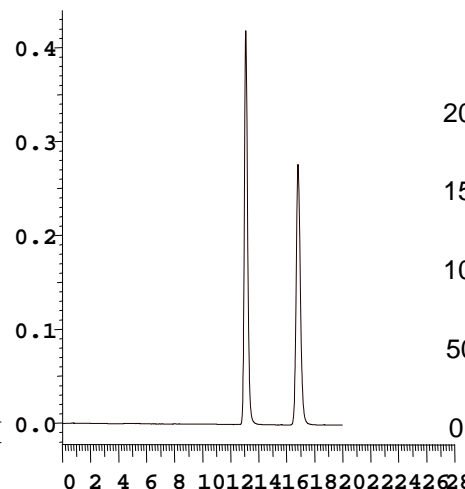
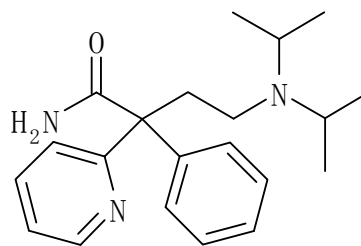
Hex/THF/DEA
=90/10/0.1
 $k_1' = 3.94$, $\alpha = 1.55$

Hydroxyzine



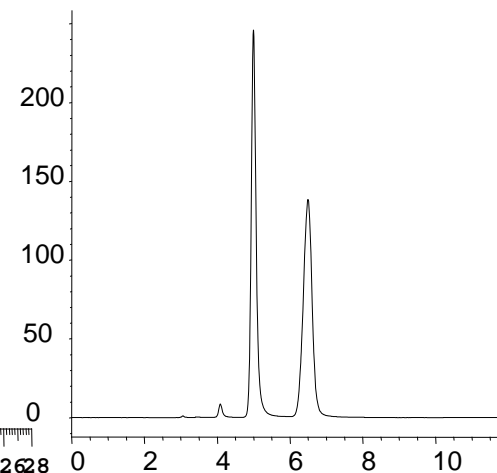
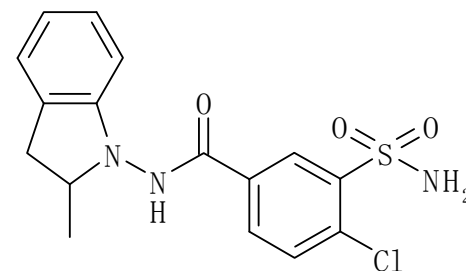
Hex/EtOAc/DEA
=40/60/0.1
 $k_1' = 2.90$, $\alpha = 2.22$

Disopyramide



Hex/Acetone/DEA
=80/20/0.1
 $k_1' = 3.36$, $\alpha = 1.37$

Indapamide

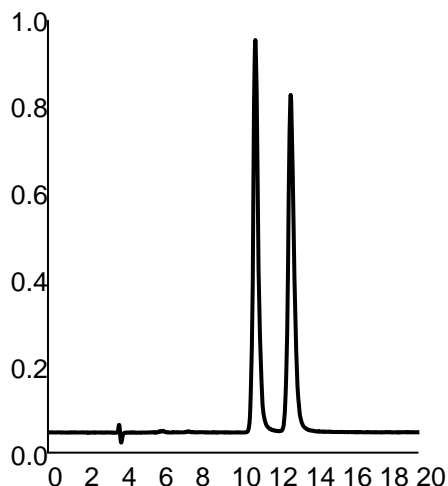
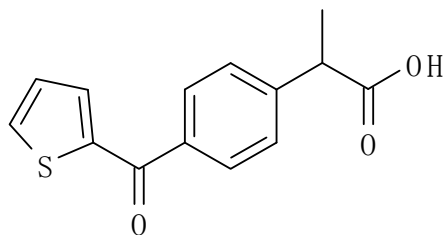


