UPLC超高效液相色谱药典应用文集

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序

药典系国家对批准上市药品标准的统一集成和对其中共性问题的统一规范。是药品生产、供应、使用和监督管理部门必须共同遵循的法定依据，制定药典标准对加强药品质量监管、保证药品质量、保障用药安全有效、维护人民健康起着十分重要的作用。药物分析技术作为药典标准制定中不可或缺的组成部分，近些年来随着医药工业的发展得到了不断的完善和进步。同时，我们也看到产业的发展和药品监管新的形势需要更精准快捷的药物分析技术及理念，以实现更科学的药品质量控制与监督已经成为各国药典的共识。在这一全球共识下，2015版中国药典在保留常规检测方法的基础上，进一步扩大了对药物分析新技术和新仪器方法的应用，大大提升了药品质量控制水平。但是，由于一些新技术的特点和应用范围并不为广大同仁所知晓，同时业界对新技术的规范使用也需要一定的认知过程，使得这些新技术的广泛应用尚需时日。

超高效液相色谱技术作为一种领先的分析技术，自2004年面世以来，其高效、环保等优势就引起了制药行业的广泛关注，2010年前后，各国药典就陆续引入了基于超高效液相色谱方法的药典各论。但由于各论的数量并不多，导致业界对这类药物分析新方法的稳定性和合规性存有一定的疑虑。

如今，随着使用超高效液相色谱方法建立标准的新药大规模问世，美国在2016版美国药典(USP39)中增加了57个基于超高效液相色谱方法的各论,各国药典也将有新的各论陆续面世。由此也引发了大量中国制药企业对超高效液相色谱技术的关注，越来越多的中国企业期待采用超高效液相色谱方法建立药物标准。为了推动超高效液相色谱技术的应用，同时帮助中国制药企业顺应发展潮流，提升产业技术实力，中国药典-沃特世联合开放实验室推出了本册《超高效液相色谱药典应用文集》。在体现联合开放实验室开放性和创新性原则的同时，能够通过本册应用文集，为今后国内外药典协同提供基础数据，也希望从法规的角度，解决有意愿使用超高效液相色谱技术的企业对于这项技术的疑惑。

国家药典委员会首席科学家

目录

中国药典（ChP）

复方丹参滴丸 8

护肝丸 / 胶囊 / 颗粒 9

欧洲药典（EP）

奈韦拉平半水合物 / Nevirapine hemihydrate 10

盐酸左卡巴斯汀 / Levocabastine Hydrochloride- Impurity C 12

盐酸左卡巴斯汀 / Levocabastine Hydrochloride 14

富马酸喹硫平 / quetiapine fumarate 17

琥铂酸索非那新 / Solifenacin succinate 21

硫酸羟氯喹 / Hydroxychloroquini sulfas 23

多粘菌素E甲磺酸钠 / Colistimethatum natricum 25

美国药典（USP）

USP<321> Drug Product Assay Tests—Organic Chemical Medicines 27

盐酸多柔比星 / Doxorubicin Hydrochloride 30

盐酸多柔比星注射液 /Doxorubicin Hydrochloride Injection 32

注射用盐酸多柔比星 / Doxorubicin Hydrochloride for Injection 34

环吡酮胺 / Ciclopirox Olamine 36

环吡酮胺乳膏 / Ciclopirox Olamine Cream，Ciclopirox Cream 38

卡马西平 / Carbamazepine 40

卡马西平口服混悬剂 / Carbamazepine Oral Suspension 42

卡马西平缓释片 / Carbamazepine Extended-Release Tablets 44

磷酸安他唑啉 / Antazoline Phosphate 46

盐酸柔红霉素 / Daunorubicin Hydrochloride 47

注射用盐酸柔红霉素 / Daunorubicin Hydrochloride for Injection 49

双氯芬酸钾片 / Diclofenac Potassium Tablets 51

双氯芬酸钠肠溶片 / Diclofenac Sodium Delayed-Release Tablets 53

双氯芬酸钠缓释片 /Diclofenac Sodium Extended-Release Tablets 55

硫酸麻黄碱注射液 / Ephedrine Sulfate Injection 57

肾上腺素 / Epinephrine 58

哈西奈德 / Halcinonide 59
米诺地尔溶液 / Minoxidil Topical Solution 60
水杨酰胺/ Salicylamide 61
马来酸氯苯那敏片 / Chlorpheniramine Maleate Tablets 62
马来酸右氯苯那敏片/ Dexchlorpheniramine Maleate Tablets 63
维生素B12片/ Cyanocobalamin Tablets 64
盐酸地尔硫卓缓释胶囊剂/ Diltiazem Hydrochloride Extended-Release Capsules 65
盐酸地尔硫卓片/ Diltiazem Hydrochloride Tablets 67
盐酸多巴胺/ Dopamine Hydrochloride 69
盐酸多巴胺注射液/ Dopamine Hydrochloride Injection 70
盐酸羟嗪/ Hydroxyzine Hydrochloride 71
盐酸羟嗪注射液/ Hydroxyzine Hydrochloride Injection 73
盐酸羟嗪片/ Hydroxyzine Hydrochloride Tablets 75
盐酸羟嗪口服溶液 / Hydroxyzine Hydrochloride Oral Solution 77
富马酸氯马斯汀/ Clemastine Fumarate 79
富马酸氯马斯汀片/ Clemastine Fumarate Tablets 80
盐酸氯米帕明/ Clomipramine Hydrochloride 81
盐酸氯米帕明胶囊/ Clomipramine Hydrochloride Capsules 83
盐酸氯米帕明复合口服混悬液/ Clomipramine Hydrochloride Compounded Oral Suspension, Veterinary 85
盐酸丙咪嗪片 / Imipramine Hydrochloride Tablets 86
甲泼尼龙/ Methylprednisolone 88
甲泼尼龙片/ Methylprednisolone Tablets 90
水杨酸局部泡沫剂/ Salicylic Acid Topical Foam 92
噻吗洛尔片/ Timolol Maleate Tablets 94
氨茶碱/ Aminophylline 96
氨茶碱注射液/ Aminophylline Injection 98
氨茶碱口服溶液 / Aminophylline Oral Solution 100
氨茶碱片 / Aminophylline Tablets 102
盐酸布比卡因/ Bupivacaine Hydrochloride 104
盐酸布比卡因注射液/ Bupivacaine Hydrochloride Injection 105
盐酸布比卡因葡萄糖注射液/ Bupivacaine Hydrochloride in Dextrose Injection 106

双嘧达莫/ Dipyridamole 108
双嘧达莫片/ Dipyridamole Tablets 110
醋酸甲羟孕酮注射液 / Medroxyprogesterone Acetate Injectable Suspension 112
醋酸甲羟孕酮片 / Medroxyprogesterone Acetate Tablets 114
茶碱/ Theophylline 116
茶碱口服液 / Theophylline Oral Solution 118
茶碱缓释片 / Theophylline Extended-Release Capsules 119
茶碱葡萄糖注射液 / Theophylline in Dextrose Injection 120
北五味子干浸膏 / Northern Schisandra Fruit Dry Extract 121
硫酸沙丁胺醇/ Albuterol Sulfate 122
沙丁胺醇片/ Albuterol Tablets 125
多西环素/多西霉素/ Doxycycline 128
多西霉素胶囊/ Doxycycline Capsules 130
多西霉素片/ Doxycycline Tablets 132
口服多西环素 / Doxycycline for Oral Suspension 134
多西环素注射用粉末 / Doxycycline for Injection 136
盐酸多西环素/ Doxycycline Hyclate 138
盐酸多西环素胶囊/ Doxycycline Hyclate Capsules 140
盐酸多西环素片/ Doxycycline Hyclate Tablets 142
溴甲纳曲酮 / Methylnaltrexone Bromide 144
硝酸硫康唑 / Sulconazole Nitrate 146
盐酸苯海索片/ Trihexyphenidyl Hydrochloride Tablets 147
伪麻黄碱硫酸盐 / Pseudoephedrine Sulfate 148
磺胺多辛乙胺嘧啶片/ Sulfadoxine and Pyrimethamine Tablets 149
三七干浸膏胶囊/ Tienchi Ginseng Root and Rhizome Dry Extract Capsules 150
三七干浸膏片/ Tienchi Ginseng Root and Rhizome Dry Extract Tablets 151
三七粉片/ Tienchi Ginseng Root and Rhizome Powder Tablets 152
三七粉胶囊/ Tienchi Ginseng Root and Rhizome Powder Capsules 153
氨氯地平与阿托伐他汀片/ Amlodipine and Atorvastatin Tablets 154
阿托伐他汀钙片/ Atorvastatin Calcium Tablets 156
泼尼松 / Prednisone 157
盐酸氯米帕明 / Clomipramine Hydrochloride 159

盐酸氯米帕明胶囊 / Clomipramine Hydrochloride Capsules 161

奥美沙坦酯片 / Olmesartan Medoxomil Tablets 163

苯佐卡因、 氨苯丁酯 、盐酸丁卡因局部喷雾剂 / Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Aerosol 164

苯佐卡因、 氨苯丁酯 、盐酸丁卡因凝胶/ Benzocaine, Butamben, and Tetracaine Hydrochloride Gel 166

苯佐卡因、 氨苯丁酯 、盐酸丁卡因局部溶液/ Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Solution 168

美国植物药法典（HMC）

灵芝/ Ganoderma lucidum Fruiting Body 170

三七/ Panax notoginseng Root and Rhizome 173

五味子 / Schisandra chinensis Fruit 175

牛樟芝 / Antrodia camphorata Fruiting Body 177

复方丹参滴丸

方法来源：收载于中国药典一部，P1219

处方： 丹参 三七 冰片

指纹图谱：

色谱柱： L1, 2.1 mm x 10 cm; 1.8 μm (ACQUITY HSS T3)

流动相： Solution A:0.02%磷酸的80%乙腈溶液

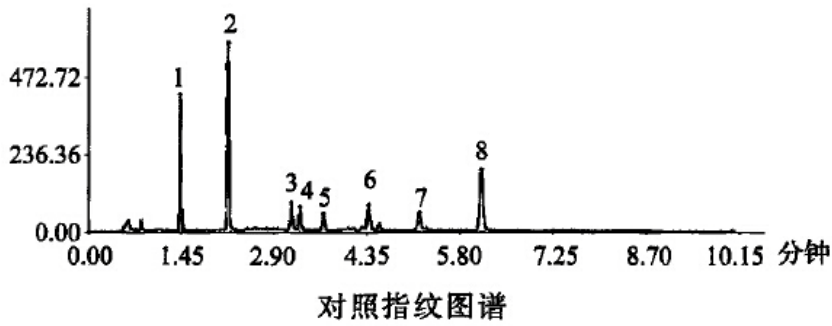
Solution B:0.02%磷酸溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	9	91
1.6	22	78
1.8	26	74
8.0	39	61
8.4	9	91
10	9	91

柱温: 40 ˚C 流速 (ml/min): 0.4 波长(nm): 280

对照指纹图谱：



对照指纹图谱

峰 1：丹参素

方法解析：中药中成分复杂，采用HPLC时，分析时间过长。现采用UPLC进行指纹图谱分析，在保证分离度的前提下，大大提高了分析速度，节约检验成本。

护肝丸 / 胶囊 / 颗粒

方法来源：收载于中国药典一部，P1219

处方： 柴胡626g 茵陈626g 板蓝根626g 五味子336g 猪胆粉40g 绿豆256g

含量测定：

色谱柱： L1, 2.1 mm × 10 cm; 1.8 μm (ACQUITY HSS T3)

流动相： Solution A:乙腈

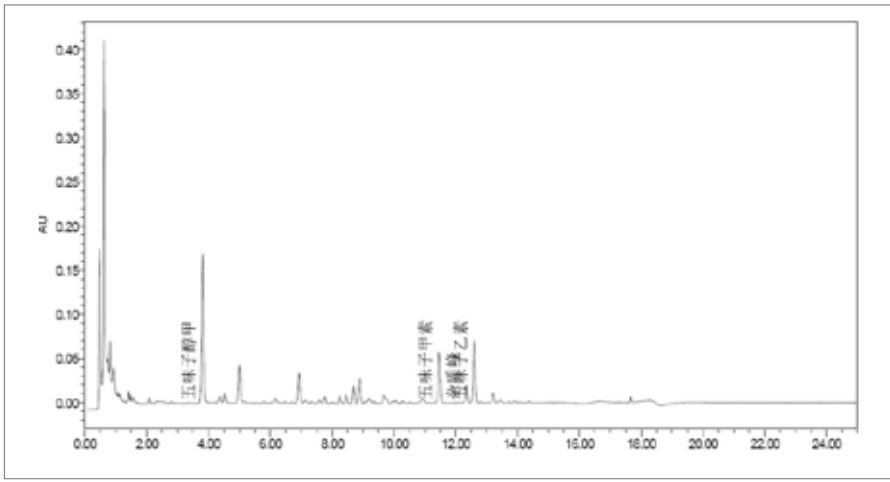
Solution B:水

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	45	55
3	45	55
15	80	20

柱温: 40 °C 流速 (ml/min): 0.4 波长(nm): 250

典型图谱：

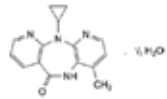


方法解析：中药中成分复杂，采用HPLC时，分析时间过长。现采用UPLC进行指纹图谱分析，在保证分离度的前提下，大大提高了分析速度，节约检验成本。

奈韦拉平半水合物
Nevirapine hemihydrate

方法来源：收载于EP7.6/ Pharmeuropa 23.2

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 5 cm; 1.8 μm(ACQUITY UPLC HSS T3)

流动相： Solution A:0.77 g乙酸铵加水900 ml，加乙酸调至 pH=5.6~5.7，加水至1000 ml

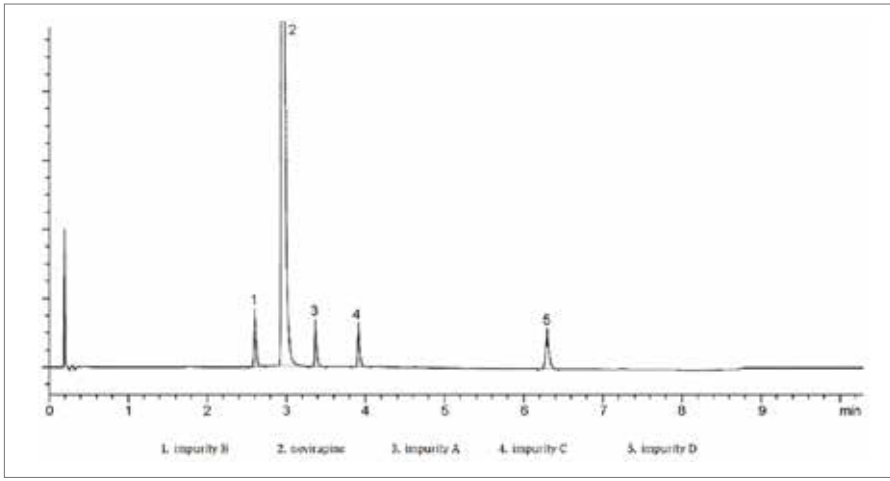
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 1.35	90	10
1.35 - 3.85	90→67	10→33
3.85 - 6.70	67→60	33→40
6.70 - 7.65	60	40

柱温: 40 °C　流速 (ml/min): 0.7　波长(nm): 282

色谱图：

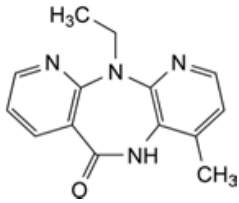


杂质谱：

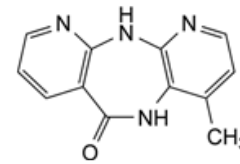
Name	相对保留时间	可接受标准 (%)
impurity B	0.9	0.2
nevirapine	1.0	-
impurity A	1.2	0.2
impurity C	1.3	0.2
单个未知杂质	-	0.10
总杂质	-	0.6

杂质结构

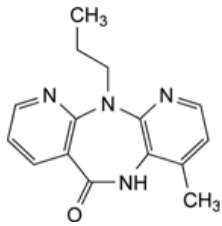
impurity A
11-ethyl-4-methyl-5,11-dihydro-6H-dipyrido[3,2-b:2′,3′-e][1,4]diazepin-6-one,



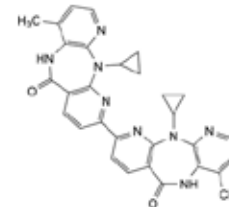
impurity B
4-methyl-5,11-dihydro-6H-dipyrido[3,2-b:2′,3′-e][1,4]diazepin-6-one



impurity C
4-methyl-11-propyl-5,11-dihydro-6H-dipyrido[3,2-b:2′,3′-e][1,=4]diazepin-6-one,



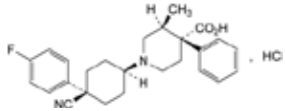
impurity D
11,11′-dicyclopropyl-4,4′-dimethyl-5,5′,11,11′-tetrahydro-6H,6′H-9,9′-bidipyrido[3,2-b:2′,3′-e][1,4]diazepine-6,6′-dione



盐酸左卡巴斯汀
Levocabastine Hydrochloride -Impurity C

方法来源：收载于Pharmeuropa 24.4, October 2012, P97

结构式：



Impurity C：

色谱柱： L11, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH Phenyl)

流动相： Solution A:17 g/L四丁基硫酸氢铵

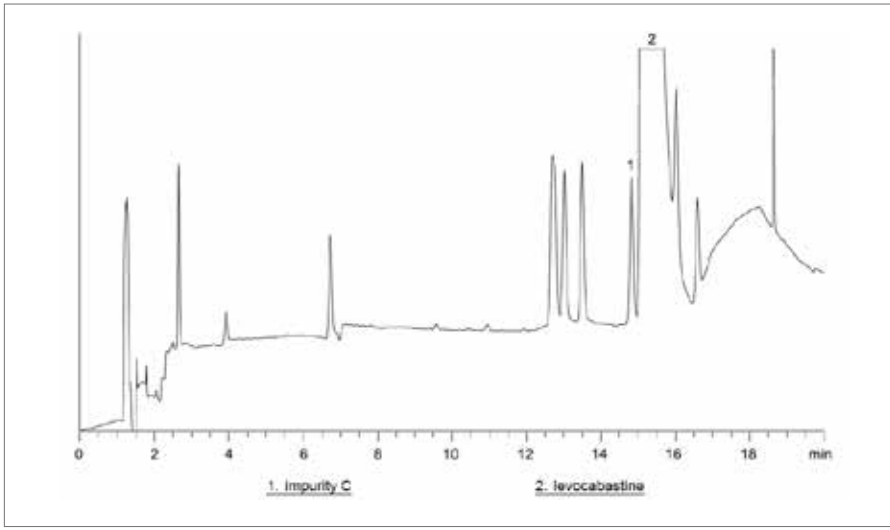
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 15	90→80	10→20
15 - 20	80→50	20→50
20 - 21	50→90	50→10
21 - 25	90	10

柱温: 35 °C　流速 (ml/min): 0.3　波长(nm): 214

色谱图：

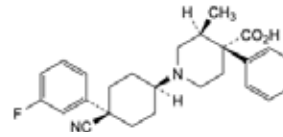


杂质谱：

Name	相对保留时间	可接受标准 (%)
impurity C	0.98	0.3
levocabastine	1.0	-

杂质结构

impurity C
(3S,4R)-1-[cis-4-cyano-4-(3-fluorophenyl)cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid,

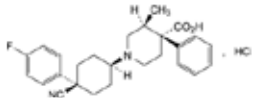


方法解析：原方法采用毛细管电泳色谱(CE)进行分析，重现性与稳定性较差，操作比较复杂。现方法改用UPLC进行分析，分析时间缩短，可操作性大大提高。

盐酸左卡巴斯汀
Levocabastine Hydrochloride

方法来源：收载于Pharmeuropa 24.4, October 2012, P98

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:17 g/L四丁基硫酸氢铵

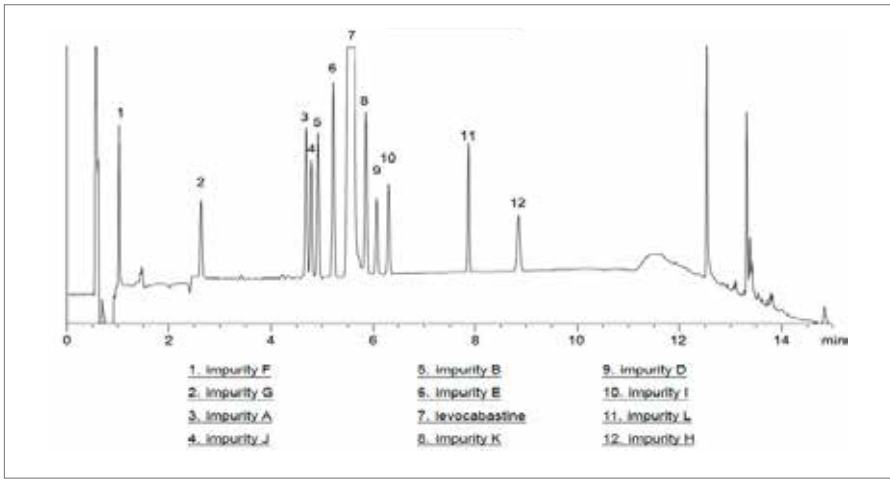
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 3	95→90	5→10
3 - 55	90→85	10→15
5.5 - 10.5	85→70	15→30
10.5 - 14	70→20	30→80
14 - 15	20	80

柱温: 60 ˚C　流速 (ml/min): 0.45　波长(nm): 214

色谱图：

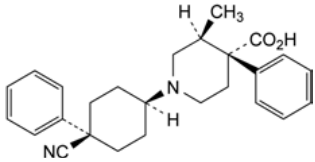


杂质谱：

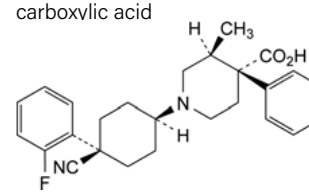
Name	相对保留时间	可接受标准 (%)
impurity A	0.85	0.2
impurity J	0.86	-
impurity B	0.90	0.15
impurity E	0.94	0.4
levocabastine	1.0	-
impurity k	1.07	-
单个未知杂质	-	0.10
总杂质	-	0.6

杂质结构

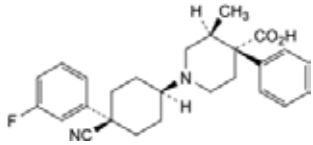
impurity A
(3S,4R)-1-(cis-4-cyano-4-phenylcyclohexyl)-3-methyl-4-phenylpiperidine-4-carboxylic acid



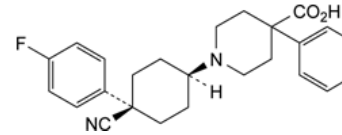
impurity B
(3S,4R)-1-[cis-4-cyano-4-(2-fluorophenyl) cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxvlic acid



impurity C
(3S,4R)-1-[cis-4-cyano-4-(3-fluorophenyl) cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid

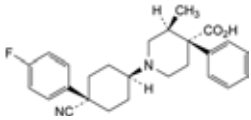


impurity D
1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-4-phenylpiperidine-4-carboxylic acid

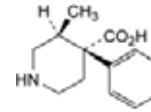


杂质结构

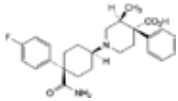
impurity E
(3S,4R)-1-[trans-4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid



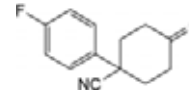
impurity F
(3S,4R)-3-methyl-4-phenylpiperidine-4-carboxylic acid



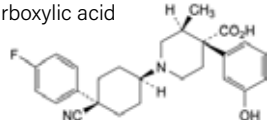
impurity G
(3S,4R)-1-[cis-4-carbamoyl-4-(4-fluorophenyl) cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid



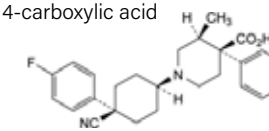
impurity H
1-(4-fluorophenyl)-4-oxocyclohexanecarbonitrile



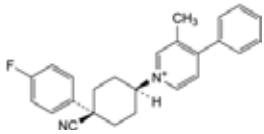
impurity I
(3S,4S)-1-[cis-4-cyano-4-(4-fluorophenyl) cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid



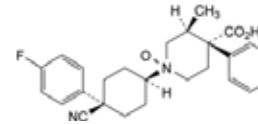
impurity J
(3S,4R)-1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-4-(3-hydroxyphenyl)-3-methylpiperidine-4-carboxylic acid



impurity K
1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenylpyridinium



impurity L
(3S,4R)-1-[(1S,4R)-4-cyano-3-(4-fluorophenyl) cyclohexyl]-3-methyl-4-phenylpiperidine-4-carboxylic acid 1-oxide.

