利用高分辨四级杆静电场轨道阱质谱快速定性和定量筛查确证中药保健品中的 114 种非法添加药物

李岳,李珉,纪宏,张宪*(北京市药品检验所,中药成分分析与生物评价北京市重点实验室,北京 102206)

摘要:目的 建立一种全新的基于高效液相色谱与四级杆静电场轨道阱串联质谱联用技术的中药保健品中 114 种非法添加药物的定性定量筛查方法。**方法** 以 0.1% 甲酸水溶液-乙腈为流动相,采用 SHISEIDO CAPCELL PAK C_{18} 色谱柱(3.0 mm × 100 mm,3 μm),HPLC 进行梯度洗脱(0 ~ 18 min,乙腈从 2% 到 100%,18 ~ 23 min,乙腈为 100%,23.1 ~ 25 min,乙腈为 2%),柱温 40 ℃,流速 0.3 mL·min^{-1};质谱采用电喷雾离子源进行扫描,四级杆静电场轨道阱串联质谱作为质量分析器进行采集,扫描范围 m/z 120 ~ 750,喷雾电压 3.5 kV,鞘气压(N_2) 275.8 kPa,辅助气压(N_2) 68.95 kPa,一次进样即同时获得母离子和碎片子离子的高分辨率高质量精度质谱数据。通过二级质谱精确质量数,对筛查到的非法添加进一步结构确认。**结果** 本方法在 25 min 内可同时检测安神类、减肥类、降压类、降脂类、降糖类、抗病毒类、止咳类、止痛类、激素类、精神类、壮阳类共 11 类 114 种非法添加化学药物,线性范围、灵敏度、重复性、回收率均满足分析要求。**结论** 使用高效液相色谱-四级杆静电场轨道阱质谱建立的筛查方法具有快速、便捷、准确的优点,能够满足目标和非目标非法添加的筛查确证需求。

关键词:非法添加筛查;超高效液相色谱法;四级杆静电场轨道阱串联质谱

Qualitative and Quantitative Screening of 114 Illegally Added Adulterants in Health Products by High Resolution Four-Stage Electrostatic Field Orbital Trap Mass Spectrometry

LI Yue,LI Min,JI Hong,ZHANG Xian*(*Analysis of Chinese Medicines and Biological Evaluation of Beijing Municipal Key Laboratory*,*Beijing Institute for Drug Control*,*Beijing* 102206,*China*)

ABSTRACT:OBJECTIVE To establish a new qualitative and quantitative screening method for 114 illegal adulterants in traditional Chinese medicine for health care based on high performance liquid chromatography(HPLC)coupled with high four-stage electrostatic field orbital well tandem mass spectrometry. **METHODS** Using 0.1% formic acid aqueous solution-acetonitrile as mobile phase,gradient elution was performed on SHISEIDO CAPCELL PAK C_{18} column(3.0 mm × 100 mm,3 μm)with column temperature of 40 ℃ and flow rate of 0.3 mL·min^{-1}. The gradient elution program was as follows:0 – 18 min,acetonitrile was from 2% to 100%;18 – 23 min,acetonitrile was 100%;23.1 – 25 min,acetonitrile was 2%. The mass spectrometry was carried out with electrospray ionization source,four stage electrostatic field track mass spectrometry as mass analyzer,and scanning range m/z 120 – 750,spray voltage 3.5 kV,sheath pressure(N_2) 275.8 kPa,auxiliary air pressure(N_2) 68.95 kPa. High resolution and high quality mass spectrometry data of parent ions and fragment ions were obtained simultaneously by one injection. The structures of illegal additions were further confirmed by the accurate mass of secondary mass spectrometry. **RESULTS** This method could simultaneously detect 114 kinds of illegally added chemical drugs of 11 categories including tranquilizers,hormones,slimming,hypoglycemic,hypotensive,lipid-lowering,psychotropic,antiviral,antitussive,analgesic and aphrodisiac drugs within 25 min. The linear range,sensitivity,repeatability and recovery rate all met the requirements of analysis. **CONCLUSION** The screening method established by four-stage electrostatic field orbital trap mass spectrometry coupled with HPLC is fast,convenient,accurate and retrospective,and can meet the needs of screening confirmation for target and non-target illegal additions.

KEY WORDS:illegal adulterant screening;liquid chromatograh;high resolution four-stage electrostatic field mass spectrometry

  随着生活水平不断提高,许多人为了增强自身免疫力,预防疾病发生,购买保健食品长期服用。一些不法商家在保健食品中添加化学药物,却不注明成分及剂量,鼓吹保健功效,达到欺骗消费者,夸大宣传疗效,增加销售量的目的,这些未进行药理和安全性研究的添加行为,违反了《食品安全法》和《药

作者简介:李岳,男,主管药师 研究方向:食品及药物分析及质量控制 *通讯作者:张宪,男,主管药师 研究方向:中药学和药物分析 Tel:(010)52779720 E-mail:zhangxian@bidc.org.cn

品管理法》,被视为非法添加[1]。使患者在不知情的情况下,持续、大量服用含有非法添加药物的保健食品,可能产生不可预知的不良反应,出现中毒现象,对社会造成极大的危害。近年来,面对不法分子添加的药物品种不断更新换代以及添加手段层出不穷,因此,为了保障人民用药安全,打击犯罪,需要建立检测范围覆盖面更宽,更能快速、准确、高选择性地筛查非法添加化学药物的方法。

在非法添加快速筛查中,主要使用的分析技术有:薄层色谱法(TLC)[2],高效液相色谱法(HPLC)[3],液质联用法(HPLC-MS)[4-7],而随着未知添加物种类增加,化合物之间极性相差较大,常规分析方法,例如 TLC 和 HPLC,常会发生色谱保留和分离行为不佳的情况,进而影响检测的准确性和有效性。此外,常用的 HPLC-MS 方法采用低分辨的四级杆[8-9]或离子阱质谱,而保健食品及中

药种类繁多,导致样品组分非常复杂,干扰因素多,容易出现假阳性[10-12]。本实验使用四级杆-静电场轨道阱高分辨率质谱同时筛查安神类等 11 类 115 种非法添加物,利用高分辨率、高选择性的特性建立根据精确质量数、保留时间、2 级碎片信息为基础更大范围的筛查库,同时对潜在的阳性样品进行分析,并建立定量方法。

1 仪器与试药

仪器:四级杆-静电场轨道阱高分辨率质谱(美国 Thermo 公司),CP225D 分析天平(德国 Sartorius 公司),Milli-Q 纯水机(美国 Millipore 公司)。

试剂:对照品信息见表 1,乙腈、甲醇为色谱纯,甲酸为优级纯。

样品:10 批保健食品为北京市药品监督管理局市场监督抽验收集。

表 1 中药保健品化学药品检测中对照品信息及对照品取样量

Tab. 1 Information and amount of reference substances

Analyte	CAS No	Batch	Source	Purity/%	m(Weigh)/mg
Alprazolam	28981-97-7	171218-201304	National Institutes for Food and Drug Control	99.5	10.06
Amobarbital	57-43-2	171221-201203	National Institutes for Food and Drug Control	99.9	10.05
Barbital	57-44-3	171220-200602	National Institutes for Food and Drug Control	100	10.05
Chlormezanone	80-77-3	17.00.09.04	LGC GmbH	99.9	10.07
Clonazepam	1622-61-3	171227-201404	National Institutes for Food and Drug Control	99.7	10.08
Clorazepate	58-25-3	171248-201403	National Institutes for Food and Drug Control	99.8	10.03
Diazaepam	439-14-5	171225-201304	National Institutes for Food and Drug Control	99.9	10.04
Estazolam	29975-16-4	171219-201003	National Institutes for Food and Drug Control	99.7	10.05
Lorazepam	86-49-1	171253-201102	National Institutes for Food and Drug Control	99.2	10.04
Midazolam	59467-64-0	171250-201002	National Institutes for Food and Drug Control	99.9	10.03
Mogadan	146-22-5	171217-200402	National Institutes for Food and Drug Control	100	10.05
Oxazepam	604-75-1	171229-201104	National Institutes for Food and Drug Control	100	10.06
Phenobarbital	50-06-6	171222-201206	National Institutes for Food and Drug Control	100	10.04
Secobarbital	76-73-3	171223-200402	National Institutes for Food and Drug Control	100	10.05
Sinomenine	115-57-7	6-SCC-122-1	Toronto Research Chemicals Inc	100	10.07
Triazolam	28911-01-5	171230-201203	National Institutes for Food and Drug Control	99.6	10.05
Zaleplon	151319-34-5	4-ANR-96-1	Zhen xiang Company	98	10.12
Zopiclone	43200-80-2	100870-200801	National Institutes for Food and Drug Control	99.9	10.07
Beclomethasone dipropionate	5534-09-8	MOL276	USP	99.8	10.02
Clobetasol propionate	25122-46-7	100302-201103	National Institutes for Food and Drug Control	99.0	10.10
Cortisol	50-23-7	40319	Dr. Ehrenstorfer GmbH	99.8	10.05
Cortisone acetate	50-04-4	40812	Dr. Ehrenstorfer GmbH	99.4	10.06
Dexamethasone acetate	1177-87-3	100122-201206	National Institutes for Food and Drug Control	99.2	10.17
Fluocinonide	356-12-7	KOK185	USP	99.7	10.08
Halcinonide	3093-35-4	HOL014	USP	99.7	10.13
Hydrocortisone acetate	50-03-3	40302	Dr. Ehrenstorfer GmbH	99.5	10.05
Metacortandracin	53-03-2	40517	Dr. Ehrenstorfer GmbH	98.5	10.11
Methylprednisolone	53-36-1	40706	Dr. Ehrenstorfer GmbH	98.9	10.02
Prednisone acetate	125-10-0	7-MIC-191-1	TRC	100	10.10
Triamcinolone	124-94-7	KOM290	USP	99.6	10.11
Triamcinolone acetonide acetate	3870-07-3	100125-201406	National Institutes for Food and Drug Control	99.1	10.08
Bumetanide	28395-03-1	100173-201303	National Institutes for Food and Drug Control	99.9	10.02
Bupropion	34911-55-2	100671-201802	National Institutes for Food and Drug Control	99.9	10.04
Caffeine	58-0-2	C0100000	European Pharmacopeia	100	10.02
Ephedrine	299-42-3	171241-201508	National Institutes for Food and Drug Control	99.8	10.01
Fenfluramine	458-24-2	608.00.08.01	LCG GmbH	99.9	10.05