MTBE/EtOH/DEA
=80/20/0.1
 $k_1' = 0.67$, $\alpha = 1.75$

CHIRALPAK® IA 分离实例

---酸性样品---

Suprofen

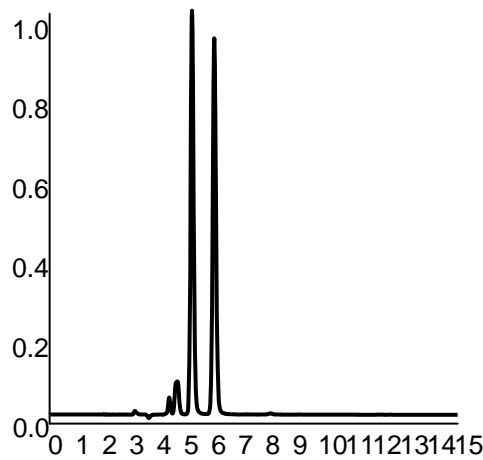
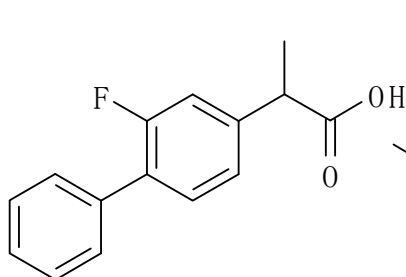


Hex/EtOAc/TFA

=70/30/0.1

$k_1' = 2.83$, $\alpha = 1.18$

Flurbiprofen

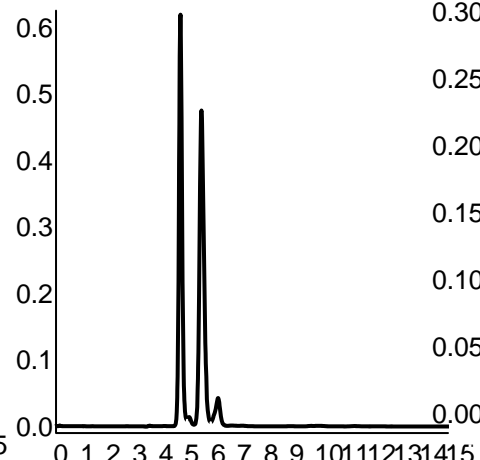
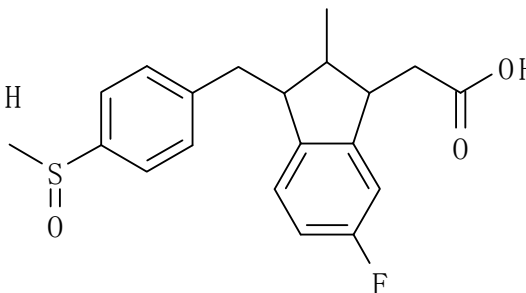


Hex/EtOH/TFA

=85/15/0.1

$k_1' = 0.74$, $\alpha = 1.37$

Sulindac

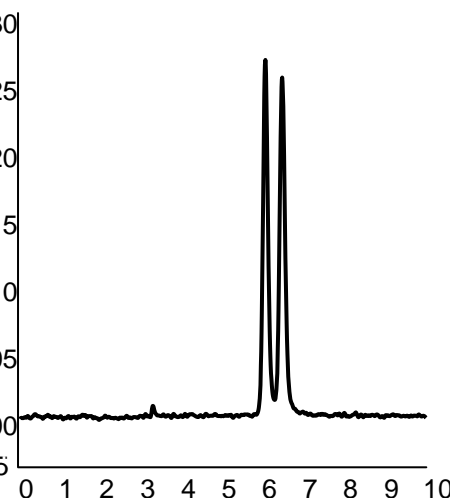
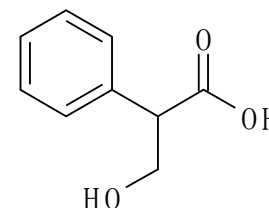


MeOH/EtOH/TFA

=50/50/0.1

$k_1' = 0.59$, $\alpha = 1.45$

Tropic acid



Hex/THF/TFA

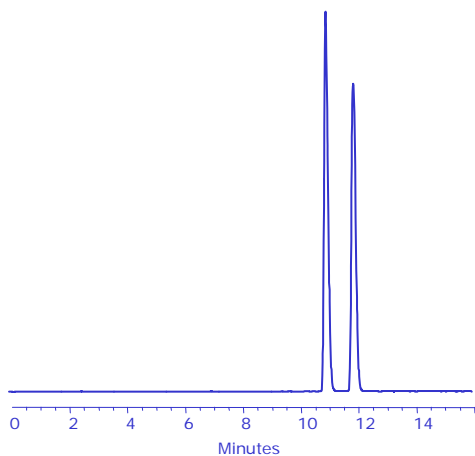
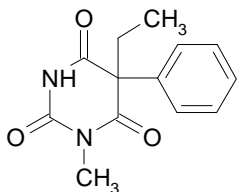
=65/35/0.1