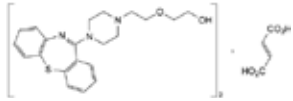


方法解析：原方法采用毛细管电泳色谱(CE)进行分析，重现性与稳定性较差，操作比较复杂。现方法改用UPLC进行分析，分析时间缩短，可操作性大大提高。

富马酸喹硫平
Quetiapine fumarate

方法来源：收载于Pharmeuropa 24.4, October 2012, P119

结构式：



有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 1.7 μm (XSelect CSH C_6-phenyl)

流动相： Buffer:3.85g/L乙酸铵，用氨水调至 pH9.0

Solution A:甲醇:buffer=10:90

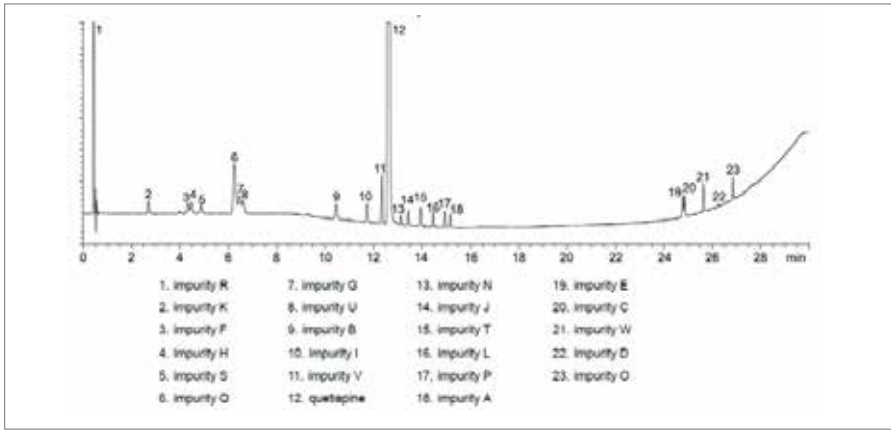
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 8	80	20
8 - 14.5	80→60	20→45
14.5 - 22.6	60→50	40→50
22.6 - 26	50→30	50→70
26 - 29	30→10	70→90
29 - 30	10	90

柱温: 50 ˚C　流速 (ml/min): 0.5　波长(nm): 240

色谱图：

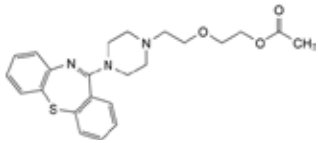


杂质谱：

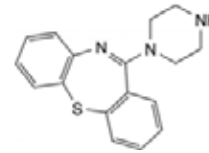
Name	相对保留时间	保留时间	可接受标准 (%)
impurity G	0.5	0.5	0.15
quetiapine	1.0	-	-
impurity N	1.04	2.0	0.15
单个未知杂质	-	1.0	0.10
总杂质	-	-	0.5

杂质结构

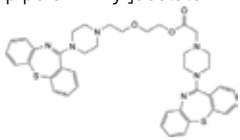
impurity A
2-[2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethyl acetate



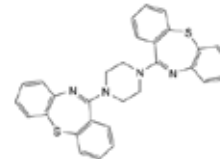
impurity B
11-(piperazin-1-yl)dibenzo[b,f][1,4]thiazepine



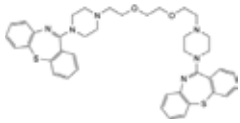
impurity C
2-[2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethyl [4-(dibenzo[b,f][1,4]thiazepin-11-yl) piperazin-1-yl]acetate



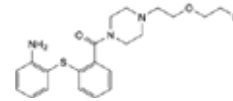
impurity D
11,11′-(piperazine-1,4-diyl) bis(dibenzo[b,f][1,4]thiazepine)



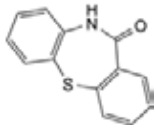
impurity E
11,11′-[ethylenebis(oxyethylenepiperazine-4,1-diyl)]bis(dibenzo[b,f][1,4] thiazepine)



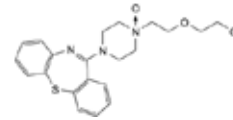
impurity F
[2-[(2-aminophenyl)sulfanyl]phenyl] [4-[2-(2-hydroxyethoxy)ethyl] piperazin-1-yl]methanone



impurity G
dibenzo[b,f][1,4]thiazepin-11(10H)-one

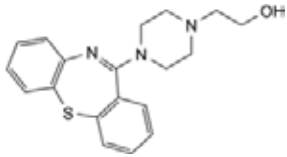


impurity H
2-[2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)-1-oxidopiperazin-1-yl]ethoxy] ethanol

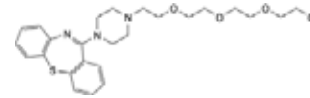


杂质结构

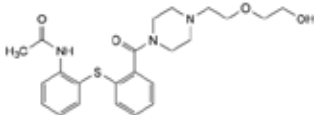
impurity I
2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethanol



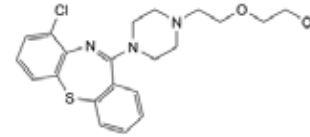
impurity J
2-[2-[2-[2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethoxy]ethoxy]ethanol



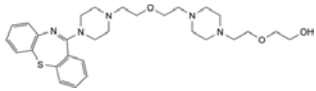
impurity K
N-[2-[[2-[[4-[2-(2-hydroxyethoxy)ethyl]piperazin-1-yl]carbonyl]phenyl]sulfanyl]phenyl]acetamide



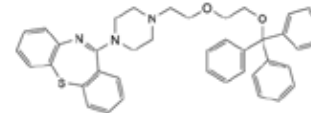
impurity L
2-[2-[4-(9-chlorodibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethanol



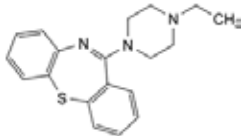
impurity N
2-[2-[4-[2-[2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethyl]piperazin-1-yl]ethoxy]ethanol



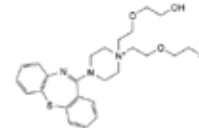
impurity O
11-[4-[2-[2-(triphenylmethoxy)ethoxy]ethyl]piperazin-1-yl]dibenzo[b,f][1,4]thiazepine



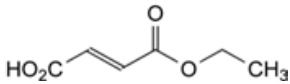
impurity P
11-(4-ethylpiperazin-1-yl)dibenzo[b,f][1,4]thiazepine



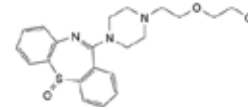
impurity Q
4-(dibenzo[b,f][1,4]thiazepin-11-yl)-1,1-bis[2-(2-hydroxyethoxy)ethyl]piperazin-1-ium



impurity R
(2E)-4-ethoxy-4-oxobut-2-enoic acid

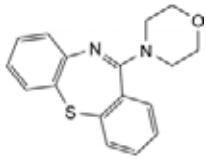


impurity S
2-[2-[4-(5-oxidodibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethanol

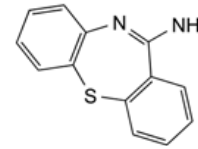


杂质结构

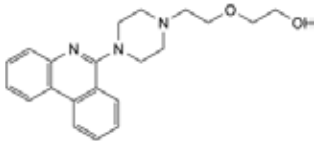
impurity T
11-(morpholin-4-yl)dibenzo[b,f][1,4]thiazepine



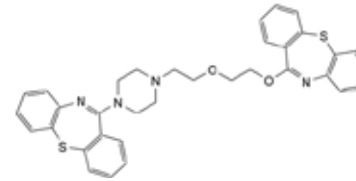
impurity U
dibenzo[b,f][1,4]thiazepin-11-amine



impurity V
2-[2-[4-(phenanthridin-6-yl)piperazin-1-yl]ethoxy]ethanol



impurity W
11-(4-[2-[2-(dibenzo[b,f][1,4]thiazepin-11-yloxy)ethoxy]ethyl]piperazin-1-yl)dibenzo[b,f][1,4]thiazepine

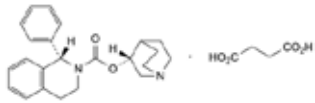


方法解析：EP8.6新增各论，采用UPLC方法，实现高峰容量，快速分析。

琥铂酸索非那新
Solifenacin succinate

方法来源：收载于Pharmeuropa 26.2, April 2014, P302

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH Shield RP18)

流动相： Buffer:0.6g磷酸铵至1L水中，加1.0ml二乙胺，用浓氨水调至 pH=11

Solution A:乙腈:Buffer=45:55

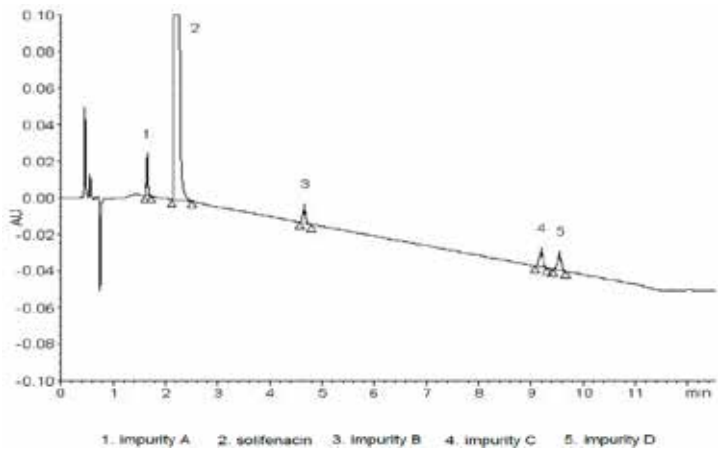
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 0.5	90	10
0.5 - 10.5	90→68	10→32
10.5 - 12.5	68	32

柱温: 40 °C　流速 (ml/min): 0.4　波长(nm): 215

色谱图：

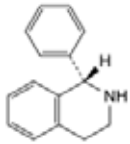


杂质谱：

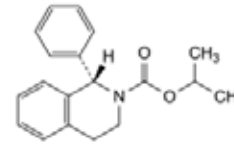
Name	相对保留时间	可接受标准 (%)
impurity A	0.7	0.2
solifenacin	-	-
单个未知杂质	-	0.10
总杂质	-	0.3

杂质结构

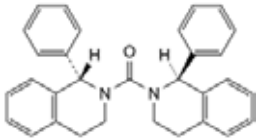
impurity A
(1S)-1-phenyl-1,2,3,4-tetrahydroisoquinoline



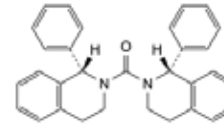
impurity B
propan-2-yl (1S)-1-phenyl-3,4-dihydroisoquinoline-2(1H)-carboxylate



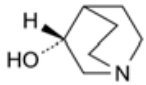
impurity C
bis[(1S)-1-phenyl-3,4-dihydroisoquinolin-2(1H)-yl]methanone



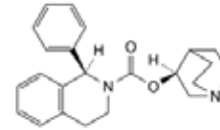
impurity D
[(1R)-1-phenyl-3,4-dihydroisoquinolin-2(1H)-yl][(1S)-1-phenyl-3,4-dihydroisoquinolin-2(1H)-yl]methanone



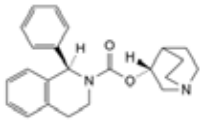
impurity E
(3R)-1-azabicyclo[2.2.2]octan-3-ol
(3-quinuclidinol)



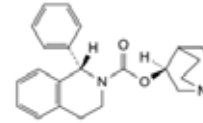
impurity F
(3S)-1-azabicyclo[2.2.2]oct-3-yl (1R)-1-phenyl-3,4-dihydroisoquinoline-2(1H)-carboxylate



impurity G
(3R)-1-azabicyclo[2.2.2]oct-3-yl (1R)-1-phenyl-3,4-dihydroisoquinoline-2(1H)-carboxylate



impurity H
(3S)-1-azabicyclo[2.2.2]oct-3-yl (1S)-1-phenyl-3,4-dihydroisoquinoline-2(1H)-carboxylate

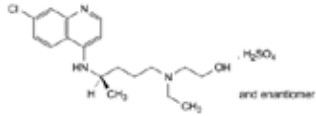


方法解析：EP8.6新增各论，采用UPLC方法，实现高峰容量，快速分析。

硫酸羟氯喹
Hydroxychloroquini sulfas

方法来源：收载于Pharmeuropa 27.2, April 2015, P52

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm (Waters ACQUITY UPLC BEH C_{18})

流动相： Buffer:1.36g磷酸二氢钾至900ml水中，加0.15g庚烷磺酸钠，用三乙胺调至 pH=7.0，加水至1000ml

Solution A:甲醇:Buffer=10:90

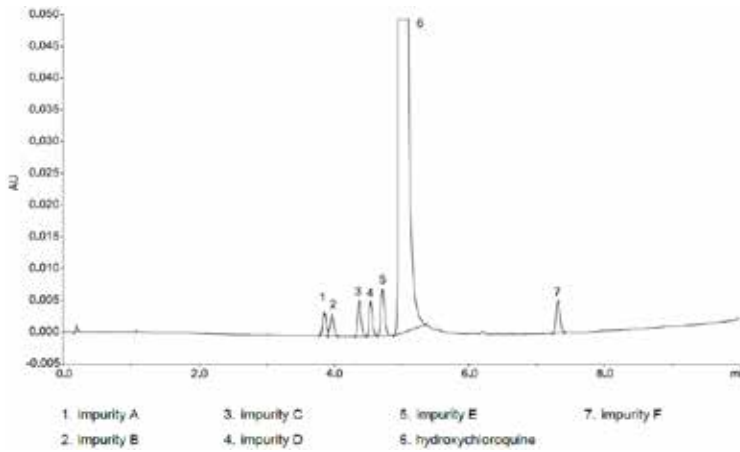
Solution B:甲醇:Buffer=85:15

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 1	90	10
1 - 12	90→68	10→32

流速 (ml/min): 0.7　波长(nm): 254

色谱图：

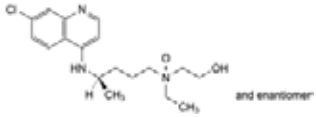


杂质谱：

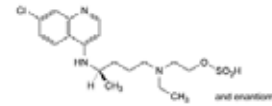
Name	相对保留时间	可接受标准 (%)
impurity B	0.8	0.15
impurity C	0.9	0.4
hydroxychloroquine	1.0	-
单个未知杂质	-	0.10
总杂质	-	0.6

杂质结构

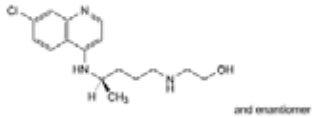
impurity A
2-[[(4RS)-4-[(7-chloroquinolin-4-yl)amino]pentyl](ethyl)nitroryl]ethanol



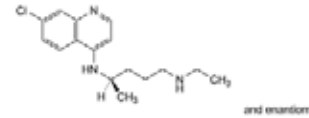
impurity B
2-[[(4RS)-4-[(7-chloroquinolin-4-yl)amino]pentyl](ethyl)amino]ethyl hydrogen sulfate



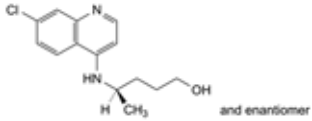
impurity C
2-[[(4RS)-4-[(7-chloroquinolin-4-yl)amino]pentyl]amino]ethanol



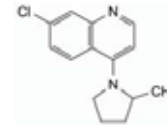
impurity D
(4RS)-N4-(7-chloroquinolin-4-yl)-N1-ethylpentane-1,4-diamine



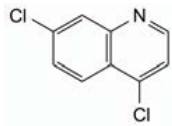
impurity E
(4R)-4-[(7-chloroquinolin-4-yl)amino]pentan-1-ol



impurity F
7-chloro-4-(2-methylpyrrolidin-1-yl)quinoline



impurity G
4,7-dichloroquinoline

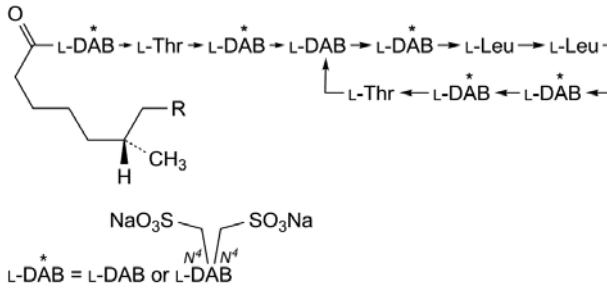


方法解析：征求意见稿，采用UPLC方法，实现高峰容量，快速分析。

多粘菌素 E 甲磺酸钠
Colistimethatum natricum

方法来源：收载于Pharmeuropa 27.3, October 2015, P70

结构式：



DAB = 2,4-diaminobutanoic acid

Colistin E1 derivative: R = CH_3

Colistin E2 derivative: R = H

Between 3 and 5 of the L-DAB residues are disubstituted at N^4

有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (Waters ACQUITY UPLC CSH)

预柱：2.1 mm × 0.5-cm; 1.7-µm

流动相： Buffer:7.8g/L磷酸二氢钠至980ml水中，用1M氢氧化钠溶液调至 pH=6.5，加水至1000ml

Solution A:乙腈:Buffer=5:95

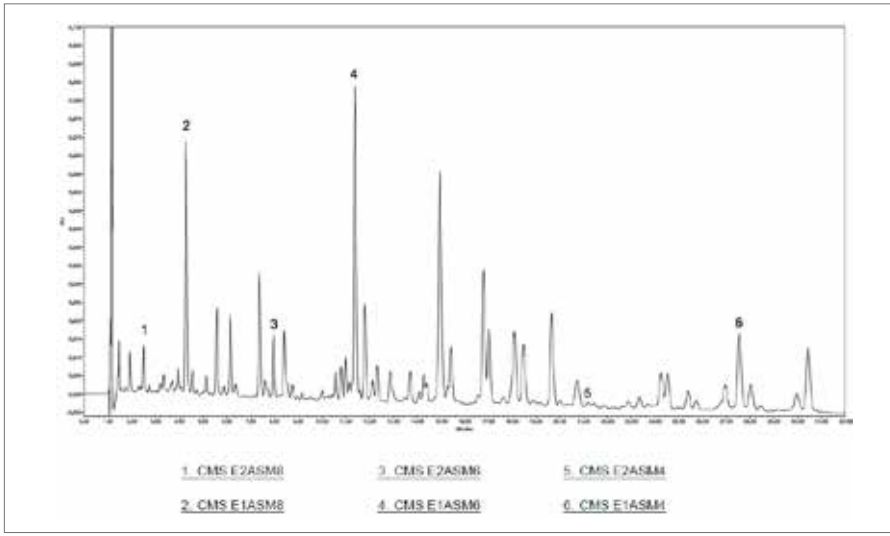
Solution B:乙腈:Buffer=50:50

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0 - 10	80→68	20→32
10 - 35	68→53	32→47
35 - 36	53→80	47→20
36 - 44	80	20
18	90	10

柱温: 30 ˚C　流速 (ml/min): 0.3　波长(nm): 210　进样温度: 5 ˚C

色谱图：



杂质谱：

Name	相对保留时间	可接受标准 (%)
CMS E2ASM8	0.22	0.5 - 2.0
CMS E1ASM8	0.39	5.0 - 9.5
CMS E2ASM6	0.71	0.5 - 2.5
CMS E1ASM6	1.0	6.5 - 9.5
CMS E2ASM4	1.77	最大 1.5
CMS E1ASM4	2.35	2.0 - 5.0
总量	-	最少 77.0

方法解析：征求意见稿，采用UPLC方法，实现高峰容量，快速分析。

USP<321> Drug Product Assay Tests—Organic Chemical Medicines

方法来源：收载于USP39-NF34

描述： OTC药物活性成分检测的鉴别及含量测定方法

含量方法1：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.15%三氟乙酸水溶液

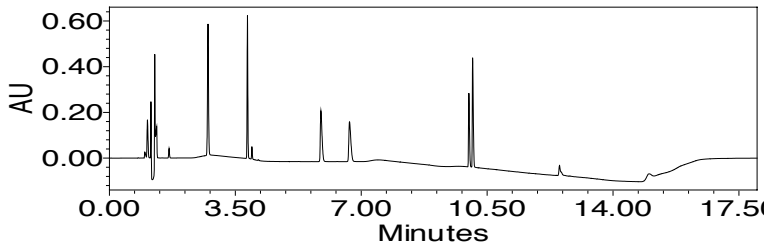
Solution B:0.02%三氟乙酸(乙腈-甲醇=75:25的混合溶液)

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
0.6	90	10
2.3	77	23
5.5	77	23
7.4	57	43
8.0	57	43
12.5	1	99
13.5	1	99

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 见峰表

色谱图(225 nm)：

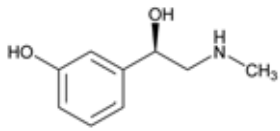


峰表：

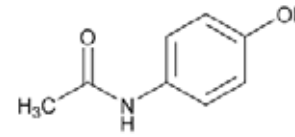
Name	波长 (nm)	保留时间 (min)
Phenylephrine	225	1.9
Acetaminophen	254	2.7
Caffeine	254	3.9
Doxylamine	264	4.0
Pseudoephedrine	210	4.1
Chlorpheniramine	225	6.1
Brompheniramine	264	7.0
Aspirin	276	7.5
Dextromethorphan	225	10.1
Diphenhydramine	225	10.2

杂质结构

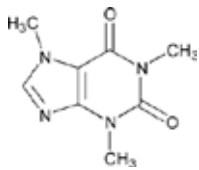
Phenylephrine



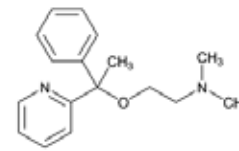
Acetaminophen



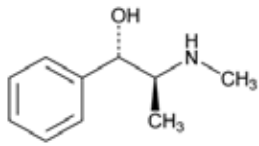
Caffeine



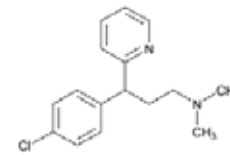
Doxylamine



Pseudoephedrine

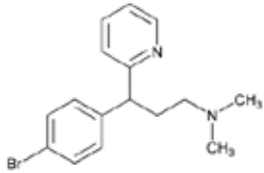


Chlorpheniramine

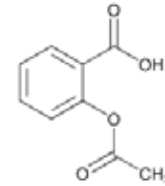


杂质结构

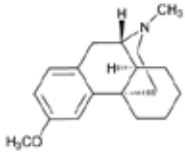
Brompheniramine



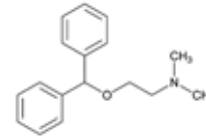
Aspirin



Dextromethorphan



Diphenhydramine



方法解析：OTC药物市场变化非常迅速，因为FDA的OTC体系允许其对制剂配方进行修改。在这种状况下，传统的一个USP各论针对一种药物制剂的形式跟不上OTC药物发展的变化。

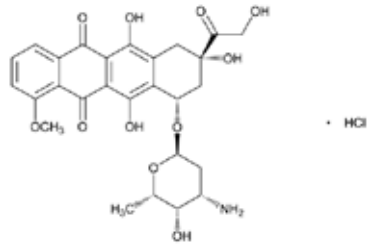
对于药典各论中的鉴别和含量测定，由于现代药品基质复杂，同时复合处方种类增加，分析方法的专属性变得极具挑战性。同时，方法开发的挑战同时也会影响检测所需的分析方法的数量。USP的目标是减少同类型产品所需分析方法的数量。近年来，高峰容量分析方法如UPLC、核壳结构色谱柱的普及，使得USP目标的实现成为了可能。

USP为持续改进药品各论的现代化，设立了通则321及通则327，用一种方法来检测一类药品，以简化药品检验。目前发布的方法，能同时对11种成分进行鉴别和定量。包括Phenylephrine hydrochloride（盐酸去氧肾上腺素），Acetaminophen（对乙酰氨基酚），Caffeine（咖啡因），Doxylamine succinate（丁二酸多西拉敏），Pseudoephedrine hydrochloride（盐酸伪麻黄碱），Chlorpheniramine maleate（马来酸氯苯那敏），Brompheniramine maleate（马来酸溴苯那敏），Aspirin（阿司匹林），Dextromethorphan hyfrobromide（氢溴酸右美沙芬），Diphenhydramine citrate（柠檬酸苯海拉明），Diphenhydramine hydrochloride（盐酸苯海拉明）。

盐酸多柔比星
Doxorubicin Hydrochloride

方法来源：收载于USP38-NF33 1S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18} /ACQUITY HCC C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:乙腈:甲醇:三氟乙酸 = 800:200:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
15	25	75
16	25	75
16.1	90	10
18	90	10

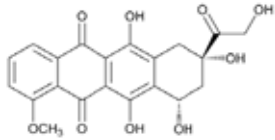
柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 254　进样温度: 4 ˚C

杂质谱：

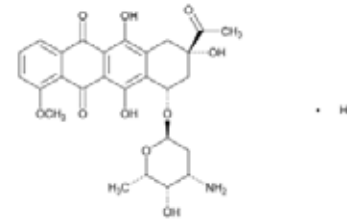
Name	相对保留时间	可接受标准 (%)
Doxorubicin	1.0	-
Doxorubicinone	1.1	0.5
Daunorubicin	1.2	0.5
Daunorubicinone	1.4	0.5
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

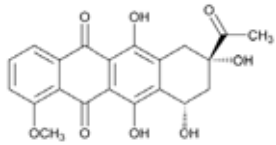
Doxorubicinone
(8S ,10S)-6,8,10,11-Tetrahydroxy-8-(hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_9$ 414.36



Daunorubicin Hydrochloride



Daunorubicinone
(8S ,10S)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_8$ 398.36



方法解析：更新前方法仅控制了总杂质（限度2.0%），更新后增加了特性杂质的控制。

更新前方法为等度方法，分析时间长，分离度不理想；更新后方法采用UPLC，大大减少了分析时间，提高了分离度。

盐酸多柔比星注射液
Doxorubicin Hydrochloride Injection

方法来源：收载于USP38-NF33 1S

定义： Doxorubicin Hydrochloride Injection is a sterile solution of Doxorubicin Hydrochloride in Sterile Water for Injection made isoosmotic with Sodium Chloride, Dextrose, or other suitable added substances. It contains NLT 90.0% and NMT 115.0% of the labeled amount of doxorubicin hydrochloride ($C_{27}H_{29}NO_{11}$ ·HCl).