Analyte	CAS No	Batch	Source	Purity/%	m(Weigh)/mg
Fluoxetine	54910-89-3	100513-201602	National Institutes for Food and Drug Control	99. 3	10. 08
Furosemide	54-31-9	100544-201503	National Institutes for Food and Drug Control	99. 3	10. 11
Phenolphthalein	77-09-8	100091-199601	National Institutes for Food and Drug Control	100	9. 99
Sertraline	79617-96-2	100702-200401	National Institutes for Food and Drug Control	100. 0	10. 04
Sibutramine	106650-56-0	100624-200401	National Institutes for Food and Drug Control	100	10. 02
Diaben	64-77-7	129178	Dr. Ehrenstorfer	99. 9	10. 06
Glibenclamide	10238-21-8	10135-201105	National Institutes for Food and Drug Control	99. 5	10. 07
Glibornuride	26944-48-9	520026-201401	National Institutes for Food and Drug Control	99. 9	10. 06
Gliclazide	21187-98-4	100269-201505	National Institutes for Food and Drug Control	99. 9	10. 06
Glimepiride	93479-97-1	100674-201503	National Institutes for Food and Drug Control	99. 6	10. 08
Glipizide	29094-61-9	100281-201604	National Institutes for Food and Drug Control	99. 7	10. 12
Gliquidone	33342-05-1	100280-201403	National Institutes for Food and Drug Control	99. 5	10. 09
Pioglitazone	112529-15-4	100634-201202	National Institutes for Food and Drug Control	100	10. 07
Atenolol	29122-68-7	100117-201606	National Institutes for Food and Drug Control	99. 7	10. 03
Benidipine	105979-17-7	101049-201001	National Institutes for Food and Drug Control	100	10. 04
Bisoprolol	104344-23-2	100711-201602	National Institutes for Food and Drug Control	99. 7	10. 05
Candesartan cilexetil	145040-37-5	100685-201602	National Institutes for Food and Drug Control	99. 8	10. 10
Captopril	62571-86-2	100318-201103	National Institutes for Food and Drug Control	99. 5	10. 08
Clonidine	4205-91-8	100071-201607	National Institutes for Food and Drug Control	100	9. 98
Dihydrochlorothiazide	58-93-5	100309-201404	National Institutes for Food and Drug Control	99. 7	10. 02
Irbesartan	138402-11-6	100607-201202	National Institutes for Food and Drug Control	99. 8	10. 02
Lacidipine	103890-78-4	100741-200802	National Institutes for Food and Drug Control	99. 9	10. 01
Lisinopril	83915-83-7	100814-201202	National Institutes for Food and Drug Control	90. 7	11. 02
Metoprolol	37350-58-6	100084-201403	National Institutes for Food and Drug Control	99. 9	10. 06
Micardis	144701-48-4	100629-201202	National Institutes for Food and Drug Control	99. 6	10. 08
Minoxidil	38304-91-5	100238-199701	National Institutes for Food and Drug Control	100	10. 03
Nifedipine	21829-25-4	100338-201605	National Institutes for Food and Drug Control	99. 8	10. 05
Quinapril	85441-61-8	100568-201302	National Institutes for Food and Drug Control	99. 0	10. 10
Reserpine	50-55-5	100041-201213	National Institutes for Food and Drug Control	99. 0	10. 08
Sotalol	3930-20-9	100737-200501	National Institutes for Food and Drug Control	100	10. 03
Terazosin	63074-08-8	100375-201103	National Institutes for Food and Drug Control	92. 4	10. 88
Troxerutin	7085-55-4	100416-201607	National Institutes for Food and Drug Control	97. 5	10. 27
Valsartan	137862-53-4	100651-201604	National Institutes for Food and Drug Control	98. 5	10. 17
Atorvastatin	134523-03-8	100590-201303	National Institutes for Food and Drug Control	95. 3	10. 52
Bezafibrate	41859-67-0	100732-201602	National Institutes for Food and Drug Control	99. 6	10. 09
Fenofibrate	49562-28-9	100733-201502	National Institutes for Food and Drug Control	99. 9	10. 00
Fluvastatin	93957-55-2	100800-201302	National Institutes for Food and Drug Control	95. 5	10. 50
Gemfibrozil	25812-30-0	100284-200602	National Institutes for Food and Drug Control	99. 5	10. 06
Lovastatin	75330-75-5	100600-201504	National Institutes for Food and Drug Control	99. 4	10. 05
Pravastatin	81131-70-6	F1/288	USP	99. 0	10. 12
Rosuvastatin	147098-20-2	101028-201202	National Institutes for Food and Drug Control	97. 6	10. 22
Simvastatin	79902-63-9	100601-201003	National Institutes for Food and Drug Control	99. 0	10. 11
Carbamazepine	298-46-4	100142-201706	National Institutes for Food and Drug Control	100. 0	10. 05
Aciclovir	59277-89-3	140630-201403	National Institutes for Food and Drug Control	99. 8	10. 02
Famciclovir	104227-87-4	100628-201102	National Institutes for Food and Drug Control	99. 9	10. 01
Lamivudine	134678-17-4	101007-201502	National Institutes for Food and Drug Control	99. 9	10. 01
Nevirapine	88255-01-0	100641-200401	National Institutes for Food and Drug Control	100. 0	99. 97
Zidovudine	30516-87-1	100672-200401	National Institutes for Food and Drug Control	100. 0	10. 02
Bambuterol	81732-65-2	101009-200701	National Institutes for Food and Drug Control	99. 7	10. 07
Benproperine	2156-27-6	100237-201303	National Institutes for Food and Drug Control	99. 8	10. 07
Clenbuterol	21898-19-1	100072-201503	National Institutes for Food and Drug Control	90. 5	11. 06
Clorprenaline	3811-25-4	100220-201603	National Institutes for Food and Drug Control	99. 9	10. 03
Dextromethorphan	125-71-3	100201-201204	National Institutes for Food and Drug Control	94. 8	10. 62
Diphenhydramine	58-73-1	100066-200807	National Institutes for Food and Drug Control	99. 9	10. 03
Diprophylline	479-18-5	100417-201603	National Institutes for Food and Drug Control	99. 9	10. 08
Doxofylline	69975-86-6	100625-201202	National Institutes for Food and Drug Control	99. 9	10. 00
Hydroxyethyltheophylline	519-37-9	100215-200601	National Institutes for Food and Drug Control	100. 0	10. 06
Pentoxyverine	77-23-6	100432-201803	National Institutes for Food and Drug Control	99. 8	10. 06
Procaterol	81262-93-3	100275-200702	National Institutes for Food and Drug Control	100. 0	10. 04
Salbutamol	18559-94-9	100328-201804	National Institutes for Food and Drug Control	99. 4	10. 03
Sulfamethoxazole	723-46-6	100025-201505	National Institutes for Food and Drug Control	99. 6	10. 04
Theophylline	58-55-9	100121-201104	National Institutes for Food and Drug Control	100. 0	10. 05
Acetaminophen	103-90-2	100018-201610	National Institutes for Food and Drug Control	99. 9	10. 05

Analyte	CAS No	Batch	Source	Purity/%	m(Weigh)/mg
Butazodine	50-33-9	100481-201702	National Institutes for Food and Drug Control	99.8	10.05
Dexamethasone	50-02-2	100129-201506	National Institutes for Food and Drug Control	99.8	10.08
Diclofenac	15307-86-5	100334-201803	National Institutes for Food and Drug Control	100.0	10.00
Indometacin	53-86-1	100258-200904	National Institutes for Food and Drug Control	99.9	10.06
Piroxicam	36322-90-4	100177-201704	National Institutes for Food and Drug Control	99.5	10.05
Trimethoprim	738-70-5	100031-201606	National Institutes for Food and Drug Control	99.8	10.11
Amino tadalafil	385769-84-6	520042-201401	National Institutes for Food and Drug Control	99.8	10.08
Homo sildenafil	642928-07-2	520046-201401	National Institutes for Food and Drug Control	99.6	10.09
Hydroxyhomo sildenafil	139755-85-4	2050-019A6	TLC PHARMACEUTICAL STANDARDS	99.9	10.02
Norneosildenafil	371959-09-0	520040-201401	National Institutes for Food and Drug Control	99.5	10.02
Pseudovardenafil	224788-34-5	520041-201401	National Institutes for Food and Drug Control	99.0	10.00
Sildenafil	139755-83-2	420012-201401	National Institutes for Food and Drug Control	99.0	10.10
Tadalafil	171596-29-5	21130	TLC PHARMACEUTICAL STANDARDS	99.9	10.01
Thioaildenafil	856190-47-1	520048-201401	National Institutes for Food and Drug Control	99.5	10.01
Vardenafil	224788-34-5	1132-035A1	TLC PHARMACEUTICAL STANDARDS	99.3	10.03

2 实验方法

2.1 色谱条件

色谱柱 SHISEIDO CAPCELL PAK C_{18}（3.0 mm × 100 mm, 3 μm,日本大阪曹达公司),流动相A:0.1%甲酸水溶液,B:乙腈;梯度洗脱:0~18 min,2% B→100% B;18~23 min,100% B;23.1~25 min,100% B→2% B;流速0.3 mL·min⁻¹;柱温:40 ℃;进样量:5 μL。

2.2 质谱条件

离子化方式:电喷雾电离(ESI⁺/ESI⁻);喷雾电压:3.5 kV;离子传输管温度:325 ℃;汽化温度:350 ℃;鞘气压(N_2):275.8 kPa;辅助气压(N_2):68.95 kPa;S-Lens:55 V;HCD 碰撞气:氮气;仪器采用包含咖啡因、MRFA、ultramark 1621 的乙腈溶液作为校正液进行外标校正。分辨率:全扫描(MS¹)为70 000 FWHM,二级扫描(MS²)为17 500 FWHM。