$k_1' = 1.01$, $\alpha = 1.14$

CHIRALPAK® IB分离实例

---中性样品---

Mephobarbital

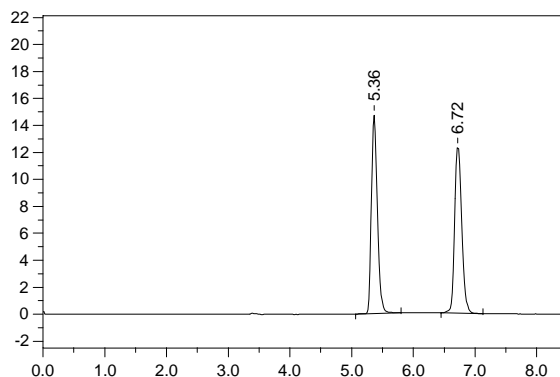
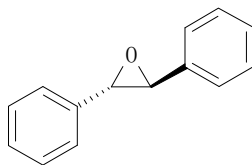


正己烷/三氯甲烷

=50/50

$\alpha=1.12$

trans-Stilbene oxide

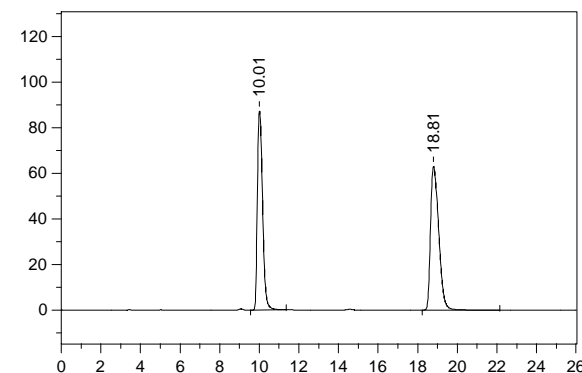
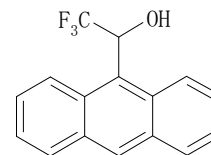


正己烷/二氯甲烷

=80/20

$k_1'=0.69, \alpha=1.62$

2,2,2-Trifluoro-1-(9-anthryl)ethanol



正己烷/四氢呋喃

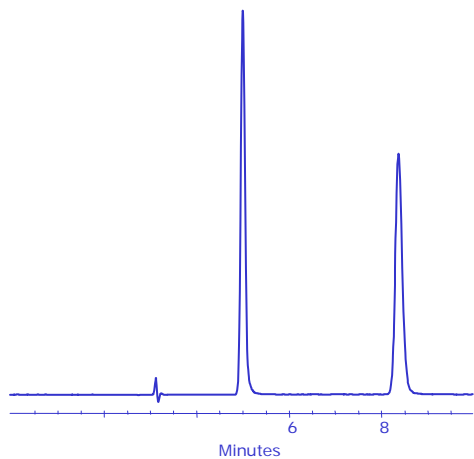
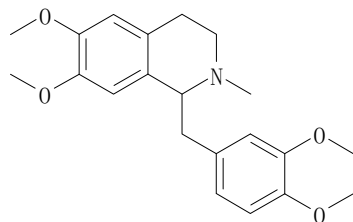
=90/10

$k_1'=2.28, \alpha=2.26$

CHIRALPAK® IB分离实例

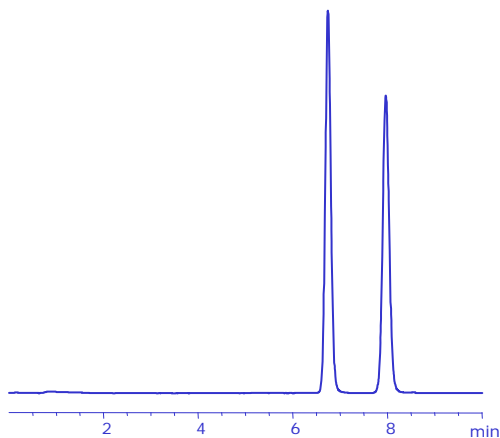
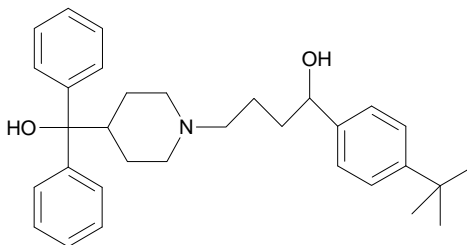
---碱性样品---