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:乙腈:甲醇:三氟乙酸 = 800:200:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
15	25	75
16	25	75
16.1	90	10
18	90	10

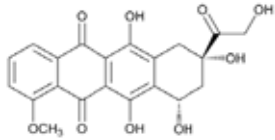
柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 254　进样温度: 4 ˚C

杂质谱：

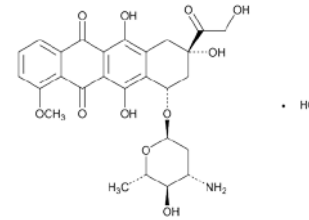
Name	相对保留时间	可接受标准 (%)
Doxorubicin	1.0	-
Epirubicin	1.05	-
Doxorubicinone	1.08	0.5
Daunorubicinone	1.35	0.5
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

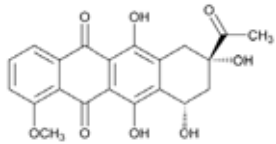
Doxorubicinone
(8S ,10S)-6,8,10,11-Tetrahydroxy-8-(hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_9$ 414.36



Epirubicin Hydrochloride



Daunorubicinone
(8S ,10S)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_8$ 398.36



方法解析：更新前方法仅控制了总杂质（限度2.0%），更新后增加了特性杂质的控制。

更新前方法为等度方法，分析时间长，分离度不理想；更新后方法采用UPLC，大大减少了分析时间，提高了分离度。

注射用盐酸多柔比星
Doxorubicin Hydrochloride for Injection

方法来源：收载于USP38-NF33 1S

定义： Doxorubicin Hydrochloride for Injection is a sterile mixture of Doxorubicin Hydrochloride and Lactose. It contains NLT 90.0% and NMT 115.0% of the labeled amount of doxorubicin hydrochloride ($C_{27}H_{29}NO_{11}$ ·HCl).

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:乙腈:甲醇:三氟乙酸 = 800:200:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
15	25	75
16	25	75
16.1	90	10
18	90	10

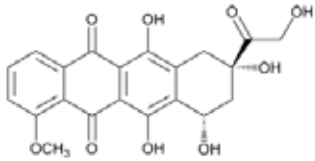
柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 254　进样温度: 4 ˚C

杂质谱：

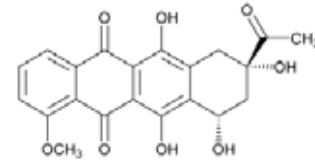
Name	相对保留时间	可接受标准 (%)
Doxorubicin	1.0	-
Doxorubicinone	1.1	0.5
Daunorubicinone	1.4	0.5
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

Doxorubicinone
(8S ,10S)-6,8,10,11-Tetrahydroxy-8-(hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_9$ 414.36



Daunorubicinone
(8S ,10S)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_8$ 398.36

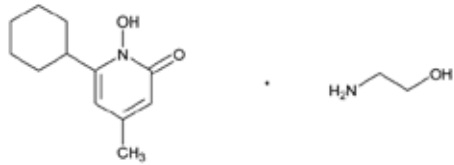


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

环吡酮胺
Ciclopirox Olamine

方法来源：收载于USP38-NF33 1S

结构式：



有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 1.8 µm

流动相： Solution A:1.26g/L甲酸铵水溶液，用甲酸调至pH3.5

Solution B:乙腈:甲醇 = 60:25

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
0.01	95	5
10.0	15	85
12.0	15	85
12.01	95	5
15.0	95	5

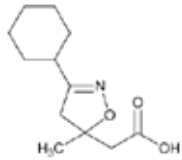
柱温: 30 °C　流速 (ml/min): 0.5　波长(nm): 300

杂质谱：

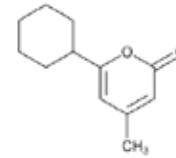
Name	相对保留时间	波长 (nm)	可接受标准 (%)
Ciclopirox related compound A	0.85	220	0.5
Ciclopirox related compound C	0.88	300	0.5
Ciclopirox	1.0	300	-
Ciclopirox related compound B	1.07	300	0.5
单个未知杂质	-	300	0.15
总杂质	-	300	0.5

杂质结构

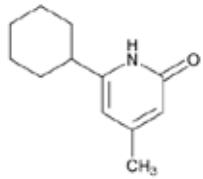
Ciclopirox Related Compound A
3-Cyclohexyl-4,5-dihydro-5-methyl-5-isoxazolyl acetic acid.
$C_{12}H_{19}NO_3$ 225.28



Ciclopirox Related Compound B
6-Cyclohexyl-4-methyl-2-pyrone.
$C_{12}H_{16}O_2$ 192.25



Ciclopirox Related Compound C
6-Cyclohexyl-4-methylpyridin-2(1H)-one.
$C_{12}H_{17}NO$ 191.27



方法解析：为了去除金属离子的干扰，所有的新色谱柱需要用冲洗溶液进行冲洗。原HPLC方法新色谱柱需要冲洗15h，然后用流动相冲洗5h。采用UPLC方法进行分析后，只需要冲洗20倍柱体积，且分析时间大大缩短。

新UPLC方法增加了对杂质C的控制。

环吡酮胺乳膏
Ciclopirox Olamine Cream, Ciclopirox Cream

方法来源：收载于USP39-NF34

定义： Ciclopirox Olamine Cream contains an amount of ciclopirox olamine ($C_{12}H_{17}NO_2$, C_2H_7NO) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of ciclopirox ($C_{12}H_{17}NO_2$)

有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 1.8 μm

流动相： Solution A:1.26g/L甲酸铵水溶液，用甲酸调至pH3.5

Solution B:乙腈:甲醇 = 60:25

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
10	15	85
12	15	85
12.01	95	5
15	95	5

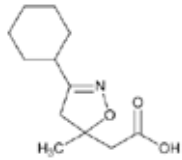
柱温: 30 ˚C　流速 (ml/min): 0.5　波长(nm): 300

杂质谱：

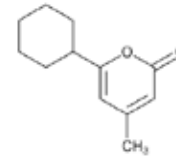
Name	相对保留时间	波长 (nm)	可接受标准 (%)
Ciclopirox related compound A	0.85	220	0.5
Ciclopirox related compound C	0.88	300	0.5
Ciclopirox	1.0	300	-
Ciclopirox related compound B	1.07	300	0.5
单个未知杂质	-	300	0.15
总杂质	-	300	0.5

杂质结构

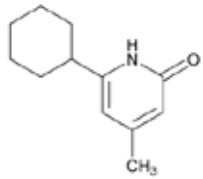
Ciclopirox Related Compound A
3-Cyclohexyl-4,5-dihydro-5-methyl-5-isoxazolyl acetic acid.
$C_{12}H_{19}NO_3$ 225.28



Ciclopirox Related Compound B
6-Cyclohexyl-4-methyl-2-pyrone.
$C_{12}H_{16}O_2$ 192.25



Ciclopirox Related Compound C
6-Cyclohexyl-4-methylpyridin-2(1H)-one.
$C_{12}H_{17}NO$ 191.27

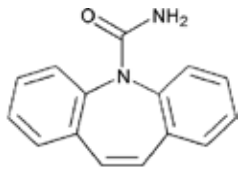


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

卡马西平
Carbamazepine

方法来源：收载于USP38-NF33 2S

结构式：



有关物质：

色谱柱： L10, 2.1 mm x 10 cm; 1.8 µm (ACQUITY UPLC HSS Cyano)

流动相： Solution A:加0.5 ml三乙胺、0.5 ml甲酸至1000 ml水

Solution B:加0.25 ml甲酸至1000 ml甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
3.0	80	20
12.0	60	40
18.0	45	55
20.0	45	55
20.1	80	20
23.0	80	20

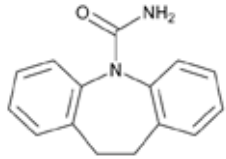
柱温: 40 ˚C　流速 (ml/min): 0.3　波长(nm): 230

杂质谱：

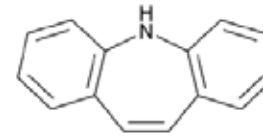
Name	相对保留时间	可接受标准 (%)
Carbamazepine related compound A	0.96	0.2
Carbamazepine	1.00	-
Carbamazepine related compound B	1.45	0.2
Carbamazepine related compound F	1.64	-
Iminodibenzyl	1.67	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Carbamazepine Related Compound A
10,11-Dihydrocarbamazepine.
$C_{15}H_{14}N_2O$ 238.28

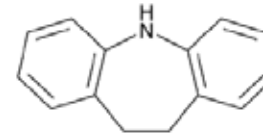


Carbamazepine Related Compound B
5H -Dibenz[b,f]azepine.
$C_{14}H_{11}N$ 193.24



Carbamazepine Related Compound F
5H -Dibenzo[b,f]azepine-5-carbonyl chloride.
$C_{15}H_{10}ClNO$ 255.70

Iminodibenzyl
10,11-Dihydro[b,f]azepine.
$C_{14}H_{13}N$ 195.28



方法解析：原HPLC等度方法改为UPLC梯度方法，提高了分离度与分析效率。

卡马西平口服混悬剂
Carbamazepine Oral Suspension

方法来源：收载于USP38-NF33 2S

定义： Carbamazepine Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$).

有关物质：

色谱柱： L10, 2.1 mm x 10 cm; 1.8 µm (ACQUITY UPLC HSS Cyano)

流动相： Solution A:加0.5 ml三乙胺、0.5 ml甲酸至1000 ml水

Solution B:加0.25 ml甲酸至1000 ml甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
3.0	80	20
12.0	60	40
18.0	45	55
20.0	45	55
20.1	80	20
23.0	80	20

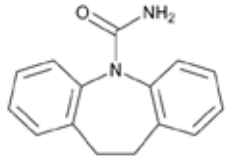
柱温: 40 ˚C　流速 (ml/min): 0.3　波长(nm): 230

杂质谱：

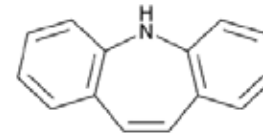
Name	相对保留时间	可接受标准 (%)
Carbamazepine related compound A	0.96	0.2
Carbamazepine	1.00	-
Carbamazepine related compound B	1.45	0.2
Carbamazepine related compound F	1.64	-
Iminodibenzyl	1.67	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Carbamazepine Related Compound A
10,11-Dihydrocarbamazepine.
$C_{15}H_{14}N_2O$ 238.28

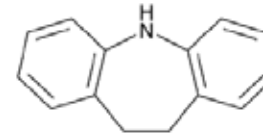


Carbamazepine Related Compound B
5H -Dibenz[b,f]azepine.
$C_{14}H_{11}N$ 193.24



Carbamazepine Related Compound F
5H -Dibenzo[b,f]azepine-5-carbonyl chloride.
$C_{15}H_{10}ClNO$ 255.70

Iminodibenzyl
10,11-Dihydro[b,f]azepine.
$C_{14}H_{13}N$ 195.28



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

卡马西平缓释片
Carbamazepine Extended-Release Tablets

方法来源：收载于USP39-NF34 1S

定义： Carbamazepine Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$).

有关物质：

色谱柱： L10, 2.1 mm x 10 cm; 1.8 µm (ACQUITY UPLC HSS Cyano)

流动相： Solution A:加0.5 ml三乙胺、0.5 ml甲酸至1000 ml水

Solution B:加0.25 ml甲酸至1000 ml甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
3.0	80	20
12.0	60	40
18.0	45	55
20.0	45	55
20.1	80	20
23.0	80	20

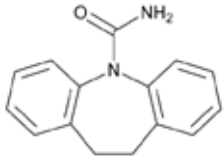
柱温: 40 ˚C　流速 (ml/min): 0.3　波长(nm): 230

杂质谱：

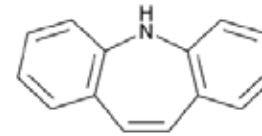
Name	相对保留时间	可接受标准 (%)
Carbamazepine related compound A	0.96	-
Carbamazepine	1.00	-
Carbamazepine related compound B	1.45	0.2
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Carbamazepine Related Compound A
10,11-Dihydrocarbamazepine.
$C_{15}H_{14}N_2O$ 238.28



Carbamazepine Related Compound B
5H -Dibenz[b,f]azepine.
$C_{14}H_{11}N$ 193.24

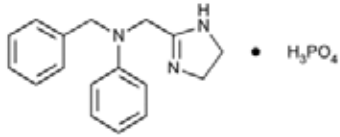


方法解析：将原来两个HPLC的杂质检测方法合并成了一个UPLC的检测方法，大大提高了分析效率。

磷酸安他唑啉
Antazoline Phosphate

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 1.7 µm (ACQUITY CSH Phenyl-Hexyl)

流动相： Solution A:1 ml甲酸加水至1000 ml

Solution B:流动相:乙腈:solution A = 17:83

等度条件：

柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 240　进样温度: 4 ˚C

杂质谱：

Name	相对保留时间	可接受标准 (%)
Antazoline phosphate	1.0	-
ntazoline related compound Aa	1.1	0.5
单个未知杂质	-	0.5
总杂质	-	1.0

杂质结构

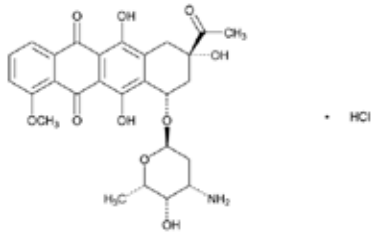
Antazoline Related Compound A
N-(2-Aminoethyl)-2-[benzyl(phenyl)amino]
acetamide.
$C_{17}H_{21}N_3O$　283.38

方法解析：采用UPLC方法代替原来的TLC方法，提高的分析效率及方法的准确性。

盐酸柔红霉素
Daunorubicin Hydrochloride

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:乙腈:甲醇:三氟乙酸 = 800:200:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	70	30
3	70	30
13	40	60
13.1	70	30
15	70	30

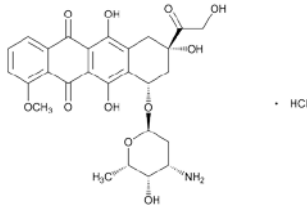
流速 (ml/min): 0.4　波长(nm): 254　进样温度: 4 °C

杂质谱：

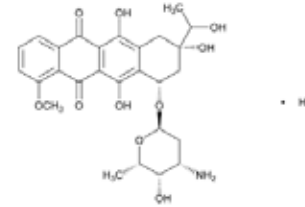
Name	相对保留时间	可接受标准 (%)
Doxorubicin	0.50	0.5
Dihydrodaunorubicin	0.72	0.5
	0.75	
Daunorubicin	1.0	-
Daunorubicinone	1.2	0.5
单个未知杂质	-	0.5
总杂质	-	2.5

杂质结构

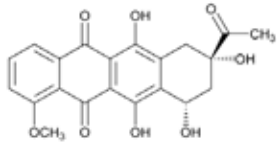
Doxorubicin
N-(2-Aminoethyl)-2-[benzyl(phenyl)amino]acetamide.
$C_{17}H_{21}N_3O$ 283.38



Dihydrodaunorubicin Hydrochloride
(8S ,10S)-10-[(3-Amino-2,3,6-trideoxy--l-lyxo-hexopyranosyl)oxy]-6,8,11-trihydroxy-8-(1-hydroxyethyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione hydrochloride.
$C_{27}H_{31}NO_{10}HCl$ 566.00



Daunorubicinone
(8S ,10S)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_8$ 398.36



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

注射用盐酸柔红霉素
Daunorubicin Hydrochloride for Injection

方法来源：收载于USP39-NF34

定义： Daunorubicin Hydrochloride for Injection is a sterile mixture of Daunorubicin Hydrochloride and Mannitol. It contains the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of daunorubicin ($C_{27}H_{29}NO_{10}$).

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:乙腈:甲醇:三氟乙酸 = 800:200:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	70	30
3	70	30
13	40	60
13.1	70	30
15	70	30

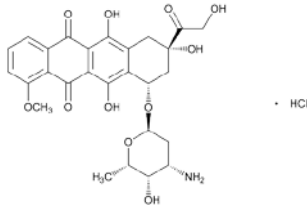
流速 (ml/min): 0.4　波长(nm): 254　进样温度: 4 °C

杂质谱：

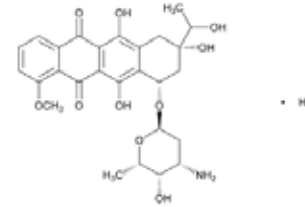
Name	相对保留时间	可接受标准 (%)
Doxorubicin	0.50	0.5
Dihydrodaunorubicin	0.72	0.5
	0.75	
Daunorubicin	1.0	-
Daunorubicinone	1.2	0.5
单个未知杂质	-	0.5
总杂质	-	2.5

杂质结构

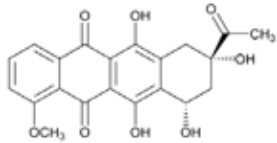
Doxorubicin
N-(2-Aminoethyl)-2-[benzyl(phenyl)amino]acetamide.
$C_{17}H_{21}N_3O$ 283.38



Dihydrodaunorubicin Hydrochloride
(8S ,10S)-10-[(3-Amino-2,3,6-trideoxy--l-lyxo-hexopyranosyl)oxy]-6,8,11-trihydroxy-8-(1-hydroxyethyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione hydrochloride.
$C_{27}H_{31}NO_{10}HCl$ 566.00



Daunorubicinone
(8S ,10S)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.
$C_{21}H_{18}O_8$ 398.36



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

双氯芬酸钾片
Diclofenac Potassium Tablets

方法来源：收载于USP39-NF34

定义： Diclofenac Potassium Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diclofenac potassium ($C_{14}H_{10}Cl_2KNO_2$).

有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 µm

流动相： Solution A:0.7708 g/L乙酸铵水溶液，加乙酸调至pH5.3

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.00	70	30
0.50	70	30
8.50	5	95
10.00	5	95
10.01	70	30
14.00	70	30

柱温: 35 ˚C　流速 (ml/min): 0.3　波长(nm): 280

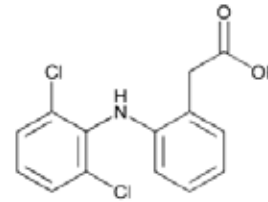
杂质谱：

Name	相对保留时间	可接受标准 (%)
Oxindole	0.4	-
Diclofenac	1.0	-
Diclofenac related compound D (diclofenac bromo analog)	1.04	-
Diclofenac related compound A	1.48	0.5
Diclofenac alcohol analog	1.55	-
Diclofenac benzaldehyde analog	1.81	-
Oxindole	0.4	-
单个未知杂质	-	0.5
总杂质	-	1.5

杂质结构

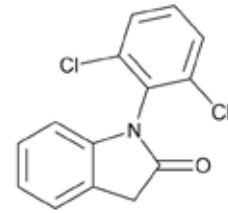
Oxindole
1,3-Dihydro-2H -indol-2-one.

Diclofenac



Diclofenac related compound D
2-{2-[(2-Bromo-6-chlorophenyl) amino]phenyl}acetic acid.

Diclofenac related compound A
1-(2,6-Dichlorophenyl)indolin-2-one (diclofenac lactam).
$C_{14}H_9Cl_2NO$ 278.13



Diclofenac alcohol analog
{2-[(2,6-Dichlorophenyl)amino] phenyl}methanol.

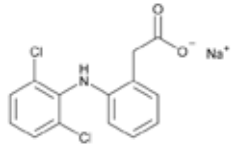
Diclofenac benzaldehyde analog
2-[(2,6-Dichlorophenyl)amino] benzaldehyde.

方法解析：增加了杂质A的限度要求，原等度HPLC方法改为UPLC方法，提高了分离度与分析效率。

双氯芬酸钠肠溶片
Diclofenac Sodium Delayed-Release Tablets

方法来源：收载于USP39-NF34

定义： Diclofenac Sodium Delayed-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$).



有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 µm

流动相： Solution A:0.7708 g/L乙酸铵水溶液，加乙酸调至pH5.3

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.00	70	30
0.50	70	30
8.50	5	95
10.00	5	95
10.01	70	30
14.00	70	30

柱温: 35 ˚C　流速 (ml/min): 0.3　波长(nm): 280

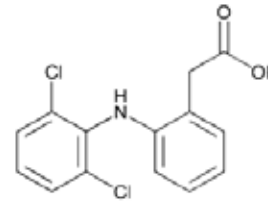
杂质谱：

Name	相对保留时间	可接受标准 (%)
Oxindole	0.4	-
Diclofenac	1.0	-
Diclofenac related compound D (diclofenac bromo analog)	1.04	-
Diclofenac related compound A	1.48	0.5
Diclofenac alcohol analog	1.55	-
Diclofenac benzaldehyde analog	1.81	-
Oxindole	0.4	-
单个未知杂质	-	0.5
总杂质	-	1.5

杂质结构

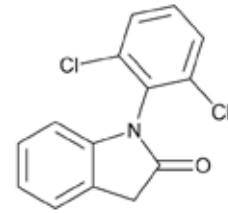
Oxindole
1,3-Dihydro-2H -indol-2-one.

Diclofenac



Diclofenac related compound D
2-{2-[(2-Bromo-6-chlorophenyl) amino]phenyl}acetic acid.

Diclofenac related compound A
1-(2,6-Dichlorophenyl)indolin-2-one (diclofenac lactam).
$C_{14}H_9Cl_2NO$ 278.13



Diclofenac alcohol analog
{2-[(2,6-Dichlorophenyl)amino] phenyl}methanol.

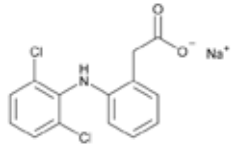
Diclofenac benzaldehyde analog
2-[(2,6-Dichlorophenyl)amino] benzaldehyde.

方法解析：增加了杂质A的限度要求，原等度HPLC方法改为UPLC方法，提高了分离度与分析效率。

双氯芬酸钠缓释片
Diclofenac Sodium Extended-Release Tablets

方法来源：收载于USP39-NF34

定义： Diclofenac Sodium Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$).



有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 µm

流动相： Solution A:0.7708 g/L乙酸铵水溶液，加乙酸调至pH5.3

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.00	70	30
0.50	70	30
8.50	5	95
10.00	5	95
10.01	70	30
14.00	70	30

柱温: 35 ˚C　流速 (ml/min): 0.3　波长(nm): 280

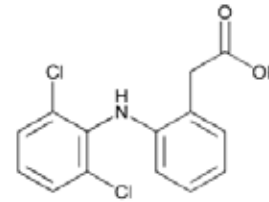
杂质谱：

Name	相对保留时间	可接受标准 (%)
Oxindole	0.4	-
Diclofenac	1.0	-
Diclofenac related compound D (diclofenac bromo analog)	1.04	-
Diclofenac related compound A	1.48	0.5
Diclofenac alcohol analog	1.55	-
Diclofenac benzaldehyde analog	1.81	-
Oxindole	0.4	-
单个未知杂质	-	0.5
总杂质	-	1.5

杂质结构

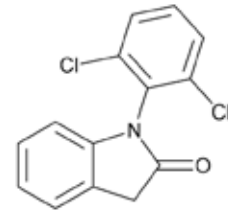
Oxindole
1,3-Dihydro-2H -indol-2-one.

Diclofenac



Diclofenac related compound D
2-{2-[(2-Bromo-6-chlorophenyl) amino]phenyl}acetic acid.

Diclofenac related compound A
1-(2,6-Dichlorophenyl)indolin-2-one (diclofenac lactam).
$C_{14}H_9Cl_2NO$ 278.13



Diclofenac alcohol analog
{2-[(2,6-Dichlorophenyl)amino] phenyl}methanol.

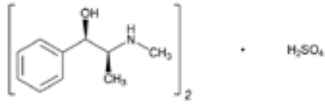
Diclofenac benzaldehyde analog
2-[(2,6-Dichlorophenyl)amino] benzaldehyde.

方法解析：增加了杂质A的限度要求，原等度HPLC方法改为UPLC方法，提高了分离度与分析效率。

硫酸麻黄碱注射液
Ephedrine Sulfate Injection

方法来源：收载于USP39-NF34

定义： Ephedrine Sulfate Injection is a sterile solution of Ephedrine Sulfate in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of ephedrine sulfate [$(C_{10}H_{15}NO)_2 \cdot H_2SO_4$].



有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 2.6 µm

流动相： Solution A:4 ml三乙胺至1 L水，加磷酸调至pH4.0

Solution B:乙腈:solutionA=1:99

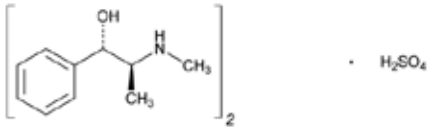
等度条件：柱温: 30 °C　流速 (ml/min): 0.6　波长(nm): 206

杂质谱：

Name	相对保留时间	可接受标准 (%)
Ephedrine	1.0	-
Pseudoephedrine	1.2	-
单个未知杂质	-	0.2
总杂质	-	2.0

杂质结构

Pseudoephedrine Sulfate
$(C_{10}H_{15}NO)_2 \cdot H_2SO_4$　428.54

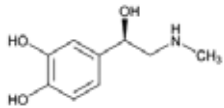


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

肾上腺素
Epinephrine

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.8 µm (ACQUITY HSS T3)

流动相： Solution A:加1.3 ml七氟丁酸至500 ml水，加0.82 ml甲酸，加水稀释至1000 ml，加氨水调至pH2.3

Solution B:加1.3 ml七氟丁酸和0.82 ml甲酸至1 L乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.00	100	0
4.5	100	0
8.8	50	50
10.8	50	50
10.9	100	0
13.9	100	0

柱温: 45 ˚C　流速 (ml/min): 0.4　波长(nm): 232

杂质谱：

Name	相对保留时间	可接受标准 (%)
Norepinephrine	0.5	4.0
Epinephrine	1	-
Adrenalone	1.1	0.2
单个未知杂质	-	0.5

杂质结构

Norepinephrine
(R)-3-(2-Amino-1-hydroxyethyl) phenol.