扫描方式:DDA(Data Dependent Acquisition 数据依赖采集);首先进行全扫描(MS¹),若全扫描中出现母离子列表当中的化合物,且质量偏差在5内,响应大于阈值2.0e³,则在下一个扫描点触发 HCD 二级碎裂,二级碎裂的归一化碰撞能量为40±20,隔离宽度为 m/z 2.0,动态排除为5 s,Apex Trigger 为2~5 s。

2.3 对照品溶液制备

取经过检测的5类型片剂和5类胶囊剂2倍服用量混合(基本涵盖市面上中药饮片和保健品片剂和胶囊剂的辅料类型)作为阴性样品。取1 g至1 000 mL量瓶中,加入体积分数80%甲醇水溶液溶解并稀释至刻度,作为空白基质溶液。再取各对照品适量(称样量见表1),用基质溶液溶解并稀释至刻度,制成质量浓度均约为1 μg·mL⁻¹的混合对照品贮备液,分别精密吸取此贮备液0.1、1、10、50 mL,至100 mL量瓶中,用基质溶液稀释至刻度,摇匀,得到约为500、100、10、1 ng·mL⁻¹的对照品溶液,再取1 ng·mL⁻¹对照品溶液1、10、50 mL,至100 mL量瓶中,用基质溶液稀释至刻度,摇匀,得到质量浓度约为0.5、0.1、0.01 ng·mL⁻¹的对照品溶液,制得系列混合对照品溶液。

2.4 样品制备

取保健品胶囊或片剂1次服用量,研细,置25 mL量瓶中,加体积分数80%甲醇水溶液超声15 min 溶解,并用体积分数80%甲醇水溶液稀释至刻度,摇匀,0.22 μm 微孔滤膜滤过,取续滤液稀释100~1 000倍,即得。

3 方法学考察及结果

3.1 空白基质干扰

取空白基质溶液和混合对照品溶液测定,空白基质溶液提取离子色谱图,无空白基质干扰。

3.2 线性

精密吸取系列浓度混合对照品溶液5 μL进样,每个浓度进样3次,峰面积取平均值。以峰面积(Y)为纵坐标,以对照品质量浓度(ρ,ng·mL⁻¹)为横坐标进行线性回归分析,记录相关系数 r^2 均大于0.991 0,显示了良好的线性关系;回归方程、相关系数、线性范围见表2。以 S/N≈10 作为定量限见表2,提取离子流色谱图见图1~2。

3.3 检出限

考察方法的灵敏度,混合对照品贮备液适量,逐步稀释后进样,以信噪比 S/N 大于等于3且能得到与标准谱图相对应的二级质谱图(MS/MS)的最低浓度,作为检测限浓度,计算检测限,结果见表2,检出限在0.01~0.1 ng·mL⁻¹之间,表明本方法具有很高的灵敏度。

表 2 中药保健品化学药品检测中各化合物的线性关系、线性相关系数及检测限测定结果

Tab. 2 Linear relationships，linear correlation coefficient and detection of limit of each compound in the detection of adulterantsin health product

Analyte	Linearity range/ng·mL^{-1}	Linear equation	r^2	LOD/ng·mL^{-1}	LOQ/ng·mL^{-1}
Alprazolam	0.1 – 500	$Y = 5\,356\,240X + 732\,045$	0.999 9	0.01	0.1
Amobarbital	1 – 500	$Y = 175\,316X + 671\,700$	0.999 1	0.1	1
Barbital	0.1 – 500	$Y = 5\,356\,240X - 7\,320\,450$	0.999 9	0.01	0.1
Chlormezanone	1 – 500	$Y = 1\,708\,690X + 3\,196\,580$	0.999 8	0.1	1
Clonazepam	0.1 – 500	$Y = 204\,892X - 3\,384\,360$	0.998 5	0.01	0.1
Clorazepate	0.1 – 500	$Y = 2\,226\,620X + 6\,264\,300$	0.999 4	0.01	0.1
Diazepam	0.1 – 500	$Y = 2\,328\,540X - 1\,047\,620$	0.998 8	0.01	0.1
Estazolam	0.1 – 500	$Y = 7\,228\,440X + 1\,020\,660$	0.999 7	0.01	0.1
Lorazepam	0.1 – 500	$Y = 58\,438.2X - 84\,706.1$	0.999 8	0.01	0.1
Midazolam	0.1 – 500	$Y = 2\,133\,820X + 7\,730\,710$	0.998 9	0.01	0.1
Mogadan	0.1 – 500	$Y = 4\,143\,850X + 1\,727\,970$	0.998 4	0.01	0.1
Oxazepam	0.1 – 500	$Y = 13\,412\,200X + 98\,455\,300$	0.996	0.01	0.1
Phenobarbital	0.1 – 500	$Y = 3\,817\,790X - 1\,454\,400$	0.999 2	0.01	0.1
Secobarbital	0.1 – 500	$Y = 10\,055\,200X + 3.795\,21$	0.999	0.01	0.1
Sinomenine	0.1 – 500	$Y = 3\,310\,680X + 3\,475\,580$	0.999 8	0.01	0.1
Triazolam	0.1 – 500	$Y = 4.544\,34X + 3.139\,55$	0.995 59	0.01	0.1
Zaleplon	0.1 – 500	$Y = 1\,887\,910X + 4\,914\,020$	0.999 4	0.01	0.1
Zopiclone	1 – 500	$Y = 20\,307\,170X + 8\,696\,080$	1	0.1	1
Beclomethasone dipropionate	0.1 – 500	$Y = 6\,563\,170X - 26\,962\,100$	0.999 1	0.01	0.1
Clobetasol propionate	0.1 – 500	$Y = 377\,466X - 1\,642\,740$	0.999 8	0.01	0.1
Cortisol	0.1 – 500	$Y = 6\,647\,130X + 43\,588\,300$	0.996 5	0.01	0.1
Cortisone acetate	0.1 – 500	$Y = 292\,398X + 871\,754$	0.999 8	0.01	0.1
Dexamethasone acetate	0.1 – 500	$Y = 4\,104\,620X + 37\,427\,100$	0.994 5	0.01	0.1
Fluocinonide	0.1 – 500	$Y = 16\,559\,100X + 3\,162\,220$	0.999 8	0.01	0.1
Halcinonide	0.1 – 500	$Y = 3\,077\,760X + 1\,798\,400$	0.999 9	0.01	0.1
Hydrocortisone acetate	0.1 – 500	$Y = 4\,832\,140X - 4\,322\,610$	0.999 6	0.01	0.1
Metacortandracin	0.1 – 500	$Y = 2\,954\,500X + 18\,407\,900$	0.997 3	0.01	0.1
Methylprednisolone	0.1 – 500	$Y = 5\,509\,800X + 27\,805\,000$	0.998 2	0.01	0.1
Prednisone acetate	0.1 – 500	$Y = 1\,258\,460X + 5\,545\,110$	0.999 1	0.01	0.1
Triamcinolone	0.1 – 500	$Y = 1\,394\,900X - 4\,328\,660$	0.999 5	0.01	0.1
Triamcinolone acetonide acetate	0.1 – 500	$Y = 1\,203\,560X + 3\,732\,380$	0.999 2	0.01	0.1
Bumetanide	0.1 – 500	$Y = 1\,464\,150X - 6\,647\,340$	0.999 3	0.01	0.1
Bupropion	0.1 – 500	$Y = 13\,140\,400X + 125\,143\,000$	0.994 6	0.01	0.1
Caffeine	0.1 – 500	$Y = 1\,517\,020X + 544\,553$	1	0.01	0.1
Ephedrine	0.1 – 500	$Y = 1\,031\,450X + 3\,595\,570$	0.998 9	0.01	0.1
Fenfluramine	0.1 – 500	$Y = 637\,070X + 508\,955$	0.999 9	0.01	0.1
Fluoxetine	1 – 500	$Y = 635\,824X + 392\,938$	0.999 9	0.1	1
Furosemide	0.1 – 500	$Y = 4\,121\,870X + 45\,756\,600$	0.992 4	0.01	0.1
Phenolphthalein	0.1 – 500	$Y = 1\,204\,420X - 919\,084$	1	0.01	0.1
Sertraline	0.1 – 500	$Y = 2\,486\,880X + 8\,495\,190$	0.999 5	0.01	0.1
Sibutramine	0.1 – 500	$Y = 88\,379X + 10\,753\,000$	0.993 2	0.01	0.1
Diaben	0.1 – 500	$Y = 4\,698\,030X + 21\,124\,800$	1	0.01	0.1
Glibenclamide	0.1 – 500	$Y = 4\,520\,970X - 1\,368\,250$	1	0.01	0.1
Glibornuride	0.1 – 500	$Y = 15\,375\,200X + 134\,200\,000$	0.995 3	0.01	0.1
Gliclazide	0.1 – 500	$Y = 2\,239\,750X - 57\,812.2$	1	0.01	0.1
Glimepiride	0.1 – 500	$Y = 1\,847\,730X - 5\,135\,810$	0.999 6	0.01	0.1
Glipizide	0.1 – 500	$Y = 5\,551\,000X + 20\,043\,600$	0.999 5	0.01	0.1
Gliquidone	0.1 – 500	$Y = 282\,106X - 673\,500$	1	0.01	0.1
Pioglitazone	0.1 – 500	$Y = 1\,563\,700X + 737\,550$	0.999 9	0.01	0.1
Atenolol	0.1 – 500	$Y = 196\,898X - 1\,757\,030$	0.998 7	0.01	0.1
Benidipine	0.1 – 500	$Y = 2\,795\,240X - 13\,032\,900$	0.998 8	0.01	0.1
Bisoprolol	0.1 – 500	$Y = 1\,918\,280X - 4\,300\,000$	0.999 8	0.01	0.1
Candesartan cilexetil	0.1 – 500	$Y = 6\,365\,520X + 1\,693\,260$	0.999 1	0.01	0.1
Captopril	1 – 500	$Y = 3.243\,59X - 12\,729\,100$	0.999 2	0.1	1