Laudanosine



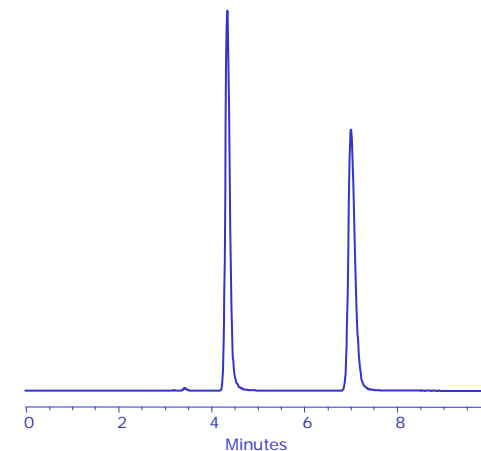
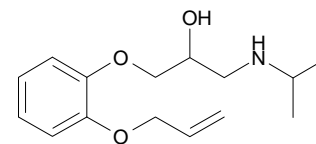
正己烷
/THF/EDA
=70/30/0.1
 $k_1' = 0.67, \alpha = 2.68$

Terfenadine



正己烷
/CHCl₃/EtNA
=65/35/0.1
 $k_1' = 1.20, \alpha = 1.33$

Oxprenolol

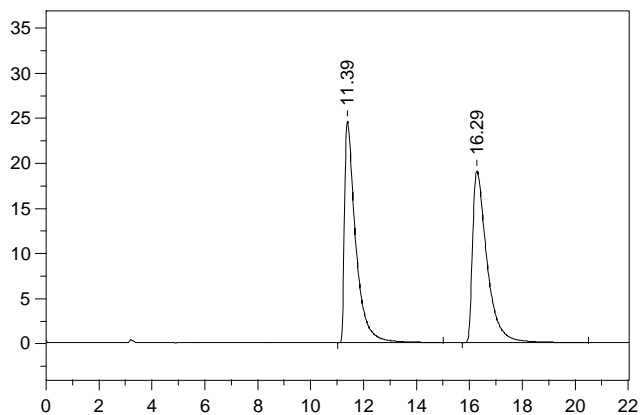
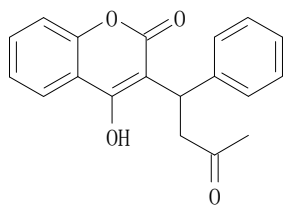


MTBE/EtOH/EDA
=95/5/0.1
 $k_1' = 0.45, \alpha = 2.98$

CHIRALPAK® IB 分离实例

---酸性样品---

Warfarin

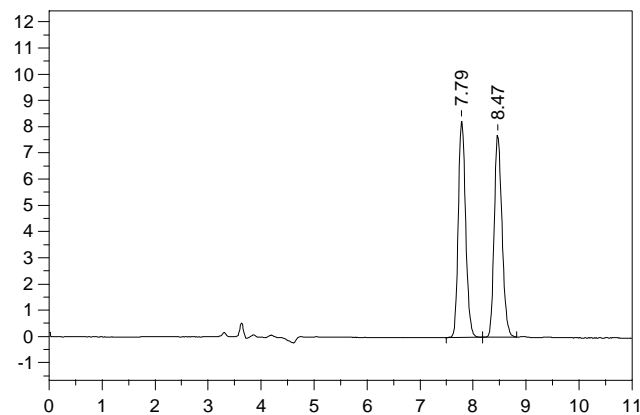
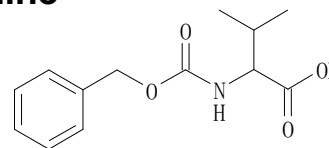