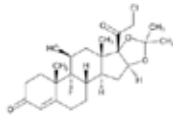
Adrenalone Hydrochloride
3′,4′-Dihydroxy-2-(methylamino) acetophenone hydrochloride
$C_9H_{11}NO_3 \cdot HCl$　217.65

方法解析：原杂质检测TLC方法改为UPLC方法，提高了检测效率与方法的准确性。增加了对Adrenalone杂质的限度控制(0.2%)。

哈西奈德
Halcinonide

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20.0	10	90
22.0	10	90
22.1	90	10
25.0	90	10

流速 (ml/min): 0.3　波长(nm): 240

杂质谱：

Name	相对保留时间	可接受标准 (%)
Dihydrotriamcinolone	0.5	-
Halcinonide	1.0	-
单个未知杂质	-	0.10
总杂质	-	3.0

杂质结构

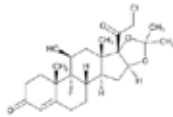
Dihydrotriamcinolone
9-Fluoro-11β,16α,17,21-
tetrahydroxypregna-4-ene-3,20-dione

方法解析：原杂质检测TLC方法改为UPLC方法，提高了检测效率与方法的准确性。

米诺地尔溶液
Minoxidil Topical Solution

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY BEH Shield RP18)

流动相： Solution A:加0.65 ml庚氟丁酸至1 L水中

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	100	0
10.0	60	40
10.1	100	0
15.0	100	0

柱温: 45 ˚C　流速 (ml/min): 0.4　波长(nm): 280

杂质谱：

Name	相对保留时间	可接受标准 (%)
Minoxidil related compound A (pyrimidine oxide analog)	0.36	-
Pyrimidine analog	0.51	-
Minoxidil	1.00	-
Minoxidil related compound E (deoxyminoxidil)	1.03	-
单个未知杂质	-	0.2
总杂质	-	2.0

杂质结构

Minoxidil related compound A
2,6-Diamino-4-chloropyrimidine 1-oxide.

Pyrimidine analog
6-Chloropyrimidine-2,4-diamine

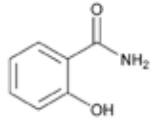
Minoxidil related compound E
6-(Piperidin-1-yl)pyrimidine-2,4-diamine.
$C_9H_{15}N_5$　193.25

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

水杨酰胺
Salicylamide

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.1%甲酸水溶液

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	92	8
6.0	55	45
6.5	5	95
8.0	5	95
8.01	92	8
12.0	92	8

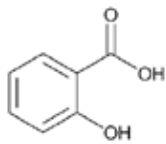
柱温: 35 ˚C　流速 (ml/min): 0.3　波长(nm): 300

杂质谱：

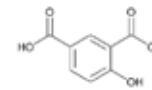
Name	相对保留时间	可接受标准 (%)
Salicylic acid related compound B	0.93	-
Salicylamide	1.00	-
Salicylic acid	1.33	0.1
单个未知杂质	-	0.10
总杂质	-	1

杂质结构

Salicylic Acid



USP Salicylic Acid Related Compound B
4-Hydroxyisophthalic acid.
$C_8H_6O_5$　182.13

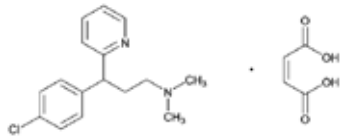


方法解析：原杂质检测TLC方法改为UPLC方法，提高了检测效率与方法的准确性。增加了对水杨酸的限度控制(0.1%)。

马来酸氯苯那敏片
Chlorpheniramine Maleate Tablets

方法来源：收载于USP39-NF34

定义： Chlorpheniramine Maleate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.15%三氟乙酸水溶液

Solution B:0.02%三氟乙酸在甲醇:乙腈=25:75混合溶液中

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
0.6	90	10
2.3	77	23
5.5	77	23
7.4	57	43
8.0	57	43
12.5	1	99
13.5	1	99

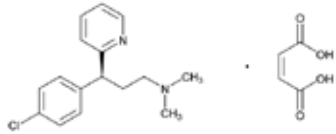
柱温: 40 °C　流速 (ml/min): 0.4　波长(nm): 225

方法解析：将原紫外分光光度法改为通则<321>中UPLC的含量测定方法。

马来酸氯苯那敏片
Chlorpheniramine Maleate Tablets

方法来源：收载于USP39-NF34 1S

结构式： Dexchlorpheniramine Maleate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of dexchlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.15%三氟乙酸水溶液

Solution B:0.02%三氟乙酸在甲醇:乙腈=25:75混合溶液中

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
0.6	90	10
2.3	77	23
5.5	77	23
7.4	57	43
8.0	57	43
12.5	1	99
13.5	1	99

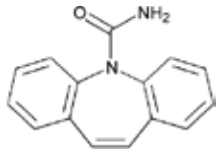
柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 225

方法解析：将原紫外分光光度法改为通则<321>中UPLC的含量测定方法。

维生素 B12 片
Cyanocobalamin Tablets

方法来源：收载于USP39-NF34

定义：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 μm (ACQUITY BEH C_{18})

流动相： Solution A:乙腈

Solution B:加470.5 mg低紫外吸收的己烷磺酸钠，1 ml磷酸，加水至1000 ml，加50%的氢氧化钾溶液调至 pH=3.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	1.0	99.0
0.5	1.0	99.0
1.2	2.3	97.7
1.4	5.0	95.0
2.5	7.0	93.0
5.0	18.0	82.0
5.5	25.0	75.0
6.5	25.0	75.0
7.0	1.0	99.0
8.0	1.0	99.0

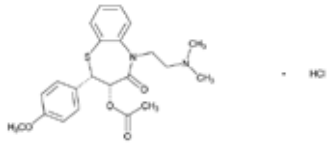
柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 361

方法解析：在含量测定项下并列了HPLC和UPLC方法，可以根据需要选择合适的方法进行测定。

盐酸地尔硫卓缓释胶囊剂
Diltiazem Hydrochloride Extended-Release Capsules

方法来源：收载于USP39-NF34

定义： Diltiazem Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.79 g/L碳酸氢铵水溶液，加稀氨水调至pH8.0

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.0	95	5
5.0	60	40
13.0	60	40
16.0	30	70
20.0	30	70
20.1	95	5
25.0	95	5

流速 (ml/min): 0.3　波长(nm): 240

杂质谱：

Name	相对保留时间	可接受标准 (%)
Diltiazem related compound H	0.44	-
Diltiazem related compound G	0.52	-
Diltiazem related compound C	0.58	-
Diltiazem related compound D	0.61	-
Diltiazem related compound E	0.66	-
Desacetyl diltiazem	0.75	0.5
Diltiazem related compound A	0.83	-
Diltiazem related compound B	0.89	-
Diltiazem	1.0	-
单个未知杂质	-	0.2
总杂质	-	1.0

杂质结构

Diltiazem related compound H
(2S ,3S)-5-(2-Aminoethyl)-3-hydroxy-2-(4-hydroxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5H)-one

Diltiazem related compound G
(2S ,3S)-3-Hydroxy-2-(3-methoxyphenyl)-5-(2-(methylamino)ethyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one

Diltiazem related compound C
(2S ,3S)-5-[2-(Dimethylamino)ethyl]-2-(4-hydroxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepin-3-yl acetate

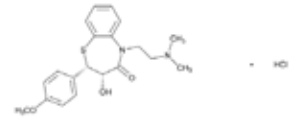
Diltiazem related compound D
(2S ,3S)-2-(4-Methoxyphenyl)-5-[2-(methylamino)ethyl]-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Diltiazem related compound E
(2S ,3S)-3-Hydroxy-2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5H)-one

Diltiazem related compound A
(2R ,3S)-5-[2-(Dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Diltiazem related compound B
(2S ,3S)-2-(4-Methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Desacetyl Diltiazem Hydrochloride
$C_{20}H_{24}N_2O_3S \cdot HCl$ 408.95



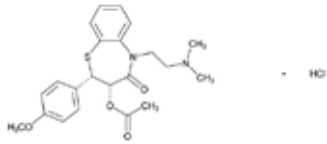
方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

含量测定方法，将原来专属性差的滴定改为了UPLC方法。

盐酸地尔硫卓片
Diltiazem Hydrochloride Tablets

方法来源：收载于USP39-NF34

定义： Diltiazem Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.79 g/L碳酸氢铵水溶液，加稀氨水调至pH8.0

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.0	95	5
5.0	60	40
13.0	60	40
16.0	30	70
20.0	30	70
20.1	95	5
25.0	95	5

流速 (ml/min): 0.3　波长(nm): 240

杂质谱：

Name	相对保留时间	可接受标准 (%)
Diltiazem related compound H	0.44	-
Diltiazem related compound G	0.52	-
Diltiazem related compound C	0.58	-
Diltiazem related compound D	0.61	-
Diltiazem related compound E	0.66	-
Desacetyl diltiazem	0.75	0.5
Diltiazem related compound A	0.83	-
Diltiazem related compound B	0.89	-
Diltiazem	1.0	-
单个未知杂质	-	0.2
总杂质	-	1.0

杂质结构

Diltiazem related compound H
(2S ,3S)-5-(2-Aminoethyl)-3-hydroxy-2-(4-hydroxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5H)-one

Diltiazem related compound G
(2S ,3S)-3-Hydroxy-2-(3-methoxyphenyl)-5-(2-(methylamino)ethyl)-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one

Diltiazem related compound C
(2S ,3S)-5-[2-(Dimethylamino)ethyl]-2-(4-hydroxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepin-3-yl acetate

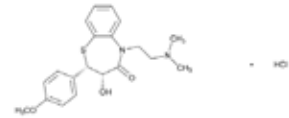
Diltiazem related compound D
(2S ,3S)-2-(4-Methoxyphenyl)-5-[2-(methylamino)ethyl]-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Diltiazem related compound E
(2S ,3S)-3-Hydroxy-2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5H)-one

Diltiazem related compound A
(2R ,3S)-5-[2-(Dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Diltiazem related compound B
(2S ,3S)-2-(4-Methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate

Desacetyl Diltiazem Hydrochloride
$C_{20}H_{24}N_2O_3S \cdot HCl$ 408.95

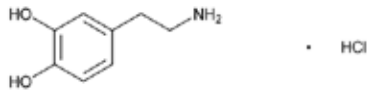


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸多巴胺
Dopamine Hydrochloride

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.9 µm

流动相： Solution A:1.0 ml七氟丁酸加水稀释至1000 ml

Solution B:1.0 ml七氟丁酸加甲醇稀释至1000 ml

流动相:Solution A:Solution B=85:15

等度条件：

柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 280

杂质谱：

Name	相对保留时间	可接受标准 (%)
Dopamine hydrochloride	1.0	-
Dopamine related compound B	1.8	0.1
Dopamine related compound A	2.3	0.1
Dopamine related compound C	4.6	0.1
单个未知杂质	-	0.1
总杂质	-	1.0

杂质结构

Dopamine related compound B
4-(2-Aminoethyl)-2-methoxyphenol
$C_9H_{13}NO_2$　167.21

Dopamine related compound A
5-(2-Aminoethyl)-2-methoxyphenol
$C_9H_{13}NO_2$　167.21

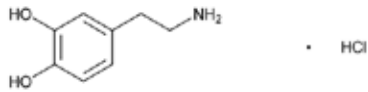
Dopamine related compound C
2-(3,4-Dimethoxyphenyl)ethan-1-amine
$C_{10}H_{15}NO_2$　181.23

方法解析：原杂质检测TLC方法改为UPLC方法，提高了检测效率与方法的准确性。

盐酸多巴胺注射液
Dopamine Hydrochloride Injection

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.9 µm

流动相： Solution A:1.0 ml七氟丁酸加水稀释至1000 ml

Solution B:1.0 ml七氟丁酸加甲醇稀释至1000 ml

流动相:Solution A:Solution B=85:15

等度条件：

柱温: 35 ˚C　流速 (ml/min): 0.5　波长(nm): 280

杂质谱：

Name	相对保留时间	可接受标准 (%)
Dopamine	1.0	-
Dopamine related compound B	1.8	-
单个未知杂质	-	0.1
总杂质	-	1.0

杂质结构

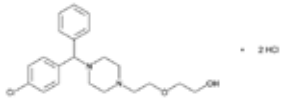
Dopamine related compound B
4-(2-Aminoethyl)-2-methoxyphenol
$C_9H_{13}NO_2$　167.21

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸羟嗪
Hydroxyzine Hydrochloride

方法来源：收载于USP40-NF35

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS C_{18} SB)

流动相： Solution A:三氟乙酸:水=0.1:99.9

Solution B:三氟乙酸:乙腈=0.5:99.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

流速 (ml/min): 0.3　波长(nm): 230

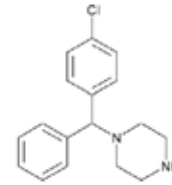
杂质谱：

Name	相对保留时间	相对相应因子	可接受标准 (%)
Decloxizine	0.87	0.68	0.3
Hydroxyzine related compound A	0.96	-	0.3
Hydroxyzine	1.0	-	-
4-Chlorobenzophenone	1.4	-	0.2
单个未知杂质	-	1.0	0.2
总杂质	-	-	0.75

杂质结构

Decloxizine
2-[2-(4-Benzhydrylpiperazin-1-yl)ethoxy]ethanol; also known as 2-{2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy}ethanol

Hydroxyzine related compound A
p-Chlorobenzhydrylpiperazine;
Also known as 1-[(4-Chlorophenyl) phenylmethyl]piperazine.
$C_{17}H_{19}ClN_2$ 286.80



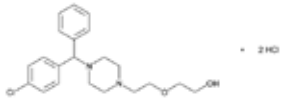
4-Chlorobenzophenone
$C_{13}H_9ClO$ 216.66

方法解析：原等度HPLC方法改为了梯度UPLC方法，提高了分析效率。
增加了对Decloxizine、4-Chlorobenzophenone和杂质A的限度控制要求。

盐酸羟嗪注射液
Hydroxyzine Hydrochloride Injection

方法来源：收载于USP39-NF34

定义： Hydroxyzine Hydrochloride Injection is a sterile solution of Hydroxyzine Hydrochloride in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS C_{18} SB)

流动相： Solution A:三氟乙酸:水=0.1:99.9

Solution B:三氟乙酸:乙腈=0.5:99.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

流速 (ml/min): 0.3　波长(nm): 230

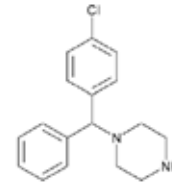
杂质谱：

Name	相对保留时间	相对相应因子	可接受标准 (%)
Decloxizine	0.87	0.68	0.3
Hydroxyzine related compound A	0.96	-	0.3
Hydroxyzine	1.0	-	-
4-Chlorobenzophenone	1.4	-	0.2
单个未知杂质	-	1.0	0.2
总杂质	-	-	0.75

杂质结构

Decloxizine
2-[2-(4-Benzhydrylpiperazin-1-yl)ethoxy]ethanol; also known as 2-{2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy}ethanol

Hydroxyzine related compound A
p-Chlorobenzhydrylpiperazine;
Also known as 1-[(4-Chlorophenyl) phenylmethyl]piperazine.
$C_{17}H_{19}ClN_2$ 286.80



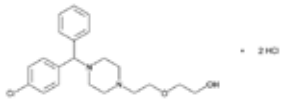
4-Chlorobenzophenone
$C_{13}H_9ClO$ 216.66

方法解析：原等度HPLC方法改为了梯度UPLC方法，提高了分析效率。
增加了对Decloxizine和杂质A的限度控制要求。

盐酸羟嗪片
Hydroxyzine Hydrochloride Tablets

方法来源：收载于USP39-NF34

定义： Hydroxyzine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS C_{18} SB)

流动相： Solution A:三氟乙酸:水=0.1:99.9

Solution B:三氟乙酸:乙腈=0.5:99.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

流速 (ml/min): 0.3　波长(nm): 230

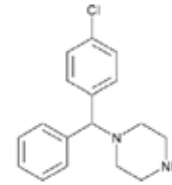
杂质谱：

Name	相对保留时间	可接受标准 (%)
Decloxizine	0.87	-
Hydroxyzine related compound A	0.96	-
Hydroxyzine	1.0	-
4-Chlorobenzophenone	1.4	0.2
单个未知杂质	-	0.3
总杂质	-	0.5

杂质结构

Decloxizine
2-[2-(4-Benzhydrylpiperazin-1-yl)ethoxy]ethanol; also known as 2-{2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy}ethanol

Hydroxyzine related compound A
p-Chlorobenzhydrylpiperazine;
Also known as 1-[(4-Chlorophenyl) phenylmethyl]piperazine.
$C_{17}H_{19}ClN_2$ 286.80



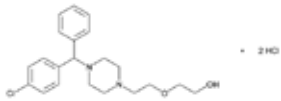
4-Chlorobenzophenone
$C_{13}H_9ClO$ 216.66

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸羟嗪口服溶液
Hydroxyzine Hydrochloride Oral Solution

方法来源：收载于USP40-NF35

定义： Hydroxyzine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS C_{18} SB)

流动相： Solution A:三氟乙酸:水=0.1:99.9

Solution B:三氟乙酸:乙腈=0.5:99.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

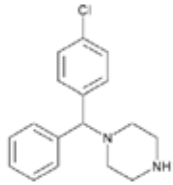
柱温: 30 ˚C　流速 (ml/min): 0.3　波长(nm): 230

杂质谱：

Name	相对保留时间	可接受标准 (%)
Hydroxyzine related compound A	0.94	-
Hydroxyzine	1.0	-
4-Chlorobenzophenone	1.4	0.2
单个未知杂质	-	0.2
总杂质	-	0.75

杂质结构

Hydroxyzine related compound A
p-Chlorobenzhydrylpiperazine;
Also known as 1-[(4-Chlorophenyl) phenylmethyl]piperazine.
$C_{17}H_{19}ClN_2$ 286.80



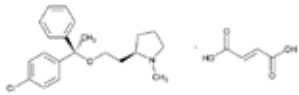
4-Chlorobenzophenone
$C_{13}H_9ClO$ 216.66

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

富马酸氯马斯汀
Clemastine Fumarate

方法来源：收载于USP39-NF34

结构式：



有关物质：

色谱柱： L7, 4.6 mm x 5 cm; 1.8 μm

流动相： buffer:4.1g/L磷酸二氢钾水溶液，加磷酸调至 pH=4.0

Solution A:甲醇:乙腈:buffer=35:35:30

Solution B:甲醇:乙腈:buffer=40:37.5:22.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
3.1	0	100
18	0	100
18.1	100	0
25	100	0

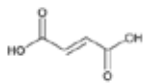
流速 (ml/min): 1.2　波长(nm): 220

杂质谱：

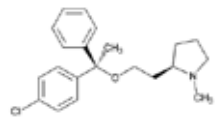
Name	相对保留时间	可接受标准 (%)
Fumaric acid	0.5	-
Clemastine	1.0	-
4-Chlorobenzophenone	1.7	0.15
单个未知杂质	-	0.10
总杂质	-	1.0

杂质结构

Fumaric acid



Clemastine



4-Chlorobenzophenone

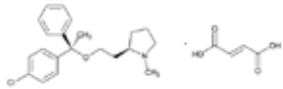
$C_{13}H_9ClO$　216.66

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

富马酸氯马斯汀片
Clemastine Fumarate Tablets

方法来源：收载于USP39-NF34 1S

定义： Clemastine Fumarate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$).



有关物质：

色谱柱： L7, 4.6 mm x 5 cm; 1.8 µm

流动相： buffer:4.1g/L磷酸二氢钾水溶液，加磷酸调至 pH=4.0

Solution A:甲醇:乙腈:buffer=35:35:30

Solution B:甲醇:乙腈:buffer=40:37.5:22.5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
3.1	0	100
18	0	100
18.1	100	0
25	100	0

流速 (ml/min): 1.2　波长(nm): 220

杂质谱：

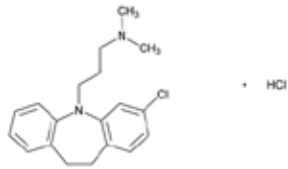
Name	相对保留时间	可接受标准 (%)
单个未知杂质	-	0.5
总杂质	-	2.0

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸氯米帕明
Clomipramine Hydrochloride

方法来源：收载于USP40-NF35 1S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:2.5ml乙酸至1 L水中，用浓氨水调至 pH=7.5

Solution B:乙腈:甲醇:THF (无稳定剂) =80:15:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
5.0	50	50
11.0	20	80
14.0	20	80
14.1	65	35
18.0	65	35

柱温: 30 ˚C　流速 (ml/min): 0.3　波长(nm): 254

杂质谱：

Name	相对保留时间	可接受标准 (%)
Imipramine	0.77	0.10
Clomipramine related compound C	0.87	0.10
Clomipramine	1.00	-
Clomipramine related compound A	1.1	0.10
Clomipramine related compound D	1.2	0.10
Clomipramine related compound F	1.5	0.10
单个未知杂质	-	0.10
总杂质	-	2.0

杂质结构

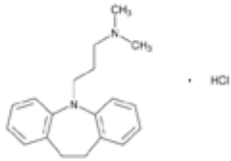
Clomipramine Related Compound A
N 1 -[3-(3-Chloro-10,11-dihydro-5H -dibenzo[b,f]azepin-5-yl)propyl]- N 1 , N 3 , N 3 -trimethylpropane-1,3-diamine dihydrochloride.
$C_{23}H_{32}ClN_3 \cdot 2HCl$ 458.89

Clomipramine Related Compound C
3-(3-Chloro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride, monohydrate.
$C_{19}H_{21}ClN_2 \cdot HCl \cdot H_2O$ 367.31

Clomipramine Related Compound D
3-(3,7-Dichloro-10,11-dihydro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride.
$C_{19}H_{22}Cl_2N_2 \cdot HCl$ 385.76

Clomipramine Related Compound F
3-Chloro-10,11-dihydro-5H -dibenzo[b,f]azepine.
$C_{14}H_{12}ClN$ 229.70

Imipramine Hydrochloride

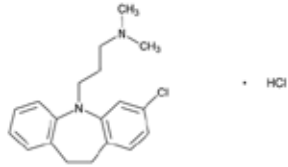


方法解析：原等度HPLC方法改为了梯度UPLC方法，提高了分析效率。
增加了5个特性杂质的限度要求。

盐酸氯米帕明胶囊
Clomipramine Hydrochloride Capsules

方法来源：收载于USP40-NF35 1S

结构式： Clomipramine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:2.5ml乙酸至1 L水中，用浓氨水调至 pH=7.5

Solution B:乙腈:甲醇:THF（无稳定剂）=80:15:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
5.0	50	50
11.0	20	80
14.0	20	80
14.1	65	35
18.0	65	35

柱温: 30 ˚C　流速 (ml/min): 0.3　波长(nm): 254

杂质谱：

Name	相对保留时间	可接受标准 (%)
Imipramine	0.77	0.20
Clomipramine related compound C	0.87	0.20
Clomipramine	1.00	-
Clomipramine related compound A	1.1	-
Clomipramine related compound D	1.2	-
Clomipramine related compound F	1.5	-
单个未知杂质	-	0.1
总杂质	-	1.0

杂质结构

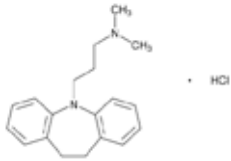
Clomipramine Related Compound A
N 1 -[3-(3-Chloro-10,11-dihydro-5H -dibenzo[b,f]azepin-5-yl)propyl]- N 1 , N 3 , N 3 -trimethylpropane-1,3-diamine dihydrochloride.
$C_{23}H_{32}ClN_3 \cdot 2HCl$ 458.89

Clomipramine Related Compound C
3-(3-Chloro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride, monohydrate.
$C_{19}H_{21}ClN_2 \cdot HCl \cdot H_2O$ 367.31

Clomipramine Related Compound D
3-(3,7-Dichloro-10,11-dihydro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride.
$C_{19}H_{22}Cl_2N_2 \cdot HCl$ 385.76

Clomipramine Related Compound F
3-Chloro-10,11-dihydro-5H -dibenzo[b,f]azepine.
$C_{14}H_{12}ClN$ 229.70

Imipramine Hydrochloride



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸氯米帕明复合口服混悬液
Clomipramine Hydrochloride Compounded Oral Suspension, Veterinary

方法来源：收载于USP39-NF34 1S

结构式： Clomipramine Hydrochloride Compounded Oral Suspension, Veterinary contains NLT 90.0% and NMT 110.0% of the labeled amount of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$).