Analyte	Linearity range/ng·mL^{-1}	Linear equation	r^2	LOD/ng·mL^{-1}	LOQ/ng·mL^{-1}
Clonidine	0.1－500	$Y = 2\ 740\ 520X - 8\ 373\ 220$	0.999 8	0.01	0.1
Dihydrochlorothiazide	0.1－500	$Y = 2\ 359\ 970X + 2\ 310\ 590$	0.999 6	0.01	0.1
Irbesartan	0.1－500	$Y = 1\ 148\ 860X - 1\ 257\ 640$	1	0.01	0.1
Lacidipine	0.1－500	$Y = 4\ 402\ 480X - 6\ 479\ 870$	0.999 9	0.01	0.1
Lisinopril	0.1－500	$Y = 1\ 751\ 920X - 2\ 471\ 180$	0.999 9	0.01	0.1
Metoprolol	0.1－500	$Y = 1\ 548\ 460X + 2\ 140\ 000$	0.999 8	0.01	0.1
Micardis	0.1－500	$Y = 2\ 391\ 620X - 5\ 402\ 850$	0.999 9	0.01	0.1
Minoxidil	0.1－500	$Y = 632\ 489X + 149\ 839$	0.999 9	0.01	0.1
Nifedipine	1－500	$Y = 10\ 372\ 400X - 1\ 488\ 060$	0.999 9	0.1	1
Quinapril	0.1－500	$Y = 607\ 646X + 904\ 054$	0.999 8	0.01	0.1
Reserpine	0.1－500	$Y = 175\ 129X + 1\ 269\ 970$	0.996 3	0.01	0.1
Sotalol	0.1－500	$Y = 495\ 306X - 4\ 260\ 460$	0.997 2	0.01	0.1
Terazosin	0.1－500	$Y = 2\ 199\ 610X + 5\ 466\ 400$	0.999 8	0.01	0.1
Troxerutin	1－500	$Y = 2\ 264\ 250X - 15\ 558\ 000$	0.997 4	0.1	1
Valsartan	0.1－500	$Y = 1\ 756\ 980X + 8\ 005\ 220$	0.998 6	0.01	0.1
Atorvastatin	0.1－500	$Y = 1\ 253\ 040X + 1\ 262\ 650$	0.999 9	0.01	0.1
Bezafibrate	0.1－500	$Y = 9\ 112\ 880X + 58\ 616\ 800$	0.997 3	0.01	0.1
Fenofibrate	0.1－500	$Y = 2\ 266\ 060X + 10\ 664\ 400$	0.998 1	0.01	0.1
Fluvastatin	1－500	$Y = 8\ 246\ 340X + 94\ 931\ 200$	0.991 7	0.1	1
Gemfibrozil	1－500	$Y = 6\ 321\ 600X + 28\ 639\ 900$	0.998 5	0.1	1
Lovastatin	0.1－500	$Y = 3\ 881\ 080X + 199\ 920$	1	0.01	0.1
Pravastatin	0.1－500	$Y = 7\ 676\ 920X + 6\ 698\ 190$	0.996	0.01	0.1
Rosuvastatin	0.1－500	$Y = 119\ 418X - 1\ 176\ 610$	0.998 3	0.01	0.1
Simvastatin	0.1－500	$Y = 9\ 528\ 490X - 15\ 350\ 200$	0.999 9	0.01	0.1
Carbamazepine	0.1－500	$Y = 3\ 205\ 440X - 4\ 568\ 840$	0.999 9	0.01	0.1
Aciclovir	0.1－500	$Y = 12\ 038\ 800X + 97\ 450\ 200$	0.995 1	0.01	0.1
Famciclovir	0.1－500	$Y = 229\ 415X - 666\ 480$	0.999 5	0.01	0.1
Lamivudine	0.1－500	$Y = 1\ 930\ 100X + 9\ 681\ 430$	0.998	0.01	0.1
Nevirapine	0.1－500	$Y = 9\ 043\ 470X + 69\ 354\ 100$	0.996 5	0.01	0.1
Zidovudine	0.1－500	$Y = 5\ 502\ 960X - 5\ 406\ 270$	1	0.01	0.1
Bambuterol	0.1－500	$Y = 1\ 841\ 630X + 627\ 448$	0.999 9	0.01	0.1
Benproperine	0.1－500	$Y = 2\ 944\ 840X - 4\ 325\ 840$	0.999 9	0.01	0.1
Clenbuterol	0.1－500	$Y = 1\ 127\ 280X - 620\ 600$	0.998 8	0.01	0.1
Clorprenaline	0.1－500	$Y = 17\ 889\ 200X - 2\ 489\ 860$	0.999 9	0.01	0.1
Dextromethorphan	0.1－500	$Y = 3\ 563\ 960X - 6\ 225\ 620$	0.999 9	0.01	0.1
Diphenhydramine	0.1－500	$Y = 1\ 920\ 950X - 6\ 489\ 780$	0.999 7	0.01	0.1
Diprophylline	0.1－500	$Y = 3\ 324\ 380X - 12\ 893\ 000$	0.999 2	0.01	0.1
Doxofylline	0.1－500	$Y = 1\ 029\ 880X + 378\ 651$	0.999 9	0.01	0.1
Hydroxyethyltheophylline	0.1－500	$Y = 245\ 216X - 1\ 448\ 790$	0.997 6	0.01	0.1
Pentoxyverine	0.1－500	$Y = 2\ 439\ 860X + 1\ 167\ 870$	0.998 7	0.01	0.1
Procaterol	0.1－500	$Y = 7\ 675\ 190X + 7\ 287\ 490$	0.995 7	0.01	0.1
Salbutamol	0.1－500	$Y = 2\ 104\ 720X + 2\ 642\ 190$	0.999 8	0.01	0.1
Sulfamethoxazole	0.1－500	$Y = 1\ 374\ 540X - 6\ 850\ 450$	0.998 7	0.01	0.1
Theophylline	1－500	$Y = 2\ 751\ 520X + 1\ 241\ 490$	0.998 6	0.1	1
Acetaminophen	0.1－500	$Y = 724\ 631X + 6\ 730\ 970$	0.996 6	0.01	0.1
Butazodine	0.1－500	$Y = 2\ 469\ 640X - 67\ 432$	1	0.01	0.1
Dexamethasone	0.1－500	$Y = 14\ 222\ 210X - 2\ 362\ 330$	0.999 9	0.01	0.1
Diclofenac	0.1－500	$Y = 44\ 940\ 870X + 53\ 251\ 000$	0.992 7	0.01	0.1
Indometacin	1－500	$Y = 1\ 268\ 570X + 3\ 535\ 890$	0.999 8	0.1	1
Piroxicam	0.1－500	$Y = 6\ 307\ 040X - 12\ 940\ 300$	0.999 8	0.01	0.1
Trimethoprim	0.1－500	$Y = 758\ 593X + 4\ 463\ 280$	0.997 8	0.01	0.1
Amino tadalafil	0.1－500	$Y = 2\ 490\ 910X - 6\ 206\ 140$	0.999 7	0.01	0.1
Homo sildenafil	0.1－500	$Y = 5\ 032\ 150X - 4\ 687\ 690$	0.999 9	0.01	0.1
Hydroxyhomo sildenafil	0.1－500	$Y = 6\ 198\ 060X + 7\ 996\ 970$	0.990 1	0.01	0.1
Norneosildenafil	0.1－500	$Y = 224\ 794X - 1\ 278\ 510$	0.999 5	0.01	0.1
Pseudovardenafil	0.1－500	$Y = 1\ 776\ 450X - 5\ 791\ 140$	0.999 3	0.01	0.1
Sildenafil	0.1－500	$Y = 809\ 263X + 11\ 087\ 800$	0.990 8	0.01	0.1
Tadalafil	0.1－500	$Y = 2\ 771\ 460X + 4\ 512\ 100$	0.999 7	0.01	0.1
Thioaildenafil	0.1－500	$Y = 590\ 600X - 863\ 466$	0.999 9	0.01	0.1
Vardenafil	0.1－500	$Y = 3\ 007\ 693X - 21\ 793\ 300$	0.991 3	0.01	0.1