正己烷/乙酸乙酯/TFA

=70/30/0.1

$k_1' = 2.69$, $\alpha = 1.59$

N-Benzoyloxycarbonyl-valine



正己烷/CHCl₃/甲醇/TFA

=70/30/1/0.1

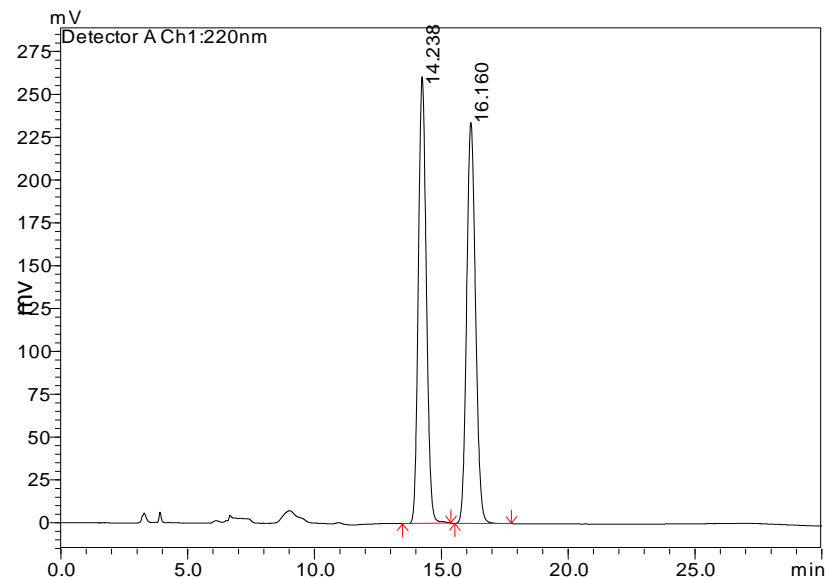
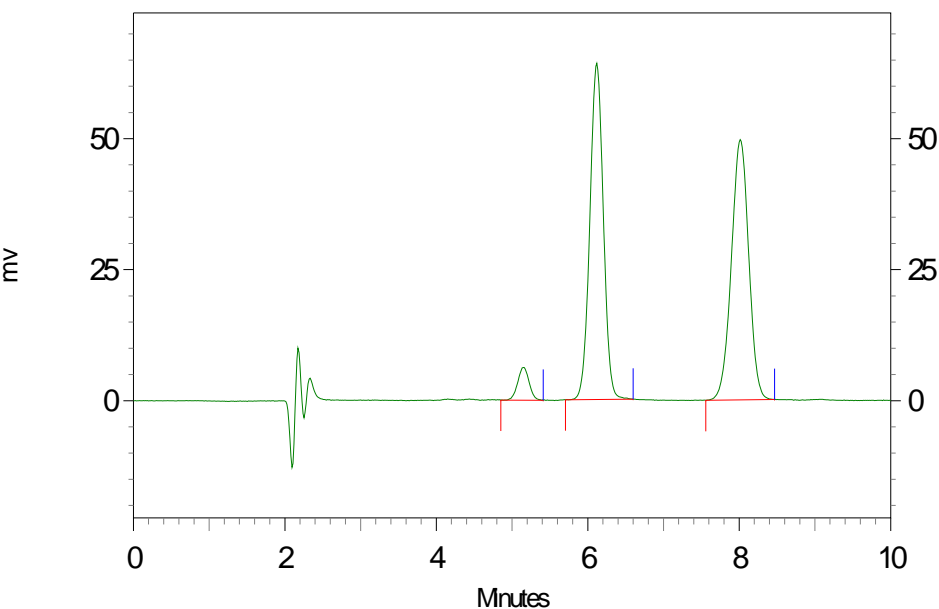
$k_1' = 1.52$, $\alpha = 1.14$