有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 2.5 µm

流动相： Solution A:甲醇-乙腈

Solution B:25 mM磷酸二氢钾加磷酸调至 pH=3.2

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	40	60
4	50	50
10	50	50
10.5	40	60
20	40	60

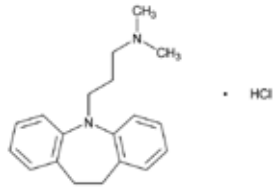
柱温: 50 ˚C　流速 (ml/min): 0.275　波长(nm): 254

方法解析：新增各论，采用UPLC进行快速高效的分析。

盐酸丙咪嗪片
Imipramine Hydrochloride Tablets

方法来源：收载于USP39-NF34 1S

结构式： Imipramine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_8)

流动相： Solution A:0.02M碳酸氢铵水溶液，用28 - 30%的氨水调至pH8.0

Solution B:乙腈:甲醇=70:30

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
1.0	90	10
5.0	60	40
7.0	60	40
10.0	48	52
13.0	48	52
14.0	20	80
16.0	20	80
16.1	90	10
18.0	90	10

柱温: 35 ˚C　流速 (ml/min): 0.4　波长(nm): 254

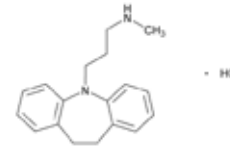
杂质谱：

Name	相对保留时间	可接受标准 (%)
Desipramine	0.82	0.10
Depramine	0.84	0.10
Imipramine	1.0	-
Iminodibenzyl	1.18	0.10
单个未知杂质	-	0.20
总杂质	-	1.5

杂质结构

Depramine
3-(5H -Dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride.
$C_{19}H_{22}N_2 \cdot HCl$ 314.85

Desipramine Hydrochloride
10,11-Dihydro-5H -[3-(methylamino) propyl]-5H -dibenz[b,f]azepine monohydrochloride.
$C_{18}H_{22}N_2 \cdot HCl$ 302.84



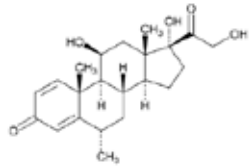
Iminodibenzyl
10,11-Dihydro-5H -dibenzo[b,f] azepine.
$C_{14}H_{13}N$ 195.28

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

甲泼尼龙
Methylprednisolone

方法来源：收载于USP39-NF34 1S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.1%甲酸水溶液

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	50	50
3.0	50	50
17.0	30	70
22.0	30	70
22.1	50	50
25.0	50	50

柱温: 40 ˚C　流速 (ml/min): 0.2　波长(nm): 254　进样温度: 4 ˚C

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methylprednisolone related compound A	0.81	1.0
Methylprednisolone	1.0	-
Methylprednisolone related compound C	1.07	1.0
Methylprednisolone related compound D	1.49	1.0
单个未知杂质	-	0.10
总杂质	-	2.0

杂质结构

Methylprednisolone Related Compound A
17,21-Dihydroxy-6α-methylpregna-1,4-diene-3,11,20-trione.
$C_{22}H_{28}O_5$ 372.45

Methylprednisolone Related Compound C
11β-Hydroxy-6?-methylandrosta-1,4-diene-3,17-dione.
$C_{20}H_{26}O_3$ 314.42

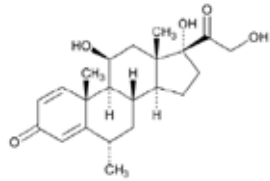
Methylprednisolone Related Compound D
11β,20-Dihydroxy-6?-methylpregna-1,4,17(20)-triene-3,21-dione.
$C_{22}H_{28}O_4$ 356.46

方法解析：原等度HPLC方法改为了梯度UPLC方法，提高了分析效率。增加了3个特性杂质的限度要求。

甲泼尼龙片
Methylprednisolone Tablets

方法来源：收载于USP39-NF34 1S

结构式： Methylprednisolone Tablets contain NLT 92.5% and NMT 107.5% of the labeled amount of methylprednisolone ($C_{22}H_{30}O_5$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.1%甲酸水溶液

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	50	50
3.0	50	50
17.0	30	70
22.0	30	70
22.1	50	50
25.0	50	50

柱温: 40 ˚C　流速 (ml/min): 0.2　波长(nm): 254　进样温度: 4 ˚C

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methylprednisolone related compound A	0.80	0.20
Methylprednisolone	1.0	-
Methylprednisolone related compound C	1.08	-
Methylprednisolone related compound D	1.51	0.20
单个未知杂质	-	0.10
总杂质	-	2.0

杂质结构

Methylprednisolone Related Compound A
17,21-Dihydroxy-6α-methylpregna-1,4-diene-3,11,20-trione.
$C_{22}H_{28}O_5$ 372.45

Methylprednisolone Related Compound C
11β-Hydroxy-6?-methylandrosta-1,4-diene-3,17-dione.
$C_{20}H_{26}O_3$ 314.42

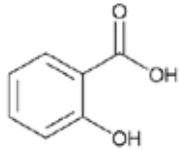
Methylprednisolone Related Compound D
11β,20-Dihydroxy-6?-methylpregna-1,4,17(20)-triene-3,21-dione.
$C_{22}H_{28}O_4$ 356.46

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

水杨酸局部泡沫剂
Salicylic Acid Topical Foam

方法来源：收载于USP39-NF34 1S

定义： Salicylic Acid Topical Foam contains NLT 90.0% and NMT 110.0% of the labeled amount of salicylic acid ($C_7H_6O_3$).



有关物质：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： 甲醇:三氟乙酸:水=35:0.1:65

等度条件：

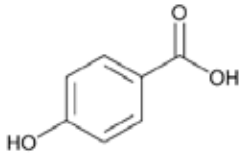
柱温: 30 ˚C　流速 (ml/min): 0.2　波长(nm): 212

杂质谱：

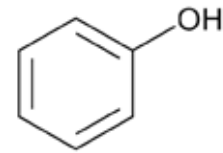
Name	相对保留时间	可接受标准 (%)
Salicylic acid related compound A	0.2	-
Phenol	0.4	-
Salicylic acid related compound B	0.6	-
Salicylic acid	1.0	-
单个未知杂质	-	0.10
总杂质	-	1.0

杂质结构

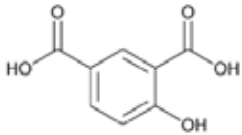
Salicylic Acid Related Compound A
4-Hydroxybenzoic acid.
$C_7H_6O_3$ 138.125



Phenol



Salicylic Acid Related Compound B
4-Hydroxyisophthalic acid.
$C_8H_6O_5$ 182.13

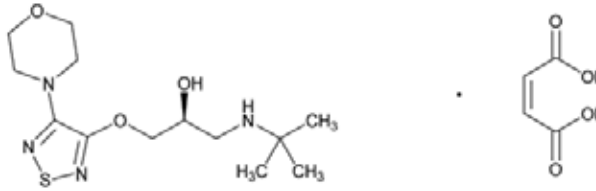


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

噻吗洛尔片
Timolol Maleate Tablets

方法来源：收载于USP39-NF34 1S

定义： Timolol Maleate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$).



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 2.6 µm

流动相： Solution A:0.5 ml三氟乙酸加水至1 L

Solution B:0.5 ml三氟乙酸加乙腈至1 L

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	84	16
2.4	84	16
8	20	80
8.1	84	16
11	84	16

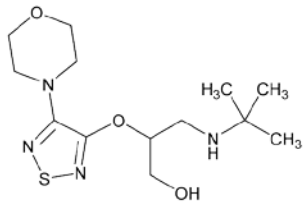
流速 (ml/min): 0.4　波长(nm): 295

杂质谱：

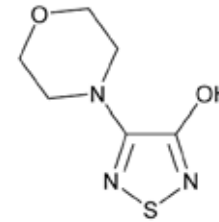
Name	相对保留时间	可接受标准 (%)
Timolol related compound B	0.5	0.4
Timolol related compound D	0.8	0.4
Timolol	1.0	-
单个未知杂质	-	0.2
总杂质	-	1.0

杂质结构

Timolol Related Compound B
3-(tert-Butylamino)-2-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-1-ol.
$C_{13}H_{24}N_4O_3S$ 316.42



Timolol Related Compound D
4-Morpholino-1,2,5-thiadiazol-3-ol.
$C_6H_9N_7O_4S$ 187.22

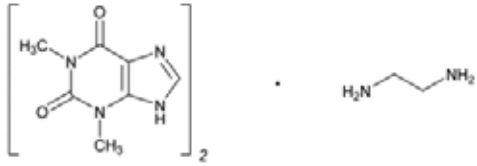


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

氨茶碱
Aminophylline

方法来源：收载于USP40-NF35

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	2

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

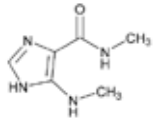
Name	相对保留时间	响应因子	可接受标准 (%)
Theophylline related compound C	0.36	-	0.10
Theophylline related compound B	0.63	-	0.10
Theophylline related compound D	0.69	-	0.10
Dimethyl uric acid	0.76	0.55	0.10
Theobromine	0.82	1.0	0.10
Theophylline	1.0	-	-
Theophylline related compound F	1.09	-	0.10
Caffeine	1.20	-	0.10
单个未知杂质	-		0.10
总杂质	-		0.3

杂质结构

Theophylline related compound C
N-(6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) formamide.
$C_7H_{10}N_4O_3$ 198.18

Theophylline related compound B
3-Methyl-1H -purine-2,6-dione;
Also known as 3-Methyl-3,7-dihydro-1H -purine-2,6-dione.
$C_6H_6N_4O_2$ 166.14

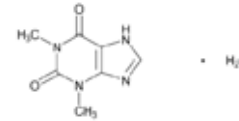
Theophylline related compound D
N-Methyl-5-(methylamino)-1H -imidazole-4-carboxamide.
$C_6H_{10}N_4O$ 154.17



Dimethyl uric acid
1,3-Dimethyl-7,9-dihydro-1H -purine-2,6,8(3H)-trione

Theobromine
3,7-Dihydro-3,7-dimethylpurine-2,6 (1H)-dione.

Theophylline



Theophylline related compound F
7-(2-Hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1H -purine-2,6-dione.
$C_9H_{12}N_4O_3$ 224.22

Caffeine

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

氨茶碱注射液
Aminophylline Injection

方法来源：收载于USP39-NF34 1S

定义： Aminophylline Injection is a sterile solution of Aminophylline in Water for Injection, or is a sterile solution of Theophylline in Water for Injection prepared with the aid of Ethylenediamine. It contains, in each mL, an amount of aminophylline ($C_{16}H_{24}N_{10}O_4$) equivalent to NLT 93.0% and NMT 107.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).
Aminophylline Injection may contain an excess of Ethylenediamine, but no other substance may be added for the purpose of pH adjustment.

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 μm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	2

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

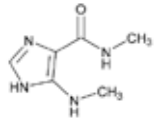
Name	相对保留时间	可接受标准 (%)
Theophylline related compound C	0.36	-
Theophylline related compound B	0.63	-
Theophylline related compound D	0.69	0.2
Dimethyl uric acid	0.76	-
Theobromine	0.82	-
Theophylline	1.0	-
Theophylline related compound F	1.09	-
Caffeine	1.20	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline related compound C
N-(6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) formamide.
$C_7H_{10}N_4O_3$ 198.18

Theophylline related compound B
3-Methyl-1H -purine-2,6-dione;
Also known as 3-Methyl-3,7-dihydro-1H -purine-2,6-dione.
$C_6H_6N_4O_2$ 166.14

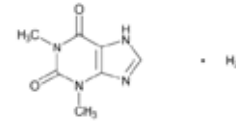
Theophylline related compound D
N-Methyl-5-(methylamino)-1H -imidazole-4-carboxamide.
$C_6H_{10}N_4O$ 154.17



Dimethyl uric acid
1,3-Dimethyl-7,9-dihydro-1H -purine-2,6,8(3H)-trione

Theobromine
3,7-Dihydro-3,7-dimethylpurine-2,6 (1H)-dione.

Theophylline



Theophylline related compound F
7-(2-Hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1H -purine-2,6-dione.
$C_9H_{12}N_4O_3$ 224.22

Caffeine

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

氨茶碱口服溶液
Aminophylline Oral Solution

方法来源：收载于USP39-NF34 1S

定义： Aminophylline Oral Solution is an aqueous solution of Aminophylline, prepared with the aid of Ethylenediamine. It contains an amount of aminophylline ($C_{16}H_{24}N_{10}O_4$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).

Aminophylline Oral Solution may contain an excess of ethylenediamine, but no other substance may be added for the purpose of pH adjustment

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	2

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

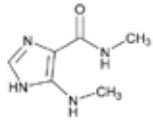
Name	相对保留时间	可接受标准 (%)
Theophylline related compound C	0.36	-
Theophylline related compound B	0.63	-
Theophylline related compound D	0.69	0.2
Dimethyl uric acid	0.76	-
Theobromine	0.82	-
Theophylline	1.0	-
Theophylline related compound F	1.09	-
Caffeine	1.20	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline related compound C
N-(6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) formamide.
$C_7H_{10}N_4O_3$ 198.18

Theophylline related compound B
3-Methyl-1H -purine-2,6-dione;
Also known as 3-Methyl-3,7-dihydro-1H -purine-2,6-dione.
$C_6H_6N_4O_2$ 166.14

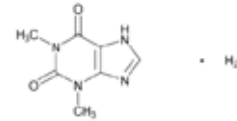
Theophylline related compound D
N-Methyl-5-(methylamino)-1H -imidazole-4-carboxamide.
$C_6H_{10}N_4O$ 154.17



Dimethyl uric acid
1,3-Dimethyl-7,9-dihydro-1H -purine-2,6,8(3H)-trione

Theobromine
3,7-Dihydro-3,7-dimethylpurine-2,6 (1H)-dione.

Theophylline



Theophylline related compound F
7-(2-Hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1H -purine-2,6-dione.
$C_9H_{12}N_4O_3$ 224.22

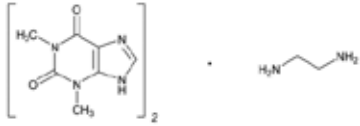
Caffeine

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

氨茶碱片
Aminophylline Tablets

方法来源：收载于USP39-NF34 1S

定义： Aminophylline Tablets contain an amount of aminophylline equivalent to NLT 93.0% and NMT 107.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	2

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

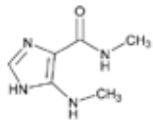
Name	相对保留时间	可接受标准 (%)
Theophylline related compound C	0.36	-
Theophylline related compound B	0.63	-
Theophylline related compound D	0.69	0.2
Dimethyl uric acid	0.76	-
Theobromine	0.82	-
Theophylline	1.0	-
Theophylline related compound F	1.09	-
Caffeine	1.20	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline related compound C
N-(6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) formamide.
$C_7H_{10}N_4O_3$ 198.18

Theophylline related compound B
3-Methyl-1H -purine-2,6-dione;
Also known as 3-Methyl-3,7-dihydro-1H -purine-2,6-dione.
$C_6H_6N_4O_2$ 166.14

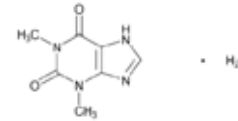
Theophylline related compound D
N-Methyl-5-(methylamino)-1H -imidazole-4-carboxamide.
$C_6H_{10}N_4O$ 154.17



Dimethyl uric acid
1,3-Dimethyl-7,9-dihydro-1H -purine-2,6,8(3H)-trione

Theobromine
3,7-Dihydro-3,7-dimethylpurine-2,6 (1H)-dione.

Theophylline



Theophylline related compound F
7-(2-Hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione.
$C_9H_{12}N_4O_3$ 224.22

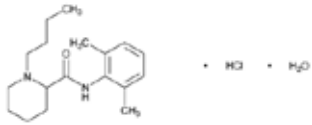
Caffeine

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸布比卡因
Bupivacaine Hydrochloride

方法来源：收载于USP39-NF34 1S

定义：



有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 µm

流动相： Solution A:10 mM乙酸铵水溶液(pH9.0)

Solution B:乙腈:甲醇:异丙醇 = 85:10:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
1.0	90	10
5.0	55	45
8.0	45	55
16.0	10	90
18.0	10	90
18.1	90	10
20.0	90	10

柱温: 45 ˚C　流速 (ml/min): 0.25　波长(nm): 230

杂质谱：

Name	相对保留时间	可接受标准 (%)
Bupivacaine related compound B	0.54	0.5
Ropivacaine related compound A	0.60	0.001
Bupivacaine	1.00	-
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

Bupivacaine Related Compound B
N-(2,6-Dimethylphenyl)piperidine-2-carboxamide.
$C_{14}H_{20}N_2O$　232.36

Ropivacaine Related Compound A
2,6-Dimethylaniline hydrochloride.
$C_8H_{11}N \cdot HCl$　157.64

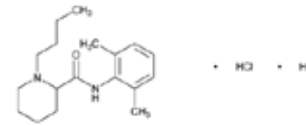
方法解析：采用UPLC方法代替原来的TLC方法，提高的分析效率及方法的准确性。

增加了Ropivacaine related compound A的限度控制方法(不超过0.001%)。

盐酸布比卡因注射液
Bupivacaine Hydrochloride Injection

方法来源：收载于USP39-NF34 1S

定义： Bupivacaine Hydrochloride Injection is a sterile solution of Bupivacaine Hydrochloride in Water for Injection. It contains NLT 93.0% and NMT 107.0% of the labeled amount of bupivacaine hydrochloride ($C_{18}H_{28}N_2O \cdot HCl$).



有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 µm

流动相： Solution A:10 mM乙酸铵水溶液(pH9.0)

Solution B:乙腈:甲醇:异丙醇 = 85:10:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
1.0	90	10
5.0	55	45
8.0	45	55
16.0	10	90
18.0	10	90
18.1	90	10
20.0	90	10

杂质谱： 柱温: 45 ˚C　流速 (ml/min): 0.25　波长(nm): 230

Name	相对保留时间	可接受标准 (%)
Bupivacaine related compound B	0.54	0.5
Ropivacaine related compound A	0.55	-
Bupivacaine	1.00	-
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

Bupivacaine Related Compound B
N-(2,6-Dimethylphenyl)piperidine-2-carboxamide.
$C_{14}H_{20}N_2O$　232.36

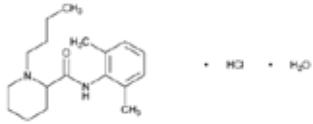
Bupivacaine Related Compound A
6-(Butylamino)-N-(2,6-dimethylphenyl)hexanamide.
$C_{18}H_{30}N_2O$　290.45

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸布比卡因葡萄糖注射液
Bupivacaine Hydrochloride in Dextrose Injection

方法来源：收载于USP39-NF34 1S

定义： Bupivacaine Hydrochloride in Dextrose Injection is a sterile solution of Bupivacaine Hydrochloride and Dextrose in Water for Injection. It contains NLT 93.0% and NMT 107.0% of the labeled amounts of bupivacaine hydrochloride ($C_{18}H_{28}N_2O \cdot HCl$) and dextrose ($C_6H_{12}O_6$). It contains no preservative.



有关物质：

色谱柱： L1, 2.0 mm x 10 cm; 1.9 μm

流动相： Solution A:10 mM乙酸铵水溶液(pH9.0)

Solution B:乙腈:甲醇:异丙醇 = 85:10:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
1.0	90	10
5.0	55	45
8.0	45	55
16.0	10	90
18.0	10	90
18.1	90	10
20.0	90	10

柱温: 45 ˚C　流速 (ml/min): 0.25　波长(nm): 230

杂质谱：

Name	相对保留时间	可接受标准 (%)
Bupivacaine related compound B	0.54	0.5
Ropivacaine related compound A	0.55	-
Bupivacaine	1.00	-
单个未知杂质	-	0.5
总杂质	-	2.0

杂质结构

Bupivacaine Related Compound B
N-(2,6-Dimethylphenyl)piperidine-2-carboxamide.
$C_{14}H_{20}N_2O$ 232.36

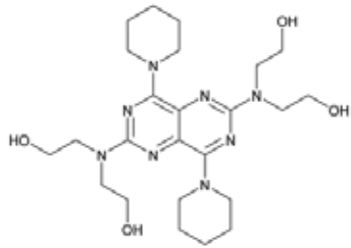
Bupivacaine Related Compound A
6-(Butylamino)-N-(2,6-dimethylphenyl)hexanamide.
$C_{18}H_{30}N_2O$ 290.45

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

双嘧达莫
Dipyridamole

方法来源：收载于USP39-NF34 1S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM甲酸铵水溶液(pH5.0)

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
2.0	80	20
17.0	5	95
19.0	5	95
21.0	80	20
25.0	80	20

柱温: 45 ˚C　流速 (ml/min): 0.25　波长(nm): 230

杂质谱：

Name	相对保留时间	可接受标准 (%)
Dipyridamole related compound B	0.6	0.1
Dipyridamole related compound F	0.7	0.1
Dipyridamole related compound D	0.9	0.1
Dipyridamole	-	-
Dipyridamole related compound E	1.2	0.1
Dipyridamole related compound C	1.5	0.1
Dipyridamole related compound A	1.9	0.1
单个未知杂质	-	0.10
总杂质	-	1.0

杂质结构

Dipyridamole Related Compound A
2,2¢-{[4,6,8-Tri(piperidin-1-yl) pyrimido[5,4-d]pyrimidin-2-yl] azanediyl}diethanol.
$C_{25}H_{40}N_8O_2$ 484.64

Dipyridamole Related Compound B
2,2′,2 ,2′ ′ ′,2′ ′ ′ ′,2′ ′ ′ ′ ′-{[8-(Piperidin-1-yl)pyrimido[5,4-d]pyrimidine-2,4,6-triyl]tris(azanetriyl)}hexaethanol.
$C_{23}H_{40}N_8O_6$ 524.61

Dipyridamole Related Compound C
2,2′-{[6-Chloro-4,8-di(piperidin-1-yl)pyrimido[5,4-d]pyrimidin-2-yl] azanediyl}diethanol.
$C_{20}H_{30}ClN_7O_2$ 435.95

Dipyridamole Related Compound D
2,2′-({6-[(2-Hydroxyethyl)amino]-4,8-di(piperidin-1-yl)pyrimido[5,4-d] pyrimidin-2-yl}azanediyl)diethanol.
$C_{22}H_{36}N_8O_3$ 460.57

Dipyridamole Related Compound E
2,2′,2 ,2′ ′ ′-{[6,8-Di(piperidin-1-yl) pyrimido[5,4-d]pyrimidine-2,4-diyl] bis(azanetriyl)}tetraethanol.
$C_{24}H_{40}N_8O_4$ 504.63

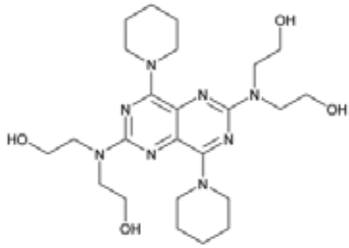
Dipyridamole Related Compound F
2,2′,2 ,2′ ′ ′-({4-[(2-Hydroxyethyl) amino]-8-(piperidin-1-yl) pyrimido[5,4-d]pyrimidine-2,6-diyl} bis(azanetriyl))tetraethanol.
$C_{21}H_{36}N_8O_5$ 480.56

方法解析：原HPLC等度方法改为UPLC梯度方法，大大提高了分析效率。
增加了6个特性杂质的限度控制。

双嘧达莫片
Dipyridamole Tablets

方法来源：收载于USP39-NF34 1S

结构式： Dipyridamole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of dipyridamole ($C_{24}H_{40}N_8O_4$).



有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM甲酸铵水溶液(pH5.0)

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
2.0	80	20
17.0	5	95
19.0	5	95
21.0	80	20
25.0	80	20

柱温: 45 ˚C　流速 (ml/min): 0.3　波长(nm): 295

杂质谱：

Name	相对保留时间	可接受标准 (%)
Dipyridamole related compound B	0.63	0.2
Dipyridamole related compound F	0.71	-
Dipyridamole related compound D	0.94	-
Dipyridamole	1.0	-
Dipyridamole related compound E	1.19	-
Dipyridamole related compound C	1.54	0.2
Dipyridamole related compound A	1.93	0.2
单个未知杂质	-	0.2
总杂质	-	1.0

杂质结构

Dipyridamole Related Compound A
2,2¢-{[4,6,8-Tri(piperidin-1-yl) pyrimido[5,4-d]pyrimidin-2-yl] azanediyl}diethanol.
$C_{25}H_{40}N_8O_2$ 484.64

Dipyridamole Related Compound B
2,2′,2 ,2′ ′ ′,2′ ′ ′ ′,2′ ′ ′ ′ ′-{[8-(Piperidin-1-yl)pyrimido[5,4-d]pyrimidine-2,4,6-triyl]tris(azanetriyl)}hexaethanol.
$C_{23}H_{40}N_8O_6$ 524.61

Dipyridamole Related Compound C
2,2′-{[6-Chloro-4,8-di(piperidin-1-yl)pyrimido[5,4-d]pyrimidin-2-yl] azanediyl}diethanol.
$C_{20}H_{30}ClN_7O_2$ 435.95

Dipyridamole Related Compound D
2,2′-({6-[(2-Hydroxyethyl)amino]-4,8-di(piperidin-1-yl)pyrimido[5,4-d] pyrimidin-2-yl}azanediyl)diethanol.
$C_{22}H_{36}N_8O_3$ 460.57

Dipyridamole Related Compound E
2,2′,2 ,2′ ′ ′-{[6,8-Di(piperidin-1-yl) pyrimido[5,4-d]pyrimidine-2,4-diyl] bis(azanetriyl)}tetraethanol.
$C_{24}H_{40}N_8O_4$ 504.63

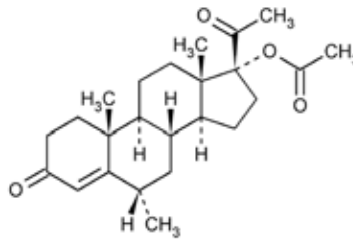
Dipyridamole Related Compound F
2,2′,2 ,2′ ′ ′-({4-[(2-Hydroxyethyl) amino]-8-(piperidin-1-yl) pyrimido[5,4-d]pyrimidine-2,6-diyl} bis(azanetriyl))tetraethanol.
$C_{21}H_{36}N_8O_5$ 480.56

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

醋酸甲羟孕酮注射液
Medroxyprogesterone Acetate Injectable Suspension

方法来源：收载于USP39-NF34 1S

定义： Medroxyprogesterone Acetate Injectable Suspension is a sterile suspension of Medroxyprogesterone Acetate in a suitable aqueous medium. It contains NLT 90.0% and NMT 110.0% of the labeled amount of medroxyprogesterone acetate ($C_{24}H_{34}O_4$).