alprazolam *m/z* 309.090 15

amobarbital *m/z* 225.124 5

barbital *m/z* 183.077 5

chlormezanone m/z 274.029 92

chlormezanone *m/z* 316.048 35

chlormezanone *m/z* 315.053 1

diazepam *m/z* 285.078 92

estazolam *m/z* 295.074 5

loazepam *m/z* 321.019 21

midazolam *m/z* 336.085 48

mogadan *m/z* 282.087 32

oxazepam *m/z* 287.058 18

phenobarbital *m/z* 231.077 52

secobarbital *m/z* 237.124 47

sinomenine *m/z* 330.169 98

triazolam *m/z* 343.051 18

zaleplon *m/z* 306.134 94

zopiclone *m/z* 389.112 34

beclomethasone dipropionate *m/z* 521.230 06

clobetasol propionate *m/z* 467.199 51

cortisol *m/z* 363.216 6

cortisone acetate *m/z* 403.211 52

dexamethasone Acetate *m/z* 435.217 74

fluocinonide *m/z* 495.218 89

t / min

halcinonide *m/z* 455.199 51

hydrocortisoneacetate *m/z* 405.227 17

metacortandracin *m/z* 359.185 3

methylprednisolone *m/z* 375.216 6

prednisoneacetate *m/z* 401.195 87

triamcinolone *m/z* 395.186 44

triamcinoloneacetonideacetate *m/z* 477.228 31

bumetanide *m/z* 365.116 57

bupropion *m/z* 240.114 97

caffeine *m/z* 195.087 65

ephedrine *m/z* 166.122 64

fenfluramine *m/z* 232.130 76

fluoxetine *m/z* 310.141 33

furosemide *m/z* 329.000 44

phenolphthalein *m/z* 319.096 49

sertraline *m/z* 306.081 08

sibutramine *m/z* 280.182 65

diaben *m/z* 271.111 09

glibenclamide *m/z* 494.151 1

glibornuride *m/z* 367.168 6

gliclazide *m/z* 324.137 64

glimepiride *m/z* 491.232 27

glipizide *m/z* 446.185 65

gliquidone *m/z* 528.216 28

t / min

pioglitazone *m/z* 357.126 74

atenolol *m/z* 267.170 31

benidipine *m/z* 506.228 56

bisoprolol *m/z* 326.232 58

candesartan cilexetil *m/z* 611.261 26

captopril *m/z* 218.084 54

clonidine *m/z* 230.024 63

dihydrochlorothiazide *m/z* 295.957 2

irbesartan *m/z* 429.239 74

lacidipine *m/z* 456.238 06

lisinopril *m/z* 406.233 65

metoprolol *m/z* 268.190 72

micardis *m/z* 515.244 15

minoxidil *m/z* 210.134 94

nifedipine *m/z* 347.123 76

quinapril *m/z* 439.222 74

reserpine *m/z* 609.280 66

sotalol *m/z* 273.126 74

terazosin *m/z* 388.197 93

troxerutin *m/z* 743.239 31

valsartan *m/z* 436.234 32

atorvastatin *m/z* 559.260 28

bezafibrate *m/z* 362.115 36
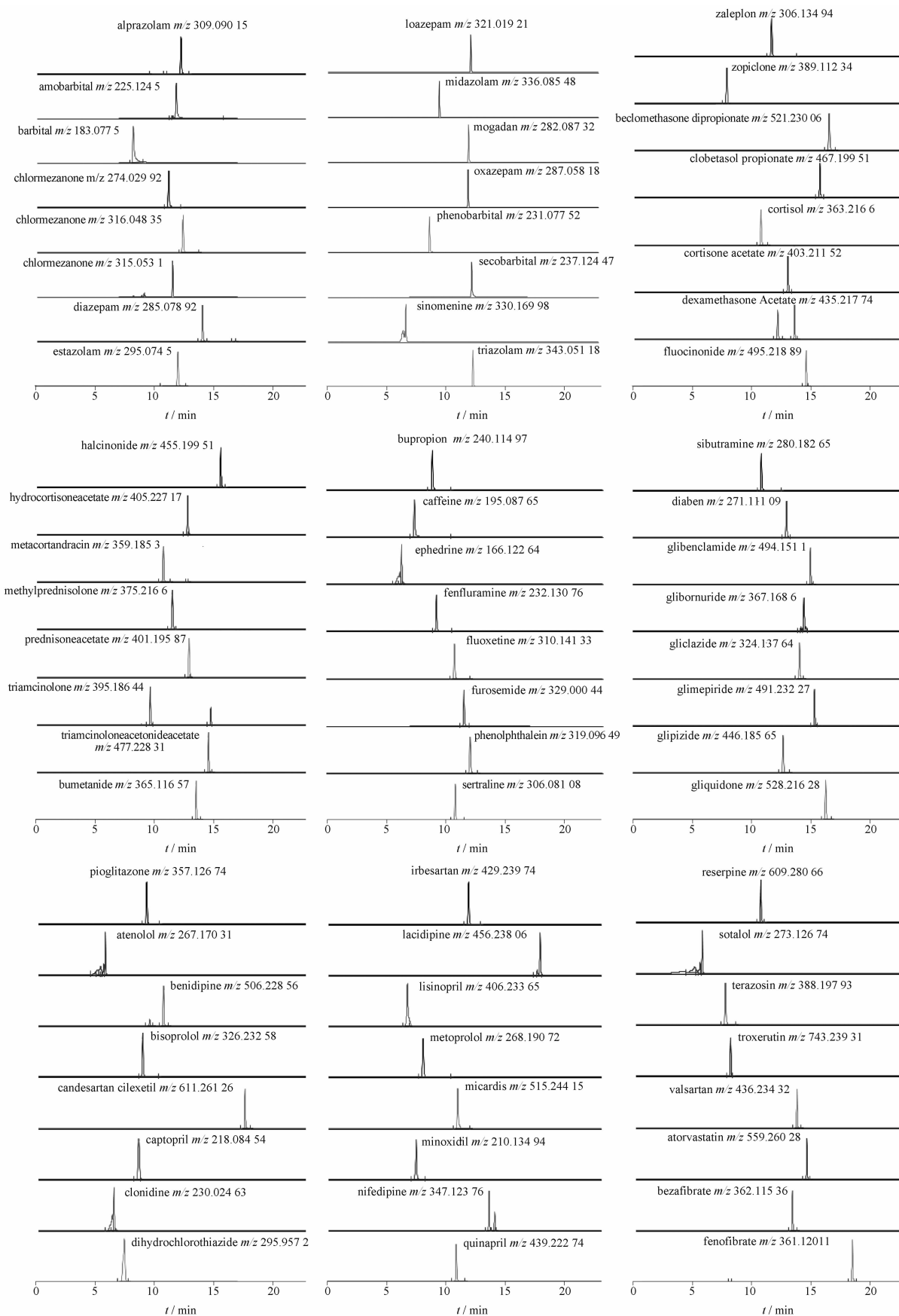
fenofibrate *m/z* 361.120 11

t / min

图 1 中药保健品化学药品检测中 72 种化合物提取离子流色谱图

Fig. 1 Extracting ion chromatograms of 72 compounds in the detection of adulterantsin health product
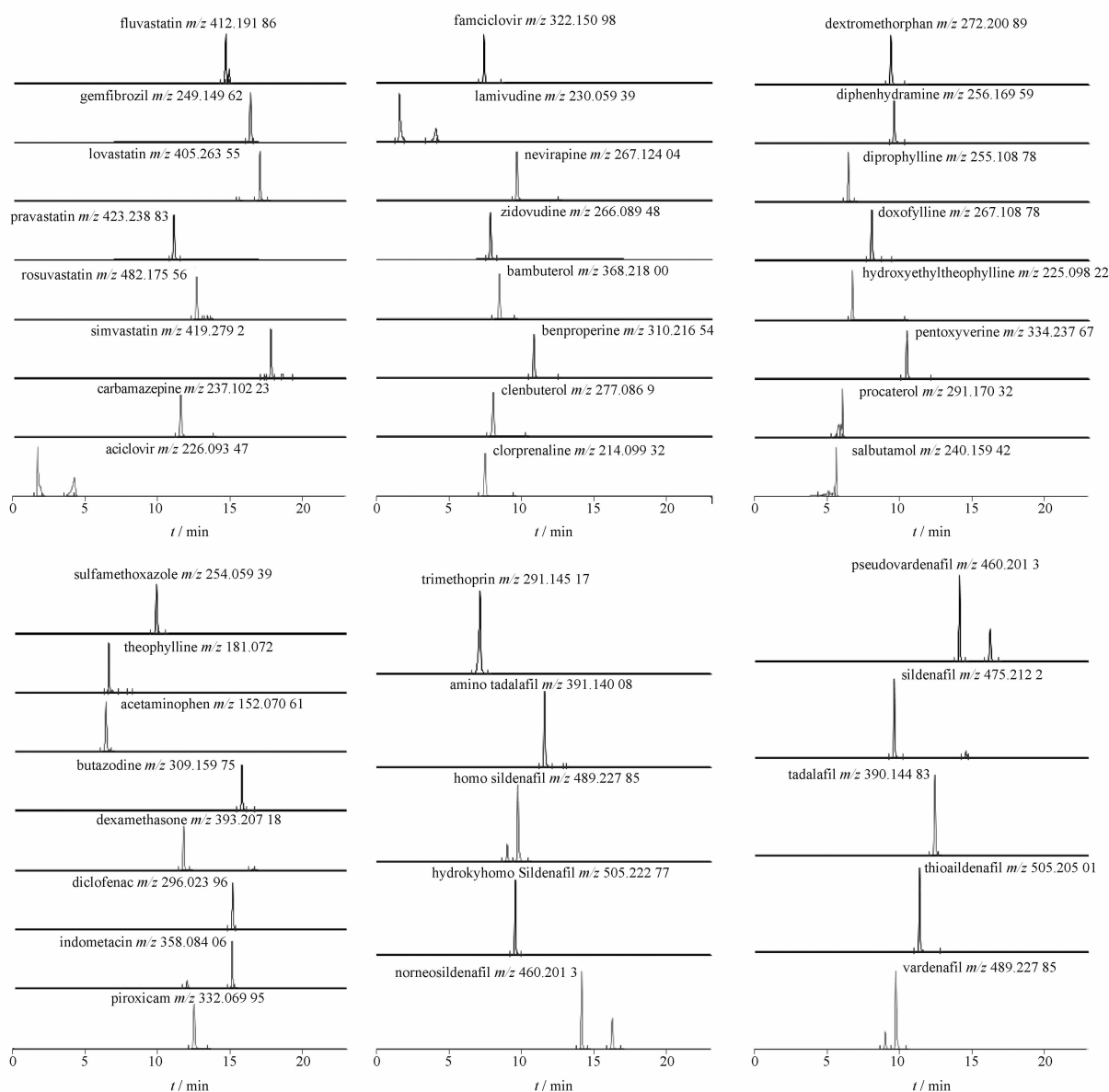
图 2 中药保健品化学药品检测中 42 种化合物提取离子流色谱图

Fig. 2 Extracting ion chromatograms of 42 compounds in the detection of adulterantsin health product

3.4 重复性

取 1 ng · mL^{-1} 对照品溶液,重复进样 5 次,记录峰面积计算精密度,各组分精密度均 <10% ,精密度良好。

3.5 回收率

取阴性样品 18 份,分别采用加样回收率方法测定加入各对照品适量,用体积分数 80% 甲醇超声溶解,并定量稀释至定量限为 0.1 mg · kg^{-1} 的化合物含量分别为低(0.1 mg · kg^{-1})、中(1 mg · kg^{-1})、高(10 mg · kg^{-1})3 个水平,以及定量限为 1 mg · kg^{-1} 的化合物含量分别为低(1 mg · kg^{-1})、中(5 mg · kg^{-1})、高(10 mg · kg^{-1})3 个水平,每个水平混合标准溶液各 6 份,分别进样,记录峰面积以外标法计算回收率,结果见表 3,4。

3.6 供试品的测定

取"2.4"项下方法制备的供试品溶液 5 μL,按"2.1"和"2.2"项下方法测定。在 10 种保健食品类中共检出 3 批阳性样品,其中,1 批检出格列本脲、厄贝沙坦,含量分别为 8.6 和 4.6 mg · kg^{-1};2 批检出西地那非,含量分别为 0.8 和 1.3 mg · kg^{-1}。

4 讨 论

4.1 流动相选择

考察色谱条件中的甲醇、乙腈、甲酸水、乙酸

表3 中药保健品化学药品检测中定量限为 0.1 mg·kg⁻¹ 化合物三水平准确度（以回收率表示）测定结果

Tab. 3 Three-level accuracy of compound with quantitative limit of 0.1 mg·kg⁻¹ in the detection of adulterants in health product(expressed in recovery rate)