CHIRALPAK® IC 分离实例

---中性样品---

Compound B

三唑酮



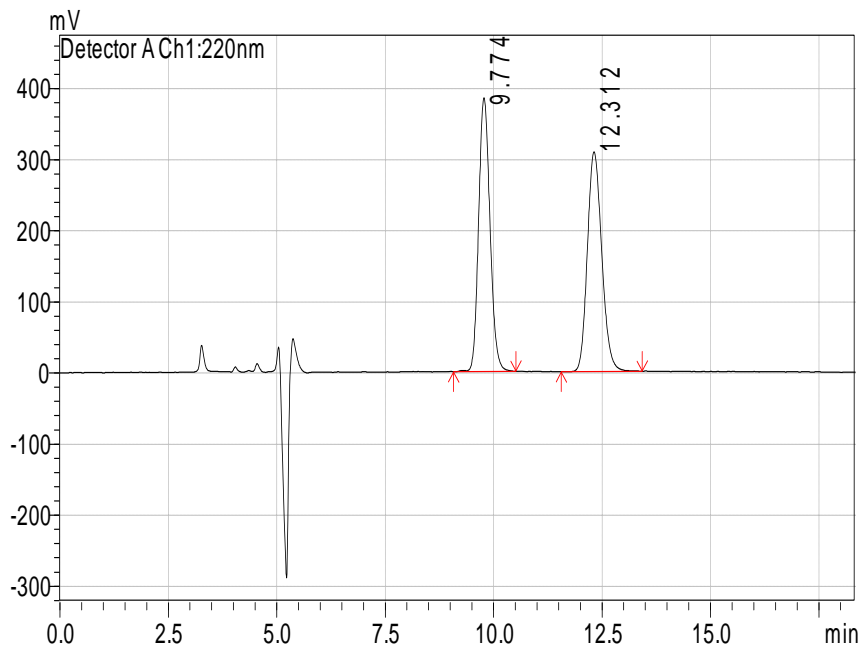
甲醇/二氧化碳=40/60
R=5.04

正己烷/异丙醇=95/5
R=3.13

CHIRALPAK® IC 分离实例

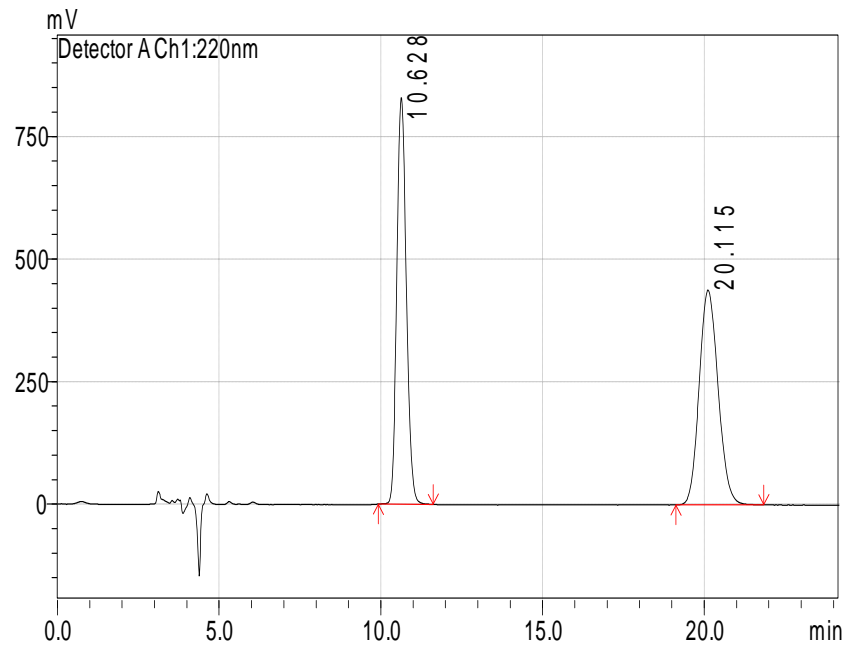
---碱性样品---

Compound C



正己烷/异丙醇/DEA
=90/10/0.1
R=4.66

Compound D

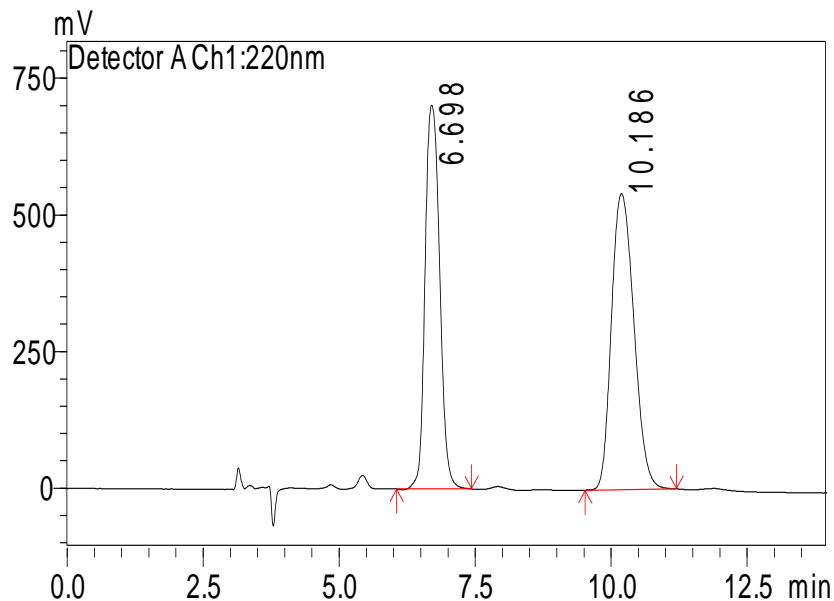