有关物质：

色谱柱： L1, 3.0 mm x 15 cm; 1.8 µm

流动相： Solution A:乙腈:四氢呋喃:水=150:50:800

Solution B:乙腈:水=70:30

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
5.0	90	10
18.0	45	55
18.01	90	10
22.0	90	10

柱温: 55 ˚C　流速 (ml/min): 0.7　波长(nm): 242

杂质谱：

Name	相对保留时间	可接受标准 (%)
6 β -Hydroxymedroxyprogesterone acetate	0.57	1.0
Homomedroxyprogesterone 13a-epimer	0.80	1.0
Medroxyprogesterone acetate related compound B	0.92	1.0
Homomedroxyprogesterone acetate	0.95	1.0
Megestrol acetate	0.96	1.0
6-Epimedroxyprogesterone acetate	0.98	1.0
Hydroxyprogesterone acetate 6-methylene analog	0.99	1.0
Medroxyprogesterone acetate	1.0	-
Medroxyprogesterone acetate related compound A	1.16	0.5
单个未知杂质	-	1.0
总杂质	-	1.5

杂质结构

Medroxyprogesterone Acetate Related Compound A
6 α -Methyl-3,20-dioxopregnan-17-yl acetate.
$C_{24}H_{36}O_4$ 388.54

Medroxyprogesterone Acetate Related Compound B
17-Hydroxy-6 α -methylpregn-4-ene-3,20-dione.
$C_{22}H_{32}O_3$ 344.49

6 β -ydroxymedroxyprogesterone acetate
6 β -Hydroxy-6 α -methyl-3,20-dioxopregn-4-ene-17-yl acetate

Homomedroxyprogesterone 13a-epimer
2,2′-({6 α -[(2-6 ,13a α -Dimethyl-13(17) a-homoandrost-4-en-3,17-dione

Homomedroxyprogesterone acetate
6 α ,13a β -Dimethyl-3,17-dioxo-13(17) a-homoandrost-4-en-13a-yl acetate.

6-Epimedroxyprogesterone acetate
6 β -Methyl-3,20-dioxopregn-4-ene-17-yl acetate

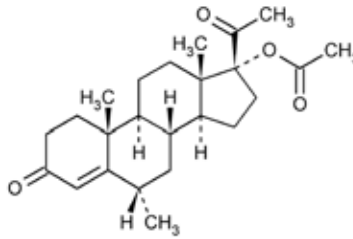
Hydroxyprogesterone acetate 6-methylene analog
6-Methylene-3,20-dioxopregn-4-ene-17-yl acetate.

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

醋酸甲羟孕酮片
Medroxyprogesterone Acetate Tablets

方法来源：收载于USP39-NF34 1S

定义： Medroxyprogesterone Acetate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of medroxyprogesterone acetate ($C_{24}H_{34}O_4$)



有关物质：

色谱柱： L1, 3.0 mm x 15 cm; 1.8 µm

流动相： Solution A:乙腈:四氢呋喃:水=150:50:800

Solution B:乙腈:水=70:30

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
5.0	90	10
18.0	45	55
18.01	90	10
22.0	90	10

柱温: 55 ˚C　流速 (ml/min): 0.7　波长(nm): 242

杂质谱：

Name	相对保留时间	可接受标准 (%)
6 β -Hydroxymedroxyprogesterone acetate	0.57	1.0
Homomedroxyprogesterone 13a-epimer	0.80	1.0
Medroxyprogesterone acetate related compound B	0.92	1.0
Homomedroxyprogesterone acetate	0.95	1.0
Megestrol acetate	0.96	1.0
6-Epimedroxyprogesterone acetate	0.98	1.0
Hydroxyprogesterone acetate 6-methylene analog	0.99	1.0
Medroxyprogesterone acetate	1.0	-
Medroxyprogesterone acetate related compound A	1.16	0.5
单个未知杂质	-	1.0
总杂质	-	1.5

杂质结构

Medroxyprogesterone Acetate Related Compound A
6 α -Methyl-3,20-dioxopregnan-17-yl acetate.
$C_{24}H_{36}O_4$ 388.54

Medroxyprogesterone Acetate Related Compound B
17-Hydroxy-6 α -methylpregn-4-ene-3,20-dione.
$C_{22}H_{32}O_3$ 344.49

6 β -ydroxymedroxyprogesterone acetate
6 β -Hydroxy-6 α -methyl-3,20-dioxopregn-4-ene-17-yl acetate

Homomedroxyprogesterone 13a-epimer
2,2′-({6 α -[(2-6 ,13a α -Dimethyl-13(17) a-homoandrost-4-en-3,17-dione

Homomedroxyprogesterone acetate
6 α ,13a β -Dimethyl-3,17-dioxo-13(17) a-homoandrost-4-en-13a-yl acetate.

6-Epimedroxyprogesterone acetate
6 β -Methyl-3,20-dioxopregn-4-ene-17-yl acetate

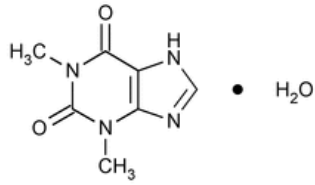
Hydroxyprogesterone acetate 6-methylene analog
6-Methylene-3,20-dioxopregn-4-ene-17-yl acetate.

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

茶碱
Theophylline

方法来源：收载于USP39-NF34 1S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7	50	50
7.3	10	90
8.3	10	90
8.31	98	2
12	98	2

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Theophylline related compound C	0.36	0.10
Theophylline related compound B	0.63	0.10
Theophylline related compound D	0.69	0.10
Theophylline	1.0	-
Theophylline related compound F	1.09	-
Caffeine	1.20	0.10
单个未知杂质	-	0.10
总杂质	-	0.5

杂质结构

Theophylline Related Compound B
3-Methyl-1H -purine-2,6-dione.
$C_6H_6N_4O_2$ 166.14

Theophylline Related Compound C
N-(6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) formamide.
$C_7H_{10}N_4O_3$ 198.18

Theophylline Related Compound D
Theophyllidine;
N-Methyl-5-(methylamino)-1H -imidazole-4-carboxamide.
$C_6H_{10}N_4O$ 154.17

Theophylline Related Compound F
Etophylline;
7-(2-Hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1H -purine-2,6-dione.
$C_9H_{12}N_4O_3$ 224.22

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

茶碱口服液
Theophylline Oral Solution

方法来源：收载于USP39-NF34 2S

定义： Theophylline Oral Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of theophylline ($C_7H_8N_4O_2$).

有关物质：

色谱柱： L7, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_8)

流动相： Solution A:10 mM乙酸铵水溶液 (pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	93.5	6.5
2.5	93.5	6.5
5.0	10	90
5.1	93.5	6.5
7.0	93.5	6.5

柱温: 40±2 ˚C　流速 (ml/min): 0.4　波长(nm): 270

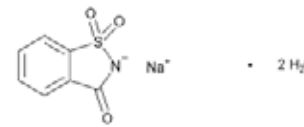
杂质谱：

Name	相对保留时间	可接受标准 (%)
Theophylline related compound D	0.45	0.2
Saccharin	0.50	-
Theophylline	1.0	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline Related Compound D
Theophyllidine;
N-Methyl-5-(methylamino)-1H
-imidazole-4-carboxamide.
$C_6H_{10}N_4O$　154.17

Saccharin Sodium



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

茶碱缓释片
Theophylline Extended-Release Capsules

方法来源：收载于USP40-NF35 1S

定义： Theophylline Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).

有关物质：

色谱柱： L7, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_8)

流动相： Solution A:10 mM乙酸铵水溶液 (pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	93.5	6.5
2.5	93.5	6.5
5.0	10	90
5.1	93.5	6.5
7.0	93.5	6.5

柱温: 40±2 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Theophylline related compound D	0.45	0.2
Theophylline	1.0	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline Related Compound D
Theophyllidine;
N-Methyl-5-(methylamino)-1H
-imidazole-4-carboxamide.
$C_6H_{10}N_4O$　154.17

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

茶碱葡萄糖注射液
Theophylline in Dextrose Injection

方法来源：收载于USP40-NF35 1S

定义： Theophylline in Dextrose Injection is a sterile solution of Theophylline and Dextrose in Water for Injection. It contains NLT 93.0% and NMT 107.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$) and NLT 95.0% and NMT 105.0% of the labeled amount of dextrose ($C_6H_{12}O_6 \cdot H_2O$).

有关物质：

色谱柱： L7, 2.1 mm x 10 cm; 1.7 μm(ACQUITY UPLC BEH C_8)

流动相： Solution A:10 mM乙酸铵水溶液(pH4.8)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	93.5	6.5
2.5	93.5	6.5
5.0	10	90
5.1	93.5	6.5
7.0	93.5	6.5

柱温: 40 ˚C　流速 (ml/min): 0.4　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Theophylline related compound D	0.44	0.2
5-HMF	0.47	-
Theophylline	1.0	-
单个未知杂质	-	0.2
总杂质	-	0.5

杂质结构

Theophylline Related Compound D
Theophyllidine;
N-Methyl-5-(methylamino)-
1H -imidazole-4-carboxamide
hydrochloride monohydrate.
$C_6H_{10}N_4O \cdot HCl \cdot H_2O$　208.65

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

北五味子干浸膏
Northern Schisandra Fruit Dry Extract

方法来源：收载于USP39-NF34 2S

定义： Northern Schisandra Fruit Dry Extract consists of dried ripe fruits of Schisandra chinensis (Turcz.) Baill. (Fam. Schisandraceae) collected in the fall, by extraction with hydroalcoholic mixtures. It contains NLT 90.0% and NMT 110.0% of the labeled amount of schisandrin on the dried basis; NLT 90.0% and NMT 110.0% of the labeled amount of total lignans, calculated as the sum of schisandrin, schisandrol B, deoxyschisandrin (schisandrin A), and -schisandrin (schisandrin B).

有关物质：

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:水

Solution B:乙腈:甲醇=1:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	47	53
30	20	80

柱温: 35 ˚C　流速 (ml/min): 0.3　波长(nm): 251

杂质谱：

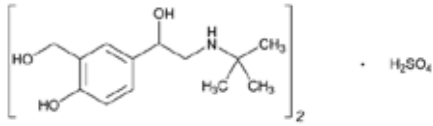
Name	相对保留时间	可接受标准 (%)
Schisandrin	1.00	1.00
Schisandrol B	1.29	1.21
Schisandrin A	2.90	1.00
Schisandrin B	3.31	1.23

方法解析：新增各论，采用UPLC进行快速高效的分析。

硫酸沙丁胺醇
Albuterol Sulfate

方法来源：收载于USP39-NF34 2S

结构式：



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
1	95	5
9	47	53
9.1	95	5
11	95	5

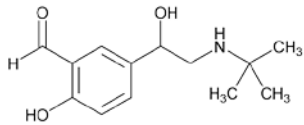
柱温: 30 ˚C　流速 (ml/min): 0.37　波长(nm): 231　进样温度: 4 ˚C

杂质谱：

Name	相对保留时间	响应因子	可接受标准 (%)
Albuterol	1.00	-	-
Levalbuterol related compound D	1.40	2.5	0.1
Albuterol related compound D	1.45	0.68	0.1
Levalbuterol related compound H	1.50	1.0	0.10
Albuterol related compound B	1.53	0.58	0.1
Albuterol dealkyl analog	1.59	0.94	0.20
Levalbuterol related compound C	1.77	0.78	0.15
Albuterol related compound C	1.84	0.57	0.1
Albuterol related compound A	1.99	0.68	0.20
Levalbuterol related compound E	2.04	0.74	0.2
Albuterol related compound E	2.17	0.67	0.3
N-Benzyl albuterone	2.73	0.64	0.10
N-Benzyl albuterol	2.80	0.79	0.05
Levalbuterol related compound F	3.19	1.1	0.10
单个未知杂质	-	1.0	0.10
总杂质	-	-	1.0

杂质结构

Levalbuterol related compound D
5-[2-(tert-Butylamino)-1-hydroxyethyl]-2-hydroxybenzaldehyde; also known as 5-[(1R S)-2-[(1,1-dimethylethyl) amino]-1-hydroxyethyl]-2-hydroxybenzaldehyde



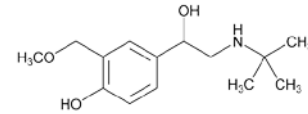
Albuterol related compound D
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-chloro-6-(hydroxymethyl)phenol; also known as (1R S)-2-[(1,1-dimethylethyl) amino]-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl]ethanol.

Levalbuterol related compound H
4-[2-(tert-Butylamino)-1-methoxyethyl]-2-(hydroxymethyl) phenol.
$C_{14}H_{23}NO_3$ 253.34

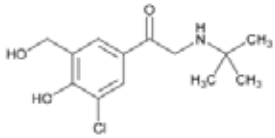
Albuterol related compound B
2-(tert-Butylamino)-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone.
$C_{13}H_{19}NO_3$ 237.29

Albuterol dealkyl analog
4-[2-(tert-Butylamino)-1-hydroxyethyl]phenol; also known as (1R S)-2-[(1,1-dimethylethyl)amino]-1-(4-hydroxyphenyl)-ethanol

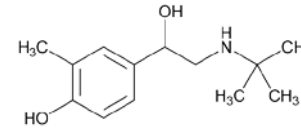
Levalbuterol related compound C
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(methoxymethyl) phenol;
Also known as α -[{(1,1-Dimethylethyl) amino}methyl]-4-hydroxy-3-(methoxymethyl)-benzenemethanol.
$C_{14}H_{23}NO_3$ 253.34



Albuterol related compound C
2-(tert-Butylamino)-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl] ethanone.
$C_{13}H_{18}ClNO_3$ 271.74

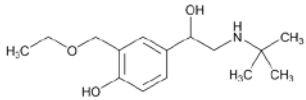


Albuterol related compound A
4-{2-[(1,1-Dimethylethyl)amino]-1-hydroxyethyl}-2-methylphenol sulfate.
$(C_{13}H_{21}NO_2)_2 \cdot H_2SO_4$ 544.70

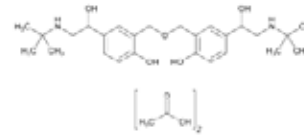


杂质结构

Levalbuterol related compound E
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(ethoxymethyl) phenol;
Also known as α -[{(1,1-Dimethylethyl) amino}methyl]-3-(ethoxymethyl)-4-hydroxy-benzenemethanol.
$C_{15}H_{25}NO_3$ 267.36



Albuterol related compound E
2,2′-Oxybis(methylene)bis{4-[2-(tert-butylamino)-1-hydroxyethyl]phenol}; also known as 1,1′[oxybis[methylen(4-hydroxy-1,3phenylene)]]bis[2-[(1,1-dimethylethyl)amino]ethanol].



N-Benzyl albuterone
2-[Benzyl(tert-butyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl] ethanone; also known as 2-[benzyl(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone.

N-Benzyl albuterol
4-{2-[Benzyl(tert-butyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl) phenol; also known as (1R S)-2-[benzyl(1,1-dimetheylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl] ethanol.

Levalbuterol related compound F
1-[4-(Benzyloxy)-3-(hydroxymethyl) phenyl]-2-(tert-butylamino)ethanol; also known as α -[{(1,1-dimethylethyl) amino}methyl]-4-(phenylmethoxy)-1,3-benzenedimethanol and (1R S)-2-[(1,1-dimethylethyl)amino]-1-[4-(benzyloxy)-3-(hydroxymethyl) phenyl]ethanol.

方法解析：原TLC方法改为UPLC方法，提高了检测效率与方法的准确性。
增加了13个特性杂质的限度控制要求。

沙丁胺醇片
Albuterol Tablets

方法来源：收载于USP39-NF34 2S

结构式： Albuterol Tablets contain an amount of albuterol sulfate [$(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$] equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of albuterol ($C_{13}H_{21}NO_3$).

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:10 mM乙酸铵水溶液(pH5.5)

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
1	95	5
9	47	53
9.1	95	5
11	95	5

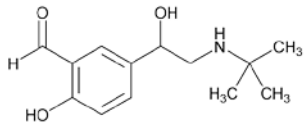
柱温: 30 ˚C　流速 (ml/min): 0.37　波长(nm): 231　进样温度: 4 ˚C

杂质谱：

Name	相对保留时间	可接受标准 (%)
Albuterol	1.00	-
Levalbuterol related compound D	1.40	0.1
Albuterol related compound D	1.45	-
Levalbuterol related compound H	1.50	-
Albuterol related compound B	1.53	-
Levalbuterol related compound C	1.82	0.15
Albuterol related compound C	1.84	-
Albuterol related compound A	1.99	-
Levalbuterol related compound E	2.04	-
Albuterol related compound E	2.25	0.3
Levalbuterol related compound F	3.19	-
单个未知杂质	-	0.2
总杂质	-	3.5

杂质结构

Levalbuterol related compound D
5-[2-(tert-Butylamino)-1-hydroxyethyl]-2-hydroxybenzaldehyde; also known as 5-[(1R S)-2-[(1,1-dimethylethyl) amino]-1-hydroxyethyl]-2-hydroxybenzaldehyde



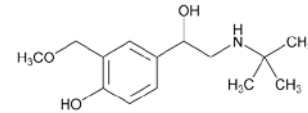
Albuterol related compound D
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-chloro-6-(hydroxymethyl)phenol; also known as (1R S)-2-[(1,1-dimethylethyl) amino]-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl]ethanol.

Levalbuterol related compound H
4-[2-(tert-Butylamino)-1-methoxyethyl]-2-(hydroxymethyl) phenol.
$C_{14}H_{23}NO_3$ 253.34

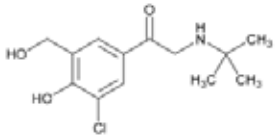
Albuterol related compound B
2-(tert-Butylamino)-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone.
$C_{13}H_{19}NO_3$ 237.29

Levalbuterol related compound F
1-[4-(Benzyloxy)-3-(hydroxymethyl) phenyl]-2-(tert-butylamino)ethanol; also known as -[{(1,1-dimethylethyl) amino}methyl]-4-(phenylmethoxy)-1,3-benzenedimethanol and (1R S)-2-[(1,1-dimethylethyl)amino]-1-[4-(benzyloxy)-3-(hydroxymethyl) phenyl]ethanol.

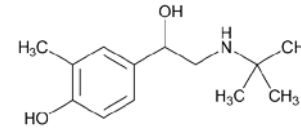
Levalbuterol related compound C
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(methoxymethyl) phenol;
Also known as α -[{(1,1-Dimethylethyl) amino}methyl]-4-hydroxy-3-(methoxymethyl)-benzenemethanol.
$C_{14}H_{23}NO_3$ 253.34



Albuterol related compound C
2-(tert-Butylamino)-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl] ethanone.
$C_{13}H_{18}ClNO_3$ 271.74

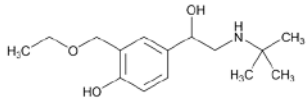


Albuterol related compound A
4-{2-[(1,1-Dimethylethyl)amino]-1-hydroxyethyl}-2-methylphenol sulfate.
$(C_{13}H_{21}NO_2)_2 \cdot H_2SO_4$ 544.70

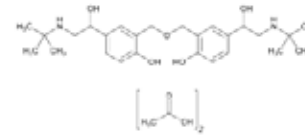


杂质结构

Levalbuterol related compound E
4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(ethoxymethyl) phenol;
Also known as α -[{(1,1-Dimethylethyl) amino}methyl]-3-(ethoxymethyl)-4-hydroxy-benzenemethanol.
$C_{15}H_{25}NO_3$ 267.36



Albuterol related compound E
2,2′-Oxybis(methylene)bis{4-[2-(tert-butylamino)-1-hydroxyethyl]phenol};
also known as 1,1′[oxybis[methylen(4-hydroxy-1,3phenylene)]]bis[2-[(1,1-dimethylethyl)amino]ethanol].

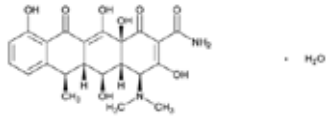


方法解析：原TLC方法改为UPLC方法，提高了检测效率与方法的准确性。
增加了3个特性杂质的限度控制要求。

多西环素 / 多西霉素 / Doxycycline

方法来源：收载于USP40-NF35 1S

结构式：



有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

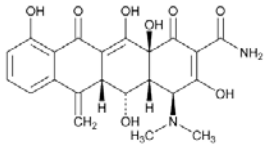
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.53	2
4-Epidoxycycline	0.66	0.3
Doxycycline related compound A (6-epidoxycycline)	0.74	2
Doxycycline	1.0	-
单个未知杂质	-	0.2

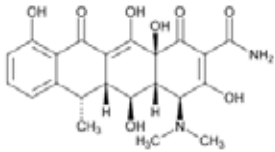
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43



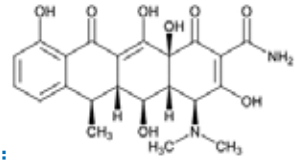
方法解析：原HPLC等度方法改为UPLC梯度方法，大大提高了分析效率。

4-Epidoxycycline的限度由原方法的0.5%收严至0.3%。

多西霉素胶囊
Doxycycline Capsules

方法来源：收载于USP40-NF35 1S

定义： Doxycycline Capsules contain NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).



· H_2O

有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

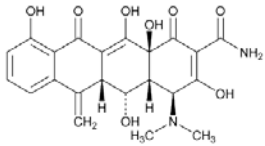
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.60	-
4-Epidoxycycline	0.70	0.35
Doxycycline related compound A (6-epidoxycycline)	0.81	-
Doxycycline	1.0	-
单个未知杂质	-	0.2
总杂质	-	1.0

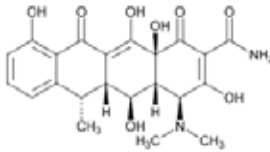
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

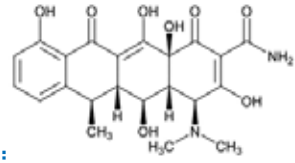


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

多西霉素片
Doxycycline Tablets

方法来源：收载于USP40-NF35 1S

定义： Doxycycline Tablets contain NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).



· H_2O

有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

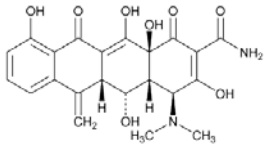
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.57	-
4-Epidoxycycline	0.69	1.5
Doxycycline related compound A (6-epidoxycycline)	0.80	-
Doxycycline	1.0	-
单个未知杂质	-	0.3
总杂质	-	2.5

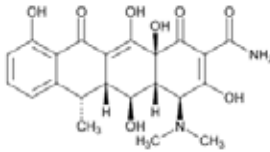
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

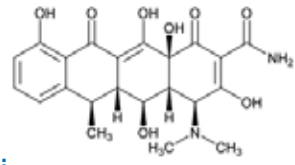


方法解析：原HPLC等度方法改为UPLC梯度方法，大大提高了分析效率。

口服多西环素
Doxycycline for Oral Suspension

方法来源：收载于USP39-NF34 2S

定义： Doxycycline for Oral Suspension contains the equivalent of NLT 90.0% and NMT 125.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) when constituted as directed. It contains one or more suitable buffers, colors, diluents, flavors, and preservatives



· H_2O

有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

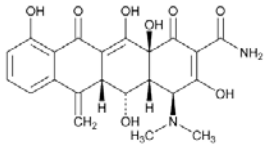
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.64	-
4-Epidoxycycline	0.79	1.5
Doxycycline related compound A (6-epidoxycycline)	0.88	-
Doxycycline	1.0	-
单个未知杂质	-	0.5
总杂质	-	2.5

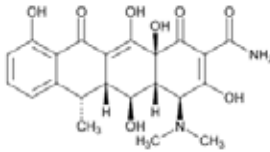
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

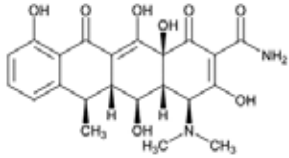


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

多西环素注射用粉末
Doxycycline for Injection

方法来源：收载于USP40-NF35 1S

定义： Doxycycline for Injection contains an amount of Doxycycline Hyclate equivalent to NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).



· H_2O

有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

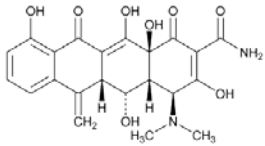
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.64	-
4-Epidoxycycline	0.79	2.2
Doxycycline related compound A (6-epidoxycycline)	0.88	-
Doxycycline	1.0	-
单个未知杂质	-	0.5
总杂质	-	5.5

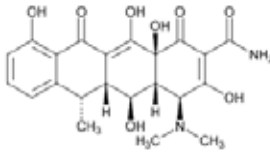
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

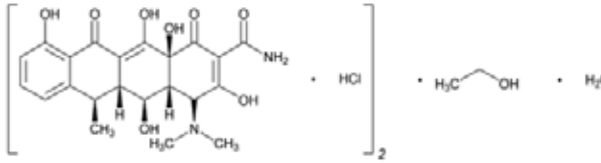


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸多西环素
Doxycycline Hyclate

方法来源：收载于USP40-NF35 1S

结构式：



有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

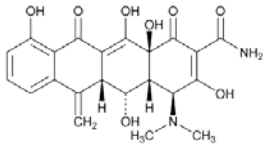
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.53	2
4-Epidoxycycline	0.66	0.5
Doxycycline related compound A (6-epidoxycycline)	0.74	2
Doxycycline	1.0	-
单个未知杂质	-	0.5

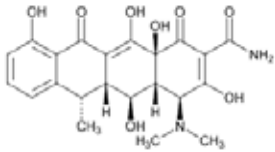
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

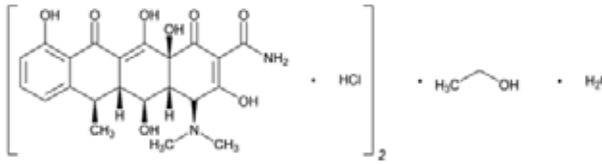


方法解析：原HPLC等度方法改为UPLC梯度方法，大大提高了分析效率。

盐酸多西环素胶囊
Doxycycline Hyclate Capsules

方法来源：收载于USP39-NF34 2S

定义： Doxycycline Hyclate Capsules contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).