Analyte	Average recovery rate/% (0.1 mg·kg⁻¹)	RSD /%	Average recovery rate/% (1 mg·kg⁻¹)	RSD /%	Average recovery rate/% (10 mg·kg⁻¹)	RSD /%
Alprazolam	94.0	3.6	94.7	8.6	101.8	5.4
Barbital	89.5	8.1	110.8	7.9	105.9	9.1
Clonazepam	60.7	9.7	93.1	5.1	91.8	6.7
Clorazepate	58.1	8.8	91.8	6.7	100.8	8.8
Diazepam	63.6	5.1	104.8	4.7	117.3	2.4
Estazolam	58.2	5.3	84.4	4.6	98.3	6.2
Lorazepam	72.4	8.8	98.2	5.0	93.9	5.3
Midazolam	70.8	4.6	93.9	5.3	92.2	8.6
Mogadan	64.8	1.8	103.5	7.0	101.4	0.8
Oxazepam	91.6	7.6	101.4	0.8	112.5	4.0
Phenobarbital	80.3	1.1	112.5	4.0	112.8	3.3
Secobarbital	61.3	0.3	85.9	5.1	101.0	3.2
Sinomenine	63.8	1.5	102.8	6.8	93.6	4.3
Triazolam	64.7	7.8	98.0	5.8	111.5	8.7
Zaleplon	96.5	8.1	113.6	8.1	96.4	3.6
Beclomethasone dipropionate	90.9	3.6	95.4	7.4	109.2	3.5
Clobetasol propionate	90.9	0.3	84.6	4.7	85.2	5.7
Cortisol	75.2	0.1	90.0	8.8	100.9	1.4
Cortisone acetate	70.9	0.5	108.8	6.1	90.7	4.1
Dexamethasone acetate	82.7	2.1	96.8	4.8	106.6	7.7
Fluocinonide	72.1	0.1	114.3	7.1	100.8	7.5
Halcinonide	74.6	0.9	97.7	6.7	94.7	2.7
Hydrocortisone acetate	71.8	8.3	97.2	5.4	107.2	4.3
Metacortandracin	97.1	0.9	103.3	3.8	105.1	4.7
Methylprednisolone	78.6	0.5	105.4	2.8	106.1	8.4
Prednisone acetate	71.8	1.7	107.0	7.6	101.5	8.3
Triamcinolone	60.6	2.8	97.3	8.5	102.1	1.4
Triamcinolone acetonide acetate	115.6	1.5	84.3	7.2	108.7	1.4
Bumetanide	103.9	5.4	102.6	5.7	103.8	7.8
Bupropion	109.4	2.9	86.7	6.9	112.6	1.3
Caffeine	80.1	2.1	107.0	4.9	95.7	6.8
Ephedrine	69.3	4.4	100.7	2.7	101.1	4.8
Fenfluramine	116.4	1.0	103.6	5.3	94.4	3.9
Furosemide	87.8	1.3	98.8	5.2	109.3	6.1
Phenolphthalein	65.8	3.5	111.6	6.5	100.0	2.3
Sertraline	78.4	4.8	93.1	6.0	104.1	2.5
Sibutramine	79.8	4.8	98.8	5.7	96.2	1.8
Diaben	115.9	5.5	111.5	4.3	92.1	4.0
Glibenclamide	107.5	4.6	91.2	5.8	103.3	1.6
Glibornuride	111.7	4.2	94.4	4.3	105.3	3.0
Gliclazide	85.7	0.6	105.9	3.4	107.1	1.0
Glimepiride	94.7	4.7	100.7	11.8	109.4	7.7
Glipizide	119.3	1.5	88.1	6.1	88.8	7.2
Gliquidone	98.0	2.1	95.2	10.0	102.1	5.4
Pioglitazone	113.2	4.5	92.5	6.5	93.2	3.7
Atenolol	102.4	5.6	97.0	6.1	87.2	2.5
Benidipine	117.2	8.7	87.2	2.5	113.9	2.2
Bisoprolol	108.2	3.7	86.2	0.1	104.1	1.8
Candesartan cilexetil	111.5	2.0	88.3	5.2	97.2	5.5
Clonidine	115.0	1.9	86.3	4.2	101.8	9.2
Dihydrochlorothiazide	105.4	2.9	85.8	7.4	95.8	0.8
Irbesartan	108.2	3.7	91.1	8.8	99.7	5.9
Lacidipine	100.7	1.9	94.0	4.3	99.4	8.9
Lisinopril	91.1	4.5	90.4	6.3	107.1	8.4
Metoprolol	98.7	5.4	92.6	5.3	99.0	8.9
Micardis	60.7	7.1	96.8	7.2	103.8	1.2
Minoxidil	102.2	4.5	89.5	6.2	97.8	5.1
Quinapril	60.2	0.4	91.2	6.8	97.6	2.9

Analyte	Average recovery rate/% (0.1 mg·kg⁻¹)	RSD /%	Average recovery rate/% (1 mg·kg⁻¹)	RSD /%	Average recovery rate/% (10 mg·kg⁻¹)	RSD /%
Reserpine	59.4	2.4	97.5	8.4	99.6	9.6
Sotalol	120.4	5.4	111.8	7.6	84.6	0.4
Terazosin	111.5	4.5	84.6	0.4	102.8	8.1
Valsartan	69.9	8.5	90.5	7.8	91.8	4.5
Atorvastatin	71.1	3.7	97.4	10.3	100.2	3.5
Bezafibrate	82.7	10.4	100.9	5.7	109.3	5.6
Fenofibrate	86.4	1.5	109.1	5.5	102.1	9.0
Lovastatin	62.9	4.9	102.8	4.0	98.3	2.7
Pravastatin	94.8	5.2	95.4	4.9	96.1	2.8
Rosuvastatin	89.3	3.8	116.5	4.2	111.4	3.8
Simvastatin	116.7	15.7	107.1	4.4	99.6	1.0
Carbamazepine	92.8	1.3	85.4	7.3	105.8	1.7
Aciclovir	102.0	4.2	90.3	6.7	113.4	4.9
Famciclovir	91.5	3.2	111.7	5.7	100.1	7.9
Lamivudine	67.0	8.5	85.2	4.5	108.3	6.5
Nevirapine	91.8	0.5	105.9	7.4	97.1	8.3
Zidovudine	107.5	3.6	104.8	5.8	98.3	8.6
Bambuterol	83.9	4.3	90.1	8.0	95.7	6.3
Benproperine	86.1	1.0	88.6	7.6	103.9	5.0
Clenbuterol	93.0	4.6	87.5	7.8	89.7	5.7
Clorprenaline	119.7	6.9	87.8	6.2	98.5	8.8
Dextromethorphan	96.4	1.8	86.9	6.8	100.8	5.4
Diphenhydramine	109.9	6.2	90.4	5.5	97.4	1.6
Diprophylline	114.0	3.4	87.1	6.5	101.1	8.7
Doxofylline	96.6	3.6	92.3	6.9	104.2	9.9
Hydroxyethyltheophylline	85.9	1.6	101.9	6.4	84.6	2.2
Pentoxyverine	91.5	3.2	84.3	11.7	101.4	8.1
Procaterol	67.0	8.5	99.2	10.4	110.6	5.6
Salbutamol	91.8	0.5	108.8	7.0	93.6	5.7
Sulfamethoxazole	107.5	3.6	98.4	6.2	101.8	6.4
Acetaminophen	86.1	1.0	109.5	5.3	104.5	8.5
Butazodine	93.0	4.6	109.9	4.5	101.6	3.4
Dexamethasone	108.8	3.3	96.4	5.7	104.6	2.0
Diclofenac	96.4	1.8	93.1	4.1	106.6	2.9
Piroxicam	120.0	3.4	98.5	3.5	101.7	3.3
Trimethoprim	96.6	3.6	91.1	5.5	105.3	6.9
Amino tadalafil	85.9	1.6	102.7	7.6	108.8	7.4
Homo sildenafil	72.1	5.2	88.7	4.7	95.4	1.7
Hydroxyhomo sildenafil	64.4	8.3	90.8	5.6	103.8	9.2
Norneosildenafil	108.6	5.0	109.6	4.9	90.0	9.3
Pseudovardenafil	88.9	3.8	89.4	6.7	112.1	2.8
Sildenafil	89.4	0.9	89.5	8.5	99.1	5.8
Tadalafil	72.2	9.9	103.4	6.8	92.8	9.9
Thioaildenafil	62.2	7.1	98.2	6.2	105.5	5.8
Vardenafil	59.1	1.6	93.0	7.1	86.3	5.5

表 4 中药保健品化学药品检测中定量限为 1 mg·kg⁻¹化合物三水平准确度(以回收率表示)测定结果

Tab. 4 Three-level accuracy of compound with quantitative limit of 1 mg·kg⁻¹ in the detection of adulterantsin health product(expressed in recovery rate)

Analyte	Average recovery rate/% (1 mg·kg⁻¹)	RSD /%	Average recovery rate/% (5 mg·kg⁻¹)	RSD /%	Average recovery rate/% (10 mg·kg⁻¹)	RSD /%
Amobarbital	94.0	3.5	101.8	5.4	95.6	8.5
Chlormezanone	90.4	0.8	92.6	4.4	88.1	3.0
Zopiclone	88.7	2.6	100.4	4.8	101.0	4.7
Fluoxetine	110.4	0.8	95.7	2.9	95.0	6.8
Captopril	114.9	3.3	100.5	5.9	111.5	3.9
Nifedipine	74.2	2.2	94.5	5.1	104.9	1.1
Troxerutin	83.6	3.9	92.9	5.8	119.4	0.7
Fluvastatin	80.5	4.9	99.7	9.8	108.2	5.4
Gemfibrozil	88.3	3.9	110.5	3.8	107.0	5.1
Theophylline	83.9	4.3	90.2	6.4	106.9	5.5
Theophylline	83.9	4.3	90.2	6.4	106.9	5.5