正己烷/异丙醇/DEA
=90/10/0.1
R=11.75

CHIRALPAK® IC 分离实例

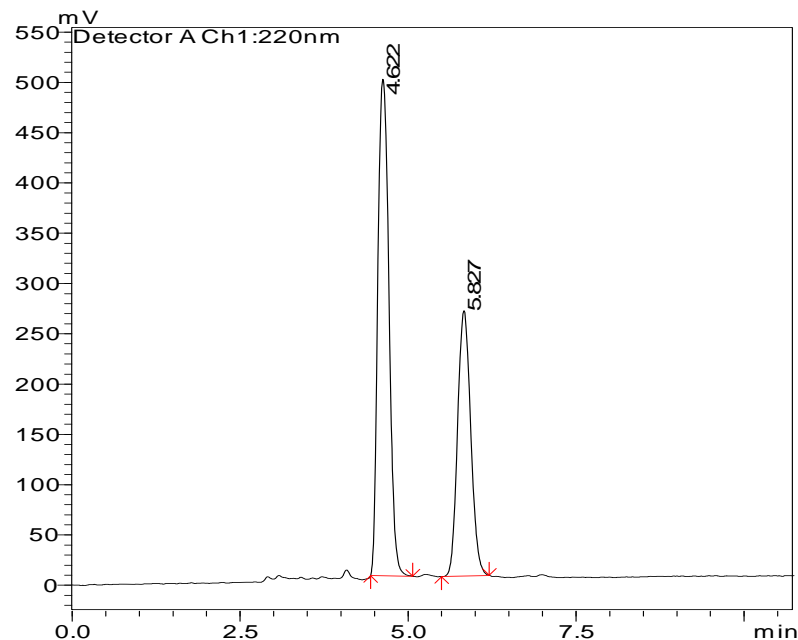
---酸性样品---

Compound E



正己烷/异丙醇/TFA
=50/50/0.1
R=5.75

Compound F



二氯甲烷/四氢呋喃/TFA
=90/10/0.1
R=3.64

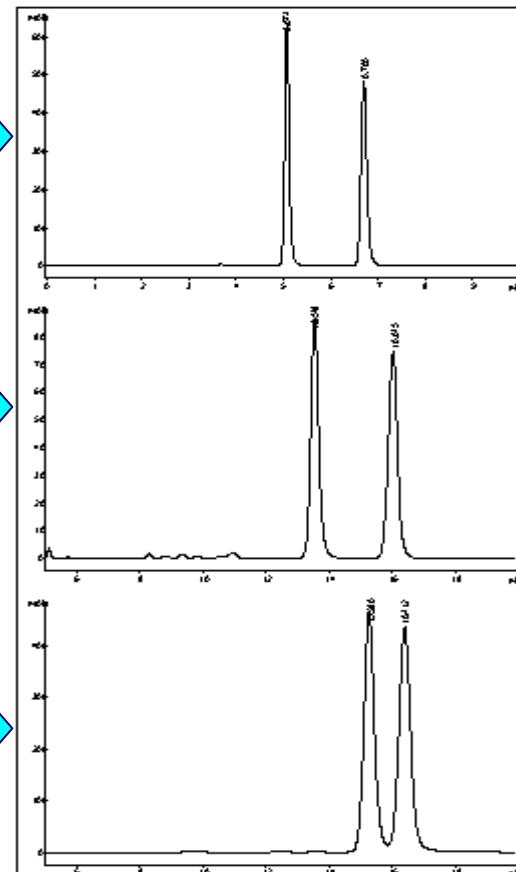
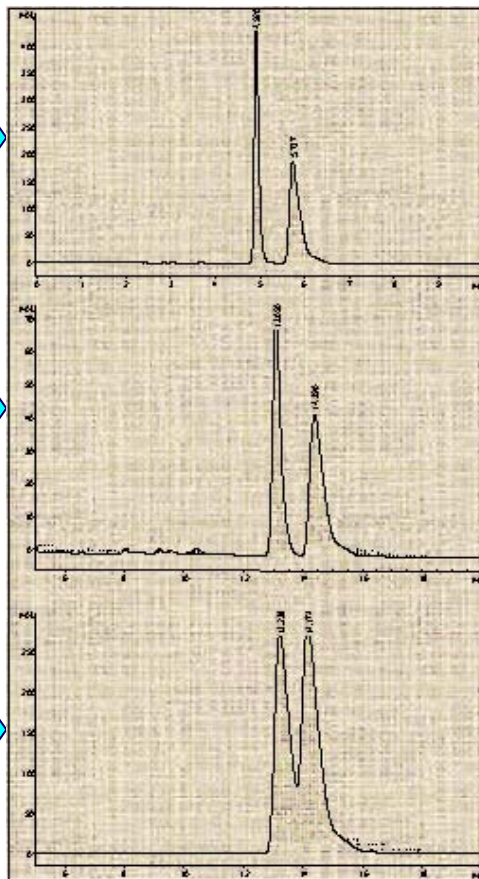
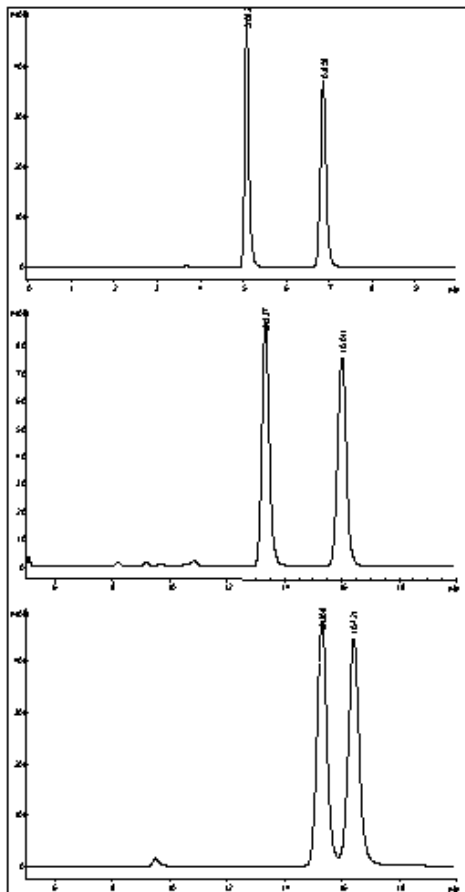
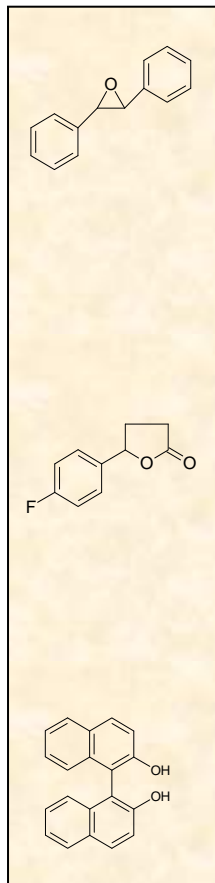
IA,IB,IC柱的修复再生

样品

新色谱柱

柱性能受损
(如受强吸附杂质的影响)

修复再生后
(可使用各种强极性溶剂)



流动相:
n-hexane/EtOH 90/10
1 ml/min, 25° C



北京金欧亚科技发展有限公司

北京崇文区左安门内大街8号伟图大厦301室

PC: 100061

Tel : 010-67136152/67100708

Fax : 010-67114016/67113925

<http://www.jinouya.cn>

E-mail: china.hplc@163.com