有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

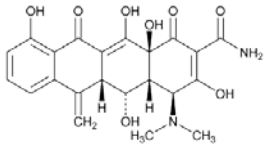
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.64	-
4-Epidoxycycline	0.79	0.5
Doxycycline related compound A (6-epidoxycycline)	0.88	-
Doxycycline	1.0	-
单个未知杂质	-	0.5
总杂质	-	2.0

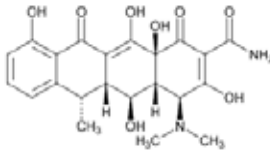
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

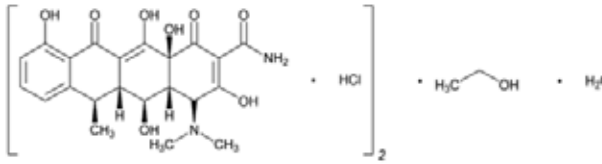


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

盐酸多西环素片
Doxycycline Hyclate Tablets

方法来源：收载于USP39-NF34 2S

定义： Doxycycline Hyclate Tablets contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).



有关物质：

色谱柱： L7, 2.1 mm x 5 cm; 1.7 µm (ACQUITY BEH C_8)

流动相： Solution A:3.1 g磷酸二氢钾, 0.5 g乙二胺四乙酸二钠，0.5 ml三乙胺加水至1000 ml，用1N盐酸溶液调至 pH=8.5±0.1

Solution B:甲醇

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

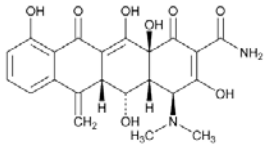
柱温: 60 ˚C　流速 (ml/min): 0.6　波长(nm): 270

杂质谱：

Name	相对保留时间	可接受标准 (%)
Methacycline	0.64	-
4-Epidoxycycline	0.79	0.5
Doxycycline related compound A (6-epidoxycycline)	0.88	-
Doxycycline	1.0	-
单个未知杂质	-	0.5
总杂质	-	2.0

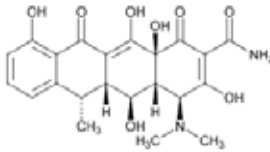
杂质结构

Methacycline
(4S ,4aR ,5S ,5aR ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide.



4-Epidoxycycline
(4R ,4aR ,5S ,5aR ,6R ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. Main degradation product.

Doxycycline related compound A (6-epidoxycycline)
(4S ,4aR ,5S ,5aR ,6S ,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide.
$C_{22}H_{24}N_2O_8$ 444.43

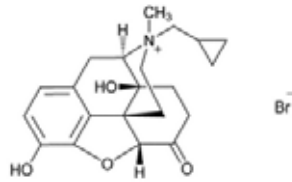


方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

溴甲纳曲酮
Methylnaltrexone Bromide

方法来源：收载于USP39-NF34 2S

定义：



$C_{21}H_{26}BrNO_4$ 436.34

Morphinanium, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-17-methyl-6-oxo-, bromide, (5α)-;

(17RS)-17-(Cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium bromide[73232-52-7].

有关物质：

色谱柱： L1, 2.1 mm x 5 cm; 1.8 µm (ACQUITY HSS T3)

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:0.1%三氟乙酸甲醇溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
1	90	10
7	75	25
13.9	30	70
14	90	10

柱温: 50 ˚C　流速 (ml/min): 0.3　波长(nm): 280　进样温度: 5 ˚C

杂质谱：

Name	相对保留时间	响应因子	可接受标准 (%)
S-Methylnaltrexone	0.92	1.0	0.15
Methylnaltrexone	1.0	-	-
N-Butenyl oxymorphone	1.26	1.0	0.15
Naltrexone	1.31	1.0	0.10
2,2′-Bismethylnaltrexone	1.63	1.6	0.15
O-Methyl methylnaltrexone	1.82	1.0	0.15
单个未知杂质	-	1.0	0.15
总杂质	-	-	1.0

杂质结构

S-Methylnaltrexone
(17S)-17-(Cyclopropylmethyl)-4,5 α -epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium bromide

N-Butenyl oxymorphone
(17RS)-17-(But-3-en-1-yl)-4,5 α -epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium bromide.

Naltrexone
17-(Cyclopropylmethyl)-4,5 α -epoxy-3,14-dihydroxymorphinan-6-one

2,2′-Bismethylnaltrexone
2,2′-Bi[(17RS)-17-(Cyclopropylmethyl)-4,5 α -epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium] dibromide

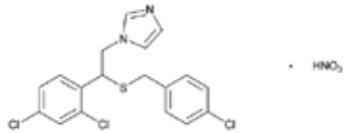
O-Methyl methylnaltrexone
(17RS)-17-(Cyclopropylmethyl)-4,5 α -epoxy-14-hydroxy-17-methyl-3-methoxy-6-oxomorphinanium bromide

方法解析：新增各论，采用UPLC进行快速高效的分析。

硝酸硫康唑
Sulconazole Nitrate

方法来源：收载于USP39-NF34 2S

结构式：



$C_{18}H_{15}Cl_3N_2S \cdot HNO_3$ 460.76

1H -Imidazole, 1-[2-[[(4-chlorophenyl)methyl]thio]-2-(2,4-dichlorophenyl)ethyl]-, mononitrate, (±);

(±)-1-[2,4-Dichloro- β -[(p-chlorobenzyl)thio]phenethyl]imidazole mononitrate [61318-91-0].

有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY BEH C_{18})

流动相： Solution A:0.1%三氟乙酸水溶液

Solution B:0.1%三氟乙酸甲醇溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	60	40
8.0	10	90
8.1	60	40
10.0	60	40

流速 (ml/min): 0.5 波长(nm): 230

杂质谱：

Name	相对保留时间	可接受标准 (%)
Sulconazole related compound A	0.61	0.1
Sulconazole nitrate	1.0	-
单个未知杂质	-	0.10
总杂质	-	1.0

杂质结构

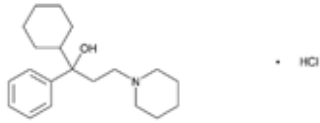
Sulconazole related compound A
1-[2-(4-Chlorobenzyl)sulfinyl-2-(2,4-dichlorophenyl)ethyl]-1H -imidazole.
$C_{18}H_{15}Cl_3N_2OS$ 413.74

方法解析：原TLC方法改为UPLC方法，提高了检测效率与方法的准确性。

盐酸苯海索片
Trihexyphenidyl Hydrochloride Tablets

方法来源：收载于USP39-NF34 2S

结构式： Trihexyphenidyl Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO \cdot HCl$).



有关物质：

色谱柱： L1, 2.1 mm x 10 cm; 2.6 µm

流动相： Solution A:1.4 g磷酸二氢钾加水至1000 ml，用磷酸调至 pH=4.0

Solution B:0.5 ml磷酸加入1000 ml乙腈中

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	95	5
20	60	40
22	60	40
22.1	95	5
24	95	5

柱温: 30 ˚C　流速 (ml/min): 0.3　波长(nm): 210

杂质谱：

Name	相对保留时间	可接受标准 (%)
Trihexyphenidyl related compound A	0.4	-
Trihexyphenidyl	1.0	-
单个未知杂质	-	1
总杂质	-	2

杂质结构

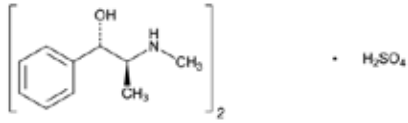
Trihexyphenidyl related compound A
1-Phenyl-3-(piperidin-1-yl)propan-1-one hydrochloride.
$C_{14}H_{19}NO \cdot HCl$　253.77

方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

伪麻黄碱硫酸盐
Pseudoephedrine Sulfate

方法来源：收载于USP40-NF35

结构式：



$(C_{10}H_{15}NO)_2 \cdot H_2SO_4$ 428.54

Benzenemethanol, α -[1-(methylamino)ethyl]-, [S-(R*,R*)]-, sulfate (2:1) (salt);

(+)-Pseudoephedrine sulfate (2:1) (salt) [7460-12-0].

有关物质：

色谱柱： L11, 2.1 mm x 10 cm; 1.9 μm

流动相： Solution A:0.4%三乙胺水溶液，加磷酸调至 pH4.0

流动相:solution A:乙腈=99:1

等度条件：流速 (ml/min): 0.4 波长(nm): 210

杂质谱：

Name	相对保留时间	可接受标准 (%)
Ephedrine	0.8	0.2
Pseudoephedrine	1.0	-
单个未知杂质	-	0.10
总杂质	-	0.3

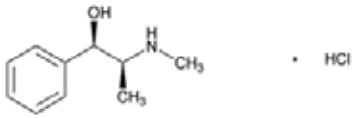
杂质结构

Ephedrine Hydrochloride

$C_{10}H_{15}NO \cdot HCl$ 201.69

Benzenemethanol, -[1-(methylamino) ethyl]-, hydrochloride, [R-(R*,S*)]-;

(-)-Ephedrine hydrochloride



方法解析：原TLC方法改为UPLC方法，提高了检测效率与方法的准确性。

磺胺多辛乙胺嘧啶片
Sulfadoxine and Pyrimethamine Tablets

方法来源：收载于USP38, P5309

结构式： Sulfadoxine and Pyrimethamine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of sulfadoxine ($C_{12}H_{14}N_4O_4S$) and NLT 90.0% and NMT 110.0% of the labeled amount of pyrimethamine ($C_{12}H_{13}ClN_4$).

有关物质：

色谱柱： L11, 2.0 mm x 10 cm; 3 µm

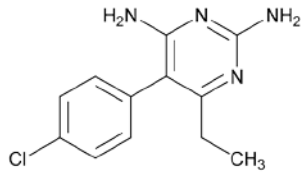
流动相： Solution A:Solution A:1 ml磷酸加水1000 ml

流动相:solution A:乙腈=83:17

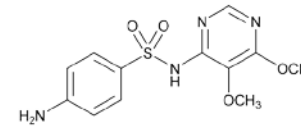
等度条件：流速 (ml/min): 0.3　波长(nm): 230

杂质结构

Pyrimethamine



Sulfadoxine



方法解析：采用UPLC方法进行快速高效的含量分析，提高了检测效率。

三七干浸膏胶囊
Tienchi Ginseng Root and Rhizome Dry Extract Capsules

方法来源：收载于USP40-NF35

结构式： Tienchi Ginseng Root and Rhizome Dry Extract Capsules contain Tienchi Ginseng Root and Rhizome Dry Extract. They contain NLT 90.0% and NMT 110.0% of the labeled amount of ginsenosides calculated as the sum of notoginsenoside R1 ($C_{47}H_{80}O_{18}$), ginsenoside Rg1 ($C_{42}H_{72}O_{14}$), ginsenoside Re ($C_{48}H_{82}O_{18}$), ginsenoside Rb1 ($C_{54}H_{92}O_{23}$), and ginsenoside Rd ($C_{48}H_{82}O_{18}$).

人参皂苷含量：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm

流动相： Solution A:0.03%磷酸水溶液

Solution B:乙腈

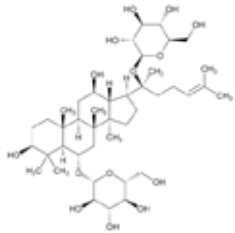
梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	83	17
2.4	80	20
3.5	70	30
4.2	69	31
5.0	58	42
5.1	0	100
6.0	0	100
6.1	83	17
7.5	83	17

柱温: 30 ˚C　流速 (ml/min): 0.8　波长(nm): 203

杂质结构

Ginsenoside Rg1



方法解析：新增各论，采用UPLC进行快速高效的分析。

三七干浸膏片
Tienchi Ginseng Root and Rhizome Dry Extract Tablets

方法来源：收载于USP40-NF35

结构式： Tienchi Ginseng Root and Rhizome Dry Extract Tablets contain Tienchi Ginseng Root and Rhizome Dry Extract. They contain NLT 90.0% and NMT 110.0% of the labeled amount of ginsenosides calculated as the sum of notoginsenoside R1 ($C_{47}H_{80}O_{18}$), ginsenoside Rg1 ($C_{42}H_{72}O_{14}$), ginsenoside Re ($C_{48}H_{82}O_{18}$), ginsenoside Rb1 ($C_{54}H_{92}O_{23}$), and ginsenoside Rd ($C_{48}H_{82}O_{18}$).

人参皂苷含量：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm

流动相： Solution A:0.03%磷酸水溶液

Solution B:乙腈

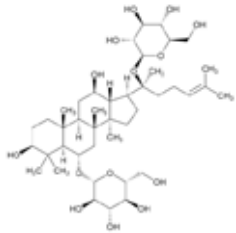
梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	83	17
2.4	80	20
3.5	70	30
4.2	69	31
5.0	58	42
5.1	0	100
6.0	0	100
6.1	83	17
7.5	83	17

柱温: 30 ˚C　流速 (ml/min): 0.8　波长(nm): 203

杂质结构

Ginsenoside Rg1



方法解析：新增各论，采用UPLC进行快速高效的分析。

三七粉片
Tienchi Ginseng Root and Rhizome Powder Tablets

方法来源：收载于USP40-NF35

结构式： Tienchi Ginseng Root and Rhizome Powder Tablets contain Tienchi Ginseng Root and Rhizome Powder. They contain NLT 5.0% of ginsenosides calculated as the sum of notoginsenoside R1 ($C_{47}H_{80}O_{18}$), ginsenoside Rg1 ($C_{42}H_{72}O_{14}$), ginsenoside Re ($C_{48}H_{82}O_{18}$), ginsenoside Rb1 ($C_{54}H_{92}O_{23}$), and ginsenoside Rd ($C_{48}H_{82}O_{18}$) from the labeled amount of Tienchi Ginseng Root and Rhizome Powder.

人参皂苷含量：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm

流动相： Solution A:0.03%磷酸水溶液

Solution B:乙腈

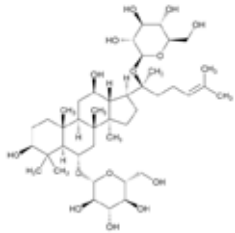
梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	83	17
2.4	80	20
3.5	70	30
4.2	69	31
5.0	58	42
5.1	0	100
6.0	0	100
6.1	83	17
7.5	83	17

柱温: 30 ˚C　流速 (ml/min): 0.8　波长(nm): 203

杂质结构

Ginsenoside Rg1



方法解析：新增各论，采用UPLC进行快速高效的分析。

三七粉胶囊
Tienchi Ginseng Root and Rhizome Powder Capsules

方法来源：收载于USP40-NF35

结构式： Tienchi Ginseng Root and Rhizome Powder Capsules contain Tienchi Ginseng Root and Rhizome Powder. They contain NLT 5.0% of ginsenosides calculated as the sum of notoginsenoside R1 ($C_{47}H_{80}O_{18}$), ginsenoside Rg1($C_{42}H_{72}O_{14}$), ginsenoside Re ($C_{48}H_{82}O_{18}$), ginsenoside Rb1 ($C_{54}H_{92}O_{23}$), and ginsenoside Rd ($C_{48}H_{82}O_{18}$) from the labeled amount of Tienchi Ginseng Root and Rhizome Powder.

人参皂苷含量：

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm

流动相： Solution A:0.03%磷酸水溶液

Solution B:乙腈

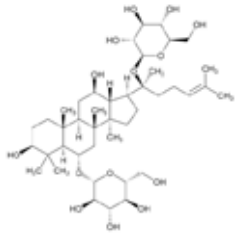
梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	83	17
2.4	80	20
3.5	70	30
4.2	69	31
5.0	58	42
5.1	0	100
6.0	0	100
6.1	83	17
7.5	83	17

柱温: 30 ˚C　流速 (ml/min): 0.8　波长(nm): 203

杂质结构

Ginsenoside Rg1



方法解析：新增各论，采用UPLC进行快速高效的分析。

氨氯地平与阿托伐他汀片
Amlodipine and Atorvastatin Tablets

方法来源：收载于USP40-NF35

定义： Amlodipine and Atorvastatin Tablets contain an amount of amlodipine besylate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and an amount of atorvastatin calcium equivalent to NLT 94.5% and NMT 105.0% of the labeled amount of atorvastatin ($C_{33}H_{34}FN_2O_5$). It may contain suitable antioxidants

有关物质：(氨氯地平相关)

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY HSS T3)

流动相： Buffer:7 mL三乙胺至1000 ml水中，加磷酸调至 pH2.5, 加1.8 g四丁基硫酸氢铵，混合均匀。

Solution A:甲醇:buffer=40:60

Solution B:乙腈:甲醇:buffer=40:40:20

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2	90	10
7	75	25
16	70	30
18	55	45
24	25	75
30	10	90
31	0	100
35	0	100
36	90	10
40	90	10

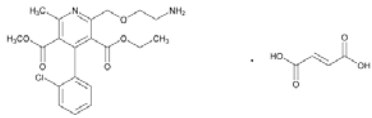
柱温: 40˚C　流速 (ml/min): 0.3　波长(nm)杂质A: 270　波长(nm)其他杂质: 360

杂质谱：

Name	相对保留时间	保留时间	可接受标准 (%)
Amlodipine related compound A	0.59	-	0.50
Amlodipine related compound F	0.73	-	-
Amlodipine	1.00	-	-
Amlodipine 4-chloro isomer	1.15	-	-
Amlodipine related compound E	1.40	-	-
Amlodipine related compound B	2.22	-	-
Atorvastatin–amlodipine adduct	3.49	0.47	0.50
单个未知杂质	-	1.0	0.20
总杂质	-		1.0

杂质结构

Amlodipine related compound A
3-Ethyl 5-methyl
[2-(2-aminoethoxymethyl)-4-
(2-chlorophenyl)-6-methyl-3,5-
pyridinedicarboxylate] fumarate.
$C_{20}H_{23}ClN_2O_5 \cdot C_4H_4O_4$ 522.93

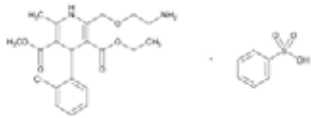


Amlodipine related Compound B
3-Ethyl 5-methyl 4-(2-chlorophenyl)-
6-methyl-2-({2-[2-(methylcarbamoyl)
benzamido]ethoxy}methyl)-1,4-
dihydropyridine-3,5-dicarboxylate.
$C_{29}H_{32}ClN_3O_7$ 570.03

Amlodipine related compound E
Diethyl 2-[(2-aminoethoxy)methyl]-
4-(2-chlorophenyl)-6-methyl-1,4-
dihydropyridine-3,5-dicarboxylate.
$C_{21}H_{27}ClN_2O_5$ 422.90

Amlodipine related compound F
Dimethyl 2-[(2-aminoethoxy)methyl]-
4-(2-chlorophenyl)-6-methyl-1,4-
dihydropyridine-3,5-dicarboxylate.
$C_{19}H_{23}ClN_2O_5$ 394.85

Amlodipine Besylate



Atorvastatin–amlodipine adduct
3-Ethyl 5-methyl 4-(2-chlorophenyl)-
2-[(2-{(3R ,5R)-7-[2-(4-fluorophenyl)-
5-isopropyl-3-phenyl-4-
(phenylcarbamoyl)-1H -pyrrol-1-
yl]-3,5-dihydroxyheptanamido}
ethoxy)methyl]-6-methyl-1,4-
dihydropyridine-3,5-dicarboxylate.

Amlodipine 4-chloro isomer
3-Ethyl 5-methyl 2-[(2-aminoethoxy)
methyl]-4-(4-chlorophenyl)-6-methyl-
1,4-dihydropyridine-3,5-dicarboxylate

方法解析：新增各论，采用UPLC进行快速高效的分析。

阿托伐他汀钙片
Atorvastatin Calcium Tablets

方法来源：收载于USP40-NF35

定义： Atorvastatin Calcium Tablets contain an amount of atorvastatin calcium [$(C_{33}H_{34}FN_2O_5)_2Ca$], equivalent to NLT 94.5% and NMT 105.0% of the labeled amount of atorvastatin

溶出实验3

色谱柱： L1, 2.1 mm x 5 cm; 2.6 µm

流动相： Solution A:甲醇:乙腈:0.1%三氟乙酸水溶液=5:5:90

Solution B:甲醇:乙腈:0.1%三氟乙酸水溶液=45:45:10

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.00	30	70
0.69	30	70
0.74	0	100
2.73	0	100
2.77	30	70
5.00	30	70

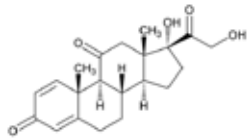
柱温: 40˚C　流速 (ml/min): 0.7　波长(nm): 248

方法解析：采用UPLC，大大加速了溶出实验的检测效率。

泼尼松
Prednisone

方法来源：收载于USP40-NF35 1S

结构式：



$C_{21}H_{26}O_5$　　358.43

Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-;

17,21-Dihydroxypregna-1,4-diene-3,11,20-trione[53-03-2].

有关物质

色谱柱： L1, 2.1 mm x 10 cm; 1.9 µm

流动相： Solution A:水

Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	75	25
3.5	75	25
8.5	30	70
9.5	30	70
9.6	75	25
12	75	25

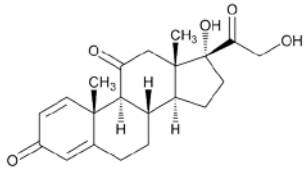
柱温: 40˚C　流速 (ml/min): 0.5　波长(nm): 254

杂质谱：

Name	相对保留时间	可接受标准 (%)
Prednisone	1.0	-
Cortisone	1.1	0.50
11-Desoxyprednisone	1.3	0.50
Prednisone acetate	1.6	0.50
单个未知杂质	-	0.10
总杂质	-	2.0

杂质结构

Prednisone



Cortisone
17,21-Dihydroxypregna-4-ene-3,11,20-trione.
$C_{21}H_{28}O_5$ 360.45

11-Desoxyprednisone
17,21-Dihydroxypregna-1,4-diene-3,20-dione

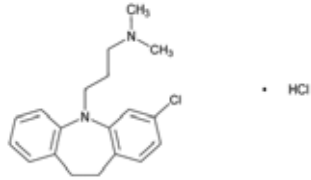
Prednisone acetate
17-Hydroxy-3,11,20-trioxopregna-1,4-diene-21-yl acetate.

方法解析：原HPLC等度方法改为UPLC梯度方法，大大提高了分析效率。
增加了3个特性杂质的限度控制。

盐酸氯米帕明
Clomipramine Hydrochloride

方法来源：收载于USP40-NF35 1S

结构式：



$C_{19}H_{23}ClN_2 \cdot HCl$　　351.31

5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl-, monohydrochloride;

3-Chloro-5-[3-(dimethylamino)propyl]-10,11-dihydro-5H -dibenz[b,f]azepine monohydrochloride [17321-77-6].

有关物质

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:2.5 ml乙酸加1000 ml水，加浓氨水调至 pH7.5

Solution B:乙腈:甲醇:THF=80:15:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
5.0	50	50
11.0	20	80
14.0	20	80
14.1	65	35
18.0	65	35

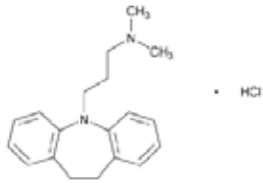
柱温: 30˚C　流速 (ml/min): 0.3　波长(nm): 254

杂质谱：

Name	相对保留时间	可接受标准 (%)
Imipramine	0.77	0.10
Clomipramine related compound C	0.87	0.10
Clomipramine	1.00	-
Clomipramine related compound A	1.1	0.10
Clomipramine related compound D	1.2	0.10
Clomipramine related compound F	1.5	0.0
单个未知杂质	-	0.10
总杂质	-	2.0

杂质结构

Imipramine Hydrochloride



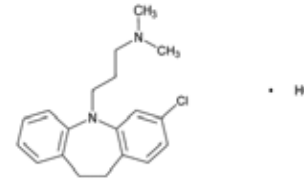
Clomipramine related compound A
N^1-[3-(3-Chloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)propyl]-N^1, N^3, N^3-trimethylpropane-1,3-diamine dihydrochloride.
$C_{23}H_{32}ClN_3 \cdot 2HCl$ 458.89

Clomipramine related compound C
3-(3-Chloro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride, monohydrate.
$C_{19}H_{21}ClN_2 \cdot HCl \cdot H_2O$ 367.31

Clomipramine related compound D
3-(3,7-Dichloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride.
$C_{19}H_{22}Cl_2N_2 \cdot HCl$ 385.76

Clomipramine related compound F
3-Chloro-10,11-dihydro-5H-dibenzo[b,f]azepine.
$C_{14}H_{12}ClN$ 229.70

Clomipramine Hydrochloride



方法解析：将原来两个HPLC等度方法合并为一个UPLC梯度方法，大大提高了分析效率。增加了5个特性杂质的限度控制。

盐酸氯米帕明胶囊
Clomipramine Hydrochloride Capsules

方法来源：收载于USP40-NF35 1S

定义： Clomipramine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$).