铵的洗脱效果,对梯度洗脱程序进行了优化。在电喷雾正离子模式下,加入适量的甲酸可以起到辅助电离,提高了响应的作用,故本方法最终采用0.1%体积比浓度的甲酸作为水相的添加剂;通过分别添加乙腈和甲醇作为有机相,发现使用乙腈时可以获得更好的峰型和更低的本底干扰,故最终选用乙腈作为有机相。

4.2 质谱条件优化

Orbitrap 具有不同的分辨率(17 500、35 000、70 000和140 000 FWHM),分辨率越高可以更好的区分目标化合物与其他质量数相近组分,考虑到筛查和定量的准确性,最终采用 70 000 FWHM 的分辨率作为全扫描分辨率,在该分辨率下,115 种化合物保留时间、准确质量数和碎片离子信息见表5,单次测定在 25 min 内基本分离,且互无干扰,理论质量数与实际测得的质量数相对偏差越小,筛查结果准确度越高。114 种分析物的实测和理论质量数偏差 2 以下为 109 种,3.5 以下为 5 种。采用理论质量数 ±5对目标化合物进行提取离子流(EIC)处理,可以获得有效的选择性。

表5 中药保健品化学药品检测中各化合物分子式、保留时间、质量偏差和二级离子

Tab. 5 Molecular formula, retention time, mass deviation and secondary ions of each compound in the detection of adulterantsin health product

Analyte	Category	Molecular formula	Retention time/min	Accurate mass/[M + H]⁺ or [M − H]⁻		Mass deviation	Precursor ion (m/z)
				Theoretical	Experimental		
Alprazolam	Tranquilize	$C_{17}H_{13}ClN_4$	12. 22	309. 090 15	309. 090 52	1. 2	281. 070 7
Amobarbital	Tranquilize	$C_{11}H_{18}N_2O_3$	11. 81	225. 124 47	225. 124 68	0. 93	182. 117 8
Barbital	Tranquilize	$C_8H_{12}N_2O_3$	8. 19	183. 077 52	183. 077 22	− 1. 64	140. 070 5,94. 915 5
Chlormezanone	Tranquilize	$C_{11}H_{12}ClNO_3S$	11. 18	274. 029 92	274. 030 21	1. 06	209. 06,154. 041 7,102. 985 2
Clonazepam	Tranquilize	$C_{15}H_{10}ClN_3O_3$	12. 39	316. 048 35	316. 048 46	0. 35	270. 055 1,302. 044 8
Clorazepate	Tranquilize	$C_{16}H_{14}ClN_3O$	9. 06	300. 089 82	300. 09	0. 6	274. 092 5,154. 416
Diazepam	Tranquilize	$C_{16}H_{13}ClN_2O$	14. 03	285. 078 92	285. 079 32	1. 4	154. 041 7,193. 088 5
Estazolam	Tranquilize	$C_{16}H_{11}ClN_4$	11. 95	295. 074 5	295. 074 65	0. 51	267. 055 4,205. 075 7
Lorazepam	Tranquilize	$C_{15}H_{10}Cl_2N_2O_2$	12. 22	321. 019 21	321. 019 35	0. 44	275. 013 3,303. 008 2,229. 052 5
Midazolam	Tranquilize	$C_{18}H_{13}ClFN_3$	9. 56	326. 085 48	326. 085 75	0. 83	291. 116 2
Mogadan	Tranquilize	$C_{15}H_{11}N_3O_3$	12. 02	282. 087 32	282. 087 8	1. 7	236. 094 1,180. 080 6
Oxazepam	Tranquilize	$C_{15}H_{11}ClN_2O_2$	11. 97	287. 058 18	287. 058 26	0. 28	241. 052 3,269. 047 1,104. 049 8
Phenobarbital	Tranquilize	$C_{12}H_{12}N_2O_3$	10. 27	231. 077 52	231. 077 96	1. 9	188. 070 7,99. 924 4
Secobarbital	Tranquilize	$C_{12}H_{18}N_2O_3$	12. 29	237. 124 47	237. 124 77	1. 27	194. 117 8,147. 901 4
Sinomenine	Tranquilize	$C_{19}H_{23}NO_4$	6. 72	330. 169 98	330. 170 32	1. 03	239. 070 1,181. 064 6
Triazolam	Tranquilize	$C_{17}H_{12}Cl_2N_4$	12. 39	343. 051 18	343. 051 33	0. 44	308. 081 8,315. 031 8
Zaleplon	Tranquilize	$C_{17}H_{15}N_5O$	11. 69	306. 134 94	306. 135 19	0. 82	236. 092 8,264. 124 1
Zopiclone	Tranquilize	$C_{17}H_{17}ClN_6O_3$	7. 94	389. 112 34	389. 112 95	1. 57	245. 022 2,217. 027 3,139. 005 6
Beclomethasone dipropionate	Hormone	$C_{28}H_{37}ClO_7$	16. 51	521. 230 06	521. 230 96	1. 73	147. 080 3,321. 148
Clobetasol propionate	Hormone	$C_{25}H_{32}ClFO_5$	15. 72	467. 199 51	467. 200 2	1. 48	57. 034
Cortisol	Hormone	$C_{21}H_{30}O_5$	10. 81	363. 216 6	363. 216 55	− 0. 14	121. 064 7
Cortisone acetate	Hormone	$C_{23}H_{30}O_6$	13. 06	403. 211 52	403. 211 49	− 0. 07	147. 080 2
Dexamethasone acetate	Hormone	$C_{24}H_{31}FO_6$	12. 19	435. 217 74	435. 217 99	0. 57	163. 111 5,343. 189 8
Fluocinonide	Hormone	$C_{26}H_{32}F_2O_7$	14. 59	495. 218 89	495. 219 39	1. 01	121. 064 7
Halcinonide	Hormone	$C_{24}H_{32}ClFO_5$	15. 55	455. 199 51	455. 200 13	1. 36	147. 800 7,263. 143 4
Hydrocortisone acetate	Hormone	$C_{23}H_{32}O_6$	12. 77	405. 227 17	405. 227 54	0. 91	147. 080 3
Metacortandracin	Hormone	$C_{21}H_{26}O_5$	10. 73	359. 185 3	359. 185 36	0. 17	147. 080 3,171. 080 2
Methylprednisolone	Hormone	$C_{22}H_{30}O_5$	11. 49	375. 216 6	375. 217 04	1. 17	161. 095 9
Prednisone acetate	Hormone	$C_{23}H_{28}O_6$	12. 9	401. 195 87	401. 196 32	1. 12	121. 064 7,309. 184 3
Triamcinolone	Hormone	$C_{21}H_{27}FO_6$	9. 63	395. 186 44	395. 186 71	0. 68	225. 127,357. 169 1
Triamcinolone acetonide acetate	Hormone	$C_{26}H_{33}FO_7$	14. 52	477. 228 31	477. 228 73	0. 88	121. 064 7
Bumetanide	Slimming	$C_{17}H_{20}N_2O_5S$	13. 49	365. 116 57	365. 116 61	0. 11	240. 138 1,184. 075 6,156. 080 7
Bupropion	Slimming	$C_{13}H_{18}ClNO$	8. 86	240. 114 97	240. 115 02	0. 21	184. 052 3,131. 073,166. 041 8
Caffeine	Slimming	$C_8H_{10}N_4O_2$	7. 36	195. 087 65	195. 087 98	1. 69	138. 066 1
Ephedrine	Slimming	$C_{10}H_{15}NO$	6. 31	166. 122 64	166. 122 63	1. 14	148. 111 8
Fenfluramine	Slimming	$C_{12}H_{16}F_3N$	9. 19	232. 130 76	232. 130 98	0. 95	159. 041 5
Fluoxetine	Slimming	$C_{17}H_{18}F_3NO$	10. 68	310. 141 33	310. 141 33	0	162. 970 3,259. 092 8,148. 111 7
Furosemide	Slimming	$C_{12}H_{11}ClN_2O_5S$	11. 5	329. 000 44	329. 001 53	3. 31	204. 983 8,285. 010 8,77. 964
Phenolphthalein	Slimming	$C_{20}H_{14}O_4$	11. 97	319. 096 49	319. 096 47	− 0. 06	225. 054 3
Sertraline	Slimming	$C_{17}H_{17}Cl_2N$	10. 75	306. 081 08	306. 081 05	− 0. 1	158. 976 2,275. 038 6
Sibutramine	Slimming	$C_{17}H_{26}ClN$	10. 88	280. 182 65	280. 182 8	0. 54	125. 015 4,139. 030 8
Diaben	Hypoglycemic	$C_{12}H_{18}N_2O_3S$	13. 01	271. 111 09	271. 111 27	0. 66	74. 096 4,155. 016 1
Glibenclamide	Hypoglycemic	$C_{23}H_{28}ClN_3O_5S$	15	494. 151 1	494. 151 73	1. 27	169. 005 1,369. 007