有关物质

色谱柱： L1, 2.1 mm x 10 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:2.5 ml乙酸加1000 ml水，加浓氨水调至 pH7.5

Solution B:乙腈:甲醇:THF=80:15:5

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
5.0	50	50
11.0	20	80
14.0	20	80
14.1	65	35
18.0	65	35

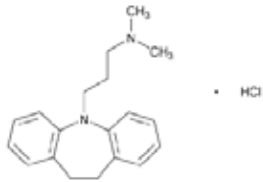
柱温: 30˚C　流速 (ml/min): 0.3　波长(nm): 254

杂质谱：

Name	相对保留时间	可接受标准 (%)
Imipramine	0.77	0.2
Clomipramine related compound C	0.87	0.2
Clomipramine	1.00	-
Clomipramine related compound A	1.1	0.10
Clomipramine related compound D	1.2	0.10
Clomipramine related compound F	1.5	0.0
单个未知杂质	-	0.1
总杂质	-	1.0

杂质结构

Imipramine Hydrochloride



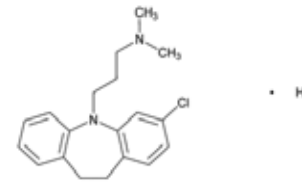
Clomipramine related compound A
N^1-[3-(3-Chloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)propyl]-N^1, N^3, N^3-trimethylpropane-1,3-diamine dihydrochloride.
$C_{23}H_{32}ClN_3 \cdot 2HCl$ 458.89

Clomipramine related compound C
3-(3-Chloro-5H -dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride, monohydrate.
$C_{19}H_{21}ClN_2 \cdot HCl \cdot H_2O$ 367.31

Clomipramine related compound D
3-(3,7-Dichloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine hydrochloride.
$C_{19}H_{22}Cl_2N_2 \cdot HCl$ 385.76

Clomipramine related compound F
3-Chloro-10,11-dihydro-5H-dibenzo[b,f]azepine.
$C_{14}H_{12}ClN$ 229.70

Clomipramine Hydrochloride



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

奥美沙坦酯片
Olmesartan Medoxomil Tablets

方法来源：收载于USP40-NF35 1S

定义： Olmesartan Medoxomil Tablets contain NLT 93.0% and NMT 105.0% of the labeled amount of olmesartan medoxomil ($C_{29}H_{30}N_6O_6$).

有关物质

色谱柱： L1, 2.1 mm x 5 cm; 1.7 μm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:3.1 g/L甲酸

Solution B:乙腈:solution A=10:90

Solution B:乙腈:solution A=90:10

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	68.8	31.2
1.5	37.5	62.5
1.6	68.8	31.2
3.0	68.8	31.2

柱温: 35˚C　流速 (ml/min): 0.6　波长(nm): 249

方法解析：新增各论，采用UPLC进行快速高效的分析。

苯佐卡因、 氨苯丁酯、盐酸丁卡因局部喷雾剂
Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Aerosol

方法来源：收载于USP40-NF35 1S

定义： Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Aerosol is Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Solution packaged in a pressurized container with a suitable inert propellant. It contains NLT 90.0% and NMT 110.0% of the labeled amounts of benzocaine ($C_9H_{11}NO_2$), butamben ($C_{11}H_{15}NO_2$), and tetracaine hydrochloride ($C_{15}H_{24}N_2O_2 \cdot HCl$).

有关物质

色谱柱： L1, 2.1 mm x 5 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.1%甲酸水溶液

Solution B:0.1%甲酸乙腈溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	91	9
2.5	50	50
3.9	50	50
4	91	9
5	91	9

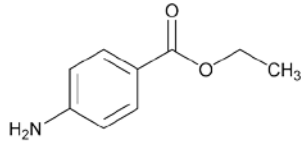
柱温: 30˚C　流速 (ml/min): 0.3　波长(nm): 254

杂质谱：

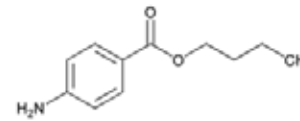
Name	相对保留时间	响应因子	可接受标准 (%)
4-Aminobenzoic acid	0.15	1.3	0.3
Benzocaine	0.70	-	-
Tetracaine	0.74	-	-
Tetracaine related compound B	0.93	0.6	0.4
Butamben	1.0	-	-
Ethyl 4-nitrobenzoate	1.04	-	0.2
单个未知杂质	-	1.0	0.4
总杂质	-		2.0

杂质结构

Benzocaine

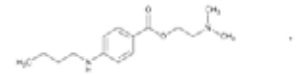


Butamben



Ethyl 4-nitrobenzoate
Ethyl p-nitrobenzoate.
$C_9H_9NO_4$ 195.17

Tetracaine Hydrochloride



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

苯佐卡因、 氨苯丁酯 、盐酸丁卡因凝胶
Benzocaine, Butamben, and Tetracaine Hydrochloride Gel

方法来源：收载于USP40-NF35 1S

定义： Benzocaine, Butamben, and Tetracaine Hydrochloride Gel is Benzocaine, Butamben, and Tetracaine Hydrochloride in a suitable gel base. It contains NLT 90.0% and NMT 110.0% of the labeled amounts of benzocaine ($C_9H_{11}NO_2$), butamben ($C_{11}H_{15}NO_2$), and tetracaine hydrochloride ($C_{15}H_{24}N_2O_2$ ·HCl).

有关物质

色谱柱： L1, 2.1 mm x 5 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.1%甲酸水溶液

Solution B:0.1%甲酸乙腈溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	91	9
2.5	50	50
3.9	50	50
4	91	9
5	91	9

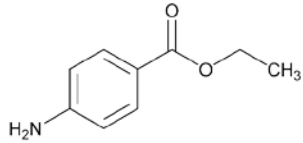
流速 (ml/min): 0.6　波长(nm): 300

杂质谱：

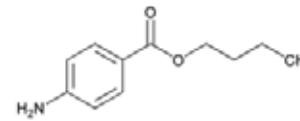
Name	相对保留时间	响应因子	可接受标准 (%)
4-Aminobenzoic acid	0.15	1.3	0.3
Benzocaine	0.70	-	-
Tetracaine	0.74	-	-
Tetracaine related compound B	0.93	0.6	0.4
Butamben	1.0	-	-
Ethyl 4-nitrobenzoate	1.04	-	0.2
单个未知杂质	-	1.0	0.4
总杂质	-		2.0

杂质结构

Benzocaine

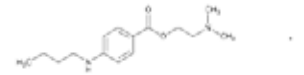


Butamben



Ethyl 4-nitrobenzoate
Ethyl p-nitrobenzoate.
$C_9H_9NO_4$ 195.17

Tetracaine Hydrochloride



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

苯佐卡因、 氨苯丁酯 、盐酸丁卡因局部溶液
Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Solution

方法来源：收载于USP40-NF35 1S

定义： Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Solution contains NLT 90.0% and NMT 110.0% of the labeled amounts of benzocaine ($C_9H_{11}NO_2$), butamben ($C_{11}H_{15}NO_2$), and tetracaine hydrochloride ($C_{15}H_{24}N_2O_2 \cdot HCl$).

有关物质

色谱柱： L1, 2.1 mm x 5 cm; 1.7 µm (ACQUITY UPLC BEH C_{18})

流动相： Solution A:0.1%甲酸水溶液

Solution B:0.1%甲酸乙腈溶液

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	91	9
2.5	50	50
3.9	50	50
4	91	9
5	91	9

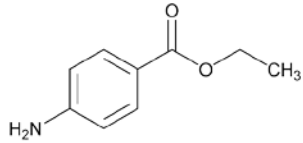
流速 (ml/min): 0.6　波长(nm): 300

杂质谱：

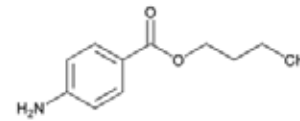
Name	相对保留时间	响应因子	可接受标准 (%)
4-Aminobenzoic acid	0.15	1.3	0.3
Benzocaine	0.70	-	-
Tetracaine	0.74	-	-
Tetracaine related compound B	0.93	0.6	0.4
Butamben	1.0	-	-
Ethyl 4-nitrobenzoate	1.04	-	0.2
单个未知杂质	-	1.0	0.4
总杂质	-		2.0

杂质结构

Benzocaine

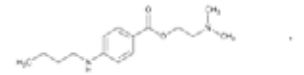


Butamben



Ethyl 4-nitrobenzoate
Ethyl p-nitrobenzoate.
$C_9H_9NO_4$ 195.17

Tetracaine Hydrochloride



方法解析：增加了杂质控制项目，采用UPLC进行快速高效的分析。

灵芝
Ganoderma lucidum Fruiting Body

方法来源：收载于USP40-NF35 1S

定义： The article consists of the dried fruiting bodies of Ganoderma lucidum (Curtis: Fr.) P. Karst. (Family Ganodermataceae). It contains NLT 0.3% of triterpene acid, calculated as the sum of ganoderenic acid C, ganoderic acid C2, ganoderic acid G, ganoderenic acid B, ganoderic acid B, ganoderic acid A, ganoderic acid H, ganoderenic acid D, ganoderic acid D, and ganoderic acid F on the dried basis.

三萜酸含量

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.075%磷酸水溶液

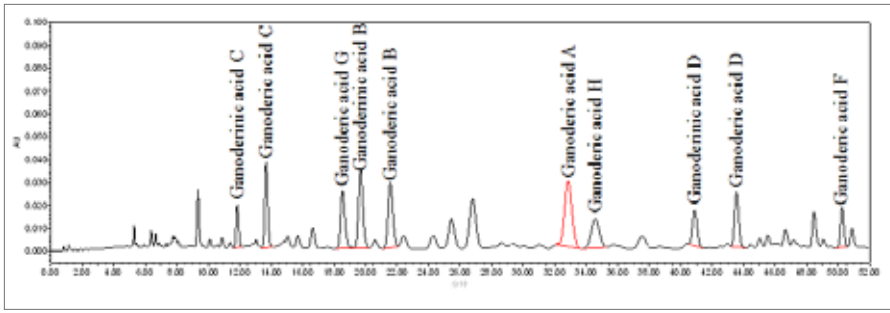
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	80	20
3	73.5	26.5
34	73.5	26.5
52	61.5	38.5
54	0	100
55	0	100
55.5	80	20

柱温: 25±1˚C　流速 (ml/min): 0.4　波长(nm): 257

色谱图：

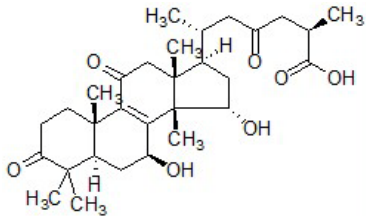


杂质谱：

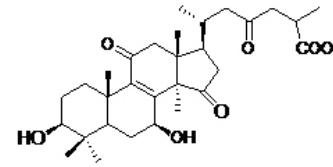
Name	相对保留时间	转换因子
Ganoderenic acid C	0.36	0.51
Ganoderic acid C2	0.42	1.05
Ganoderic acid G	0.56	1.18
Ganoderenic acid B	0.60	0.45
Ganoderic acid B	0.66	1.10
Ganoderic acid A	1.00	1.00
Ganoderic acid H	1.05	1.54
Ganoderenic acid D	1.25	0.51
Ganoderic acid D	1.33	1.08
Ganoderic acid F	1.54	1.45

杂质结构

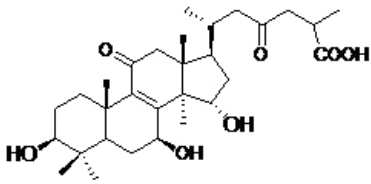
Ganoderic acid A



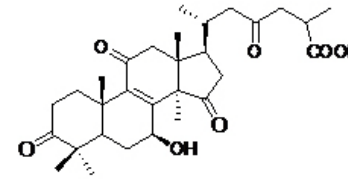
Ganoderic acid B



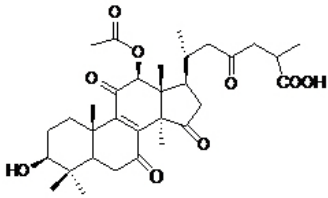
Ganoderic acid C2



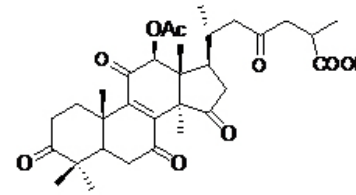
Ganoderic acid D



Ganoderic acid H

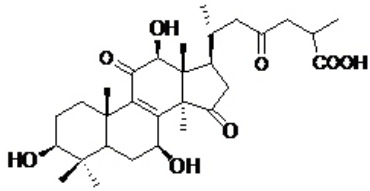


Ganoderic acid F

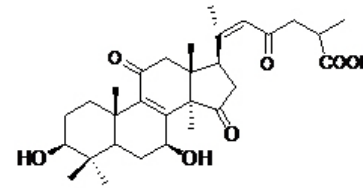


杂质结构

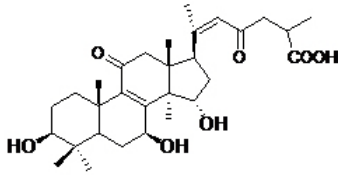
Ganoderic acid G



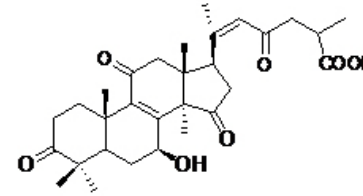
Ganoderenic acid B



Ganoderenic acid C



Ganoderenic acid D



方法解析：中药中成分复杂，采用HPLC时，分析时间过长。现采用UPLC进行指纹图谱分析，在保证分离度的前提下，大大提高了分析速度，节约检验成本。

三七
Panax notoginseng Root and Rhizome

方法来源：收载于HMC

定义： The article consists of the dried roots, rootlets, and rhizomes of *Panax notoginseng* (Burk.) F. H. Chen (Family Araliaceae) collected before flowering in autumn. It contains NLT 5.0% of total saponins calculated as the sum of notoginsenoside R1, ginsenoside Rg1, ginsenoside Re, ginsenoside Rb1, and ginsenoside Rd, and NLT 0.6% of notoginsenoside R1, on the dried basis.

人参皂苷含量

色谱柱： L1, 2.1 mm x 5 cm; 1.7 µm

流动相： Solution A:0.03%磷酸水溶液

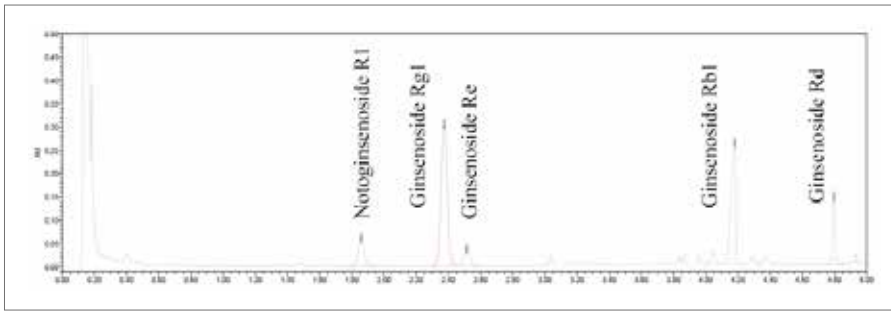
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	83	17
2.4	80	20
3.5	70	30
4.2	69	31
5.0	58	42
5.1	0	100
6.0	0	100
6.1	83	17
7.5	83	17

柱温: 30±1˚C　流速 (ml/min): 0.8　波长(nm): 203

色谱图：



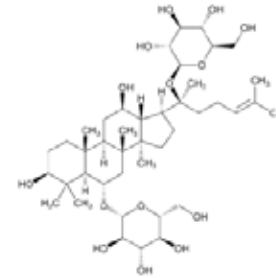
杂质谱：

Name	相对保留时间	转换因子
Notoginsenoside R1	0.78	1.09
Ginsenoside Rg1	1.00	1.00
Ginsenoside Re	1.06	1.02
Ginsenoside Rb1	1.78	1.26
Ginsenoside Rd	2.04	1.03

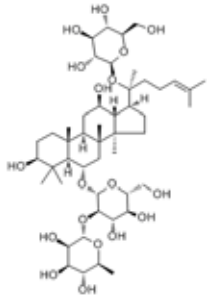
杂质结构

Notoginsenoside R1

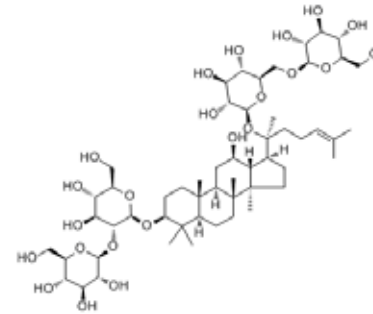
Ginsenoside Rg1



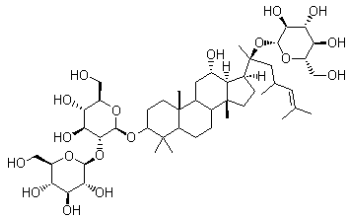
Ginsenoside Re



Ginsenoside Rb1



Ginsenoside Rd



方法解析：中药中成分复杂，采用HPLC时，分析时间过长。现采用UPLC进行指纹图谱分析，在保证分离度的前提下，大大提高了分析速度，节约检验成本。

五味子
Schisandra chinensis Fruit

方法来源：收载于HMC

定义： The article consists of the dried ripe fruits of *Schisandra chinensis* (Turcz.) Baill. (Family Schisandraceae) collected in the fall. It contains NLT 0.40% of schisandrin (schisandrol A, $C_{24}H_{32}O_7$) on the dried basis; and NLT 0.95% of total lignans calculated as the sum of schisandrin, schisandrol B ($C_{23}H_{28}O_7$), schisandrin A (deoxyschisandrin, $C_{24}H_{32}O_6$), and schisandrin B (γ -schisandrin, $C_{23}H_{28}O_6$), on the dried basis.

含量

色谱柱： L1, 2.1 mm x 15 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:水

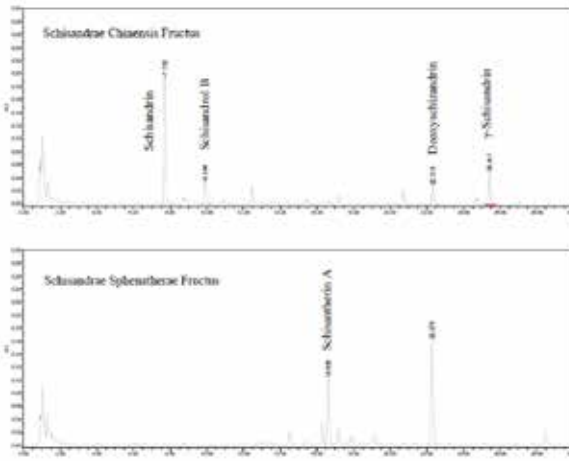
Solution B:乙腈:甲醇=1:1

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0	47	53
30	20	80

柱温: 35˚C　流速 (ml/min): 0.3　波长(nm): 251

色谱图：

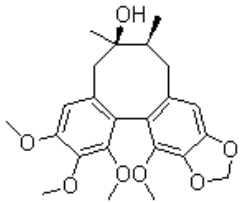


杂质谱：

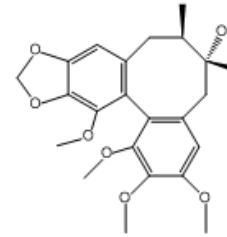
Name	相对保留时间	转换因子
Schisandrin	1.00	1.00
Schisandrol B	1.29	1.21
Schisandrin A	2.90	1.00
Schisandrin B	3.31	1.23

杂质结构

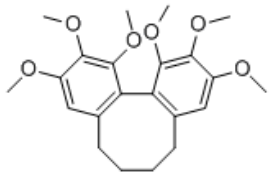
Schisandrin



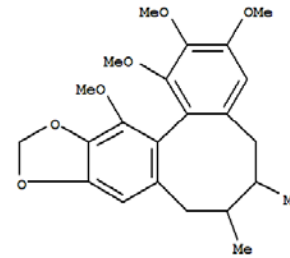
Schisandrol B



Schisandrin A



Schisandrin B



方法解析：中药中成分复杂，采用HPLC时，分析时间过长。现采用UPLC进行指纹图谱分析，在保证分离度的前提下，大大提高了分析速度，节约检验成本。

牛樟芝
Antrodia camphorata Fruiting Body

方法来源：收载于HMC

定义： The article consists of the dried ripe fruits of *Schisandra chinensis* (Turcz.) Baill. (Family Schisandraceae) collected in the fall. It contains NLT 0.40% of schisandrin (schisandrol A, $C_{24}H_{32}O_7$) on the dried basis; and NLT 0.95% of total lignans calculated as the sum of schisandrin, schisandrol B ($C_{23}H_{28}O_7$), schisandrin A (deoxyschisandrin, $C_{24}H_{32}O_6$), and schisandrin B (γ -schisandrin, $C_{23}H_{28}O_6$), on the dried basis.

三萜类含量

色谱柱： L1, 2.1 mm x 10 cm; 1.8 µm (ACQUITY UPLC HSS T3)

流动相： Solution A:0.1%甲酸水溶液

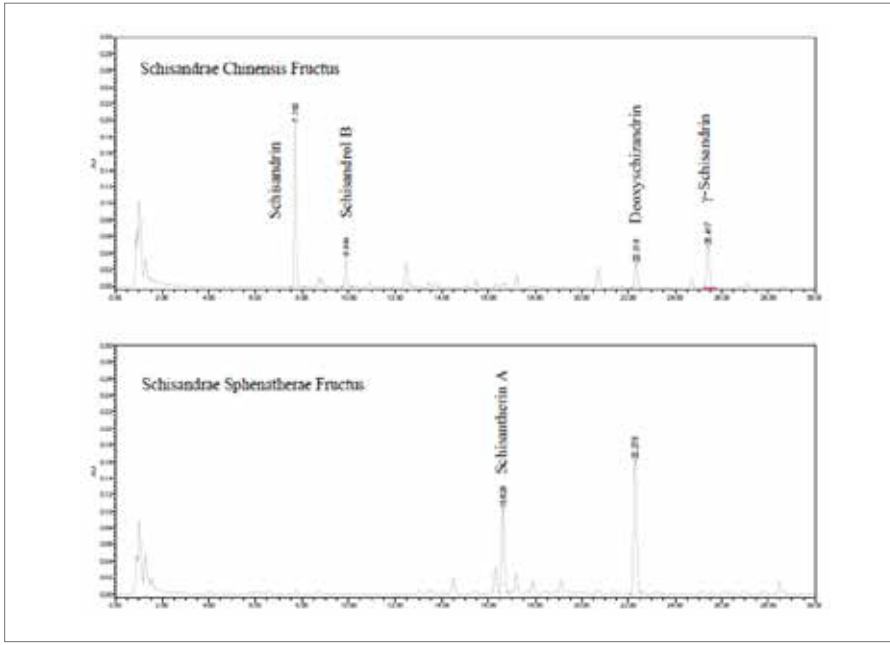
Solution B:乙腈

梯度条件：

Time (min)	Solution A (%)	Solution B (%)
0.0	70	30
7.5	50	50
10.8	40	60
13.8	35	65
16.8	32	68
18.5	25	75
30.6	15	85
35.6	0	100
35.7	70	30
38.0	70	30

柱温: 35˚C　流速 (ml/min): 0.3　波长(nm): 251

色谱图：

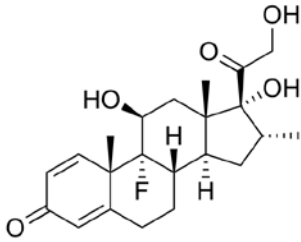


杂质谱：

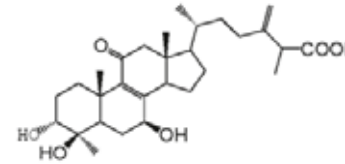
Name	相对保留时间	转换因子
Dexamethasone	1.00	1.00
(R,S)-Antcin K	1.29	0.34
1,4-Dimethoxy-2,3-methylenedioxy-5-methylbenzene	1.69	0.28
(*R*,*S*)-Antcin C	2.38	0.21
(*R*,*S*)-Antcin H	2.50	0.15
Dehydrosulfurenic acid	2.84	0.33
(*R*,*S*)-Antcin B	3.07	0.21
(*R*,*S*)-Antcin A	3.76	0.24
Dehydroeburicoic acid	5.87	0.47

杂质结构

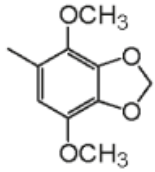
Dexamethasone



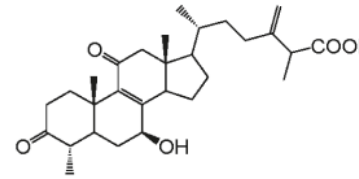
(*R,S*)-Antcin K



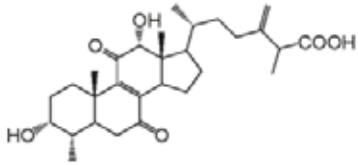
1,4-Dimethoxy-2,3-methylenedioxy-5-methylbenzene



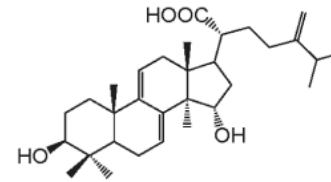
(*R,S*)-Antcin C



(*R,S*)-Antcin H

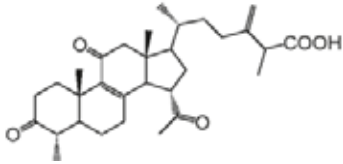


Dehydrosulfurenic acid

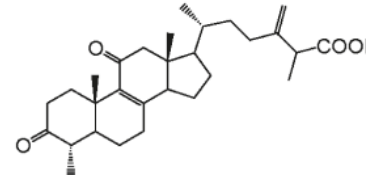


杂质结构

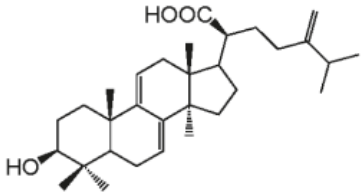
(*R*,*S*)-Antcin B



(*R*,*S*)-Antcin A



Dehydroeburicoic acid



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NOTES

NOTES

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