Analyte	Category	Molecular formula	Retention time/min	Accurate mass/[M+H]⁺or[M−H]⁻ Theoretical	Accurate mass/[M+H]⁺or[M−H]⁻ Experimental	Mass deviation	Precursor ion (m/z)
Glibornuride	Hypoglycemic	$C_{18}H_{26}N_2O_4S$	14.46	367.168 6	367.169 13	1.44	152.143 4
Gliclazide	Hypoglycemic	$C_{15}H_{21}N_3O_3S$	14.06	324.137 64	324.137 66	0.06	110.096 4,127.123
Glimepiride	Hypoglycemic	$C_{24}H_{34}N_4O_5S$	15.34	491.232 27	491.232 6	0.67	126.091 4,352.132 5
Glipizide	Hypoglycemic	$C_{21}H_{27}N_5O_4S$	12.71	446.185 65	446.186 28	1.41	321.101 5,167.016 2
Gliquidone	Hypoglycemic	$C_{27}H_{33}N_3O_6S$	16.27	528.216 28	528.216 74	0.87	404.115 8,167.016 1,131.060 4
Pioglitazone	Hypoglycemic	$C_{19}H_{20}N_2O_3S$	9.32	357.126 74	357.126 86	0.34	134.096 4
Atenolol	Hypotensive	$C_{14}H_{22}N_2O_3$	5.83	267.170 32	267.170 84	1.95	145.060 47,74.060 8
Benidipine	Hypotensive	$C_{28}H_{31}N_3O_6$	10.73	506.228 56	506.228 97	0.81	91.054 8,174.127 6,315.097
Bisoprolol	Hypotensive	$C_{18}H_{31}NO_4$	9	326.232 59	326.232 64	0.15	116.107 3,74.060 9
Candesartan cilexetil	Hypotensive	$C_{33}H_{34}N_6O_6$	17.63	611.261 26	611.261 78	0.85	423.155 9,207.091 7
Captopril	Hypotensive	$C_9H_{15}NO_3S$	8.64	218.084 54	218.084 7	0.73	70.065 9,116.070 9,75.027 1
Clonidine	Hypotensive	$C_9H_9Cl_2N_3$	6.57	230.024 63	230.025 01	1.65	212.998
Dihydrochlorothiazide	Hypotensive	$C_7H_8ClN_3O_4S_2$	7.45	295.957 2	295.958 19	3.35	77.963 9,204.983 8,268.946 4
Irbesartan	Hypotensive	$C_{25}H_{28}N_6O$	11.89	429.239 74	429.239 99	0.58	207.091 5
Lacidipine	Hypotensive	$C_{26}H_{33}NO_6$	17.87	456.238 06	456.238 22	0.35	400.174 9,354.133
Lisinopril	Hypotensive	$C_{21}H_{31}N_3O_5$	6.75	406.233 65	406.234 01	0.89	80.081 4
Metoprolol	Hypotensive	$C_{15}H_{25}NO_3$	8.09	268.190 72	268.190 95	0.86	116.107 3,74.060 8
Micardis	Hypotensive	$C_{33}H_{30}N_4O_2$	10.98	515.244 15	515.244 45	0.58	276.136 7,497.233 1
Minoxidil	Hypotensive	$C_9H_{15}N_5O$	7.51	210.134 94	210.135 1	0.76	193.132 2,164.093 1,84.081 5
Nifedipine	Hypotensive	$C_{17}H_{18}N_2O_6$	13.59	347.123 76	347.124 15	1.12	254.104 6,195.091 6
Quinapril	Hypotensive	$C_{25}H_{30}N_2O_5$	10.85	439.222 75	439.222 93	0.41	234.148 6,117.070 1
Reserpine	Hypotensive	$C_{33}H_{40}N_2O_9$	10.81	609.280 66	609.280 76	0.16	195.065 1,174.091 3
Sotalol	Hypotensive	$C_{12}H_{20}N_2O_3S$	5.83	273.126 74	273.127 14	1.46	133.076,213.069,255.115 9
Terazosin	Hypotensive	$C_{19}H_{25}N_5O_4$	7.81	388.197 93	388.198 18	0.64	290.160 8,247.118 8,71.05
Troxerutin	Hypotensive	$C_{33}H_{42}O_{19}$	8.23	743.239 31	743.239 2	−0.15	435.128 2,85.029 1
Valsartan	Hypotensive	$C_{24}H_{29}N_5O_3$	13.84	436.234 32	436.234 83	1.17	207.091 5,235.098 3
Atorvastatin	Lipid-lowering	$C_{33}H_{35}FN_2O_5$	14.69	559.260 28	559.260 56	0.5	440.223 8,250.103
Bezafibrate	Lipid-lowering	$C_{19}H_{20}ClNO_4$	13.48	362.115 36	362.115 75	1.08	138.994 5,121.065
Fenofibrate	Lipid-lowering	$C_{20}H_{21}ClO_4$	18.54	361.120 11	361.120 27	0.44	233.036 1,138.994 5
Fluvastatin	Lipid-lowering	$C_{24}H_{26}FNO_4$	14.72	412.191 86	412.192 2	0.82	224.086 7,266.133 6
Gemfibrozil	Lipid-lowering	$C_{15}H_{22}O_3$	16.39	249.149 62	249.150 19	2.29	139.042 3,77.006 3
Lovastatin	Lipid-lowering	$C_{24}H_{36}O_5$	17.06	405.263 55	405.263 85	0.74	199.148 1,173.132 6
Pravastatin	Lipid-lowering	$C_{23}H_{36}O_7$	11.13	423.238 83	423.240 17	3.17	101.059 4,59.012 3
Rosuvastatin	Lipid-lowering	$C_{22}H_{28}FN_3O_6S$	12.71	482.175 56	482.175 84	0.58	258.139 9,300.150 4
Simvastatin	Lipid-lowering	$C_{25}H_{38}O_5$	17.83	419.279 2	419.279 42	0.52	199.148 1,173.132 5
Carbamazepine	Psychotropic	$C_{15}H_{12}N_2O$	11.6	237.102 23	237.102 26	0.13	79.950 6
Aciclovir	Antiviral	$C_8H_{11}N_5O_3$	1.74	226.093 47	226.093 61	0.62	152.056 5
Famciclovir	Antiviral	$C_{14}H_{19}N_5O_4$	7.51	322.150 98	322.151 25	0.84	136.061 7,202.108 5
Lamivudine	Antiviral	$C_8H_{11}N_3O_3S$	1.77	230.059 39	230.059 6	0.91	112.050 4
Nevirapine	Antiviral	$C_{15}H_{14}N_4O$	9.76	267.124 04	267.124 27	0.86	226.084 7
Zidovudine	Antiviral	$C_{10}H_{13}N_5O_4$	7.95	266.089 48	266.090 24	2.86	223.071 8
Bambuterol	Antitussive	$C_{18}H_{29}N_3O_5$	8.55	368.218	368.217 99	−0.03	294.114 6,72.044 4
Benproperine	Antitussive	$C_{21}H_{27}NO$	10.9	310.216 54	310.216 55	0.03	126.128,91.054 4
Clenbuterol	Antitussive	$C_{12}H_{18}Cl_2N_2O$	8.14	277.086 9	277.087 07	0.61	203.013 6,132.068 2,168.044 9
Clorprenaline	Antitussive	$C_{11}H_{16}ClNO$	7.59	214.099 32	214.099 49	0.79	154.041 7,196.088 7,118.065 1
Dextromethorphan	Antitussive	$C_{18}H_{25}NO$	9.45	272.200 89	272.201 05	0.59	215.143 1,147.080 5
Diphenhydramine	Antitussive	$C_{17}H_{21}NO$	9.67	256.169 59	256.169 74	0.59	167.085 6
Diprophylline	Antitussive	$C_{10}H_{14}N_4O_4$	6.52	255.108 78	255.109 1	1.25	181.071 8,124.050 5
Doxofylline	Antitussive	$C_{11}H_{14}N_4O_4$	8.12	267.108 78	267.108 92	0.52	181.072 1,87.044 1,124.050 6
Hydroxyethyltheophylline	Antitussive	$C_9H_{12}N_4O_3$	6.8	225.098 22	225.098 34	0.53	181.072,124.050 6
Pentoxyverine	Antitussive	$C_{20}H_{31}NO_3$	10.55	334.237 67	334.237 85	0.54	100.112 1,72.080 8
Procaterol	Antitussive	$C_{16}H_{22}N_2O_3$	6.12	291.170 32	291.170 72	1.37	273.159 6,231.124 7
Salbutamol	Antitussive	$C_{13}H_{21}NO_3$	5.7	240.159 42	240.159 7	1.17	148.075 6
Sulfamethoxazole	Antitussive	$C_{10}H_{11}N_3O_3S$	9.84	254.059 39	254.059 55	0.63	156.011 4,108.044 4,92.049 5
Theophylline	Antitussive	$C_7H_8N_4O_2$	6.55	181.072	181.072 07	0.39	124.050 6
Acetaminophen	Analgesic	$C_8H_9NO_2$	6.37	152.070 61	152.070 79	1.18	110.06
Butazodine	Analgesic	$C_{19}H_{20}N_2O_2$	15.74	309.159 75	309.159 85	0.32	160.112,120.044 4
Dexamethasone	Analgesic	$C_{22}H_{29}FO_5$	11.71	393.207 18	393.207 43	0.64	147.080 2,237.127 1
Diclofenac	Analgesic	$C_{14}H_{11}Cl_2NO_2$	15.09	296.023 96	296.024 26	1.01	214.041 6,250.018 3
Indometacin	Analgesic	$C_{19}H_{16}ClNO_4$	15.06	358.084 06	358.084 38	0.89	138.994 6
Piroxicam	Analgesic	$C_{15}H_{13}N_3O_4S$	12.46	332.069 95	332.070 04	0.27	95.060 3,121.039 6,164.081 8

续表5（continued）

Analyte	Category	Molecular formula	Retention time/min	Accurate mass/[M + H]⁺or [M − H]⁻ Theoretical	Accurate mass/[M + H]⁺or [M − H]⁻ Experimental	Mass deviation	Precursor ion (m/z)
Trimethoprim	Analgesic	$C_{14}H_{18}N_4O_3$	7.16	291.145 17	291.145 39	0.76	123.066 5,230.116 2
Amino tadalafil	Aphrodisiac	$C_{21}H_{18}N_4O_4$	11.57	391.140 08	391.140 08	0	135.044,269.102 9,262.086
Homo sildenafil	Aphrodisiac	$C_{23}H_{32}N_6O_4S$	9.78	489.227 85	489.228 27	0.86	72.081 6,58.066 1
Hydroxyhomo sildenafil	Aphrodisiac	$C_{23}H_{32}N_6O_5S$	9.58	505.222 77	505.222 99	0.44	99.092 1
Norneosildenafil	Aphrodisiac	$C_{22}H_{29}N_5O_4S$	14.13	460.201 3	460.201 42	0.26	283.118 7,84.081 4
Pseudovardenafil	Aphrodisiac	$C_{22}H_{29}N_5O_4S$	16.25	460.201 3	460.201 63	0.72	169.097,151.086 5
Sildenafil	Aphrodisiac	$C_{22}H_{30}N_6O_4S$	9.65	475.212 2	475.212 43	0.48	58.066 1,100.1
Tadalafil	Aphrodisiac	$C_{22}H_{19}N_3O_4$	12.44	390.144 83	390.144 81	−0.05	135.044,268.107 7
Thioaildenafil	Aphrodisiac	$C_{23}H_{32}N_6O_3S_2$	11.38	505.205 01	505.205 2	0.38	99.092 1,113.107 6
Vardenafil	Aphrodisiac	$C_{23}H_{32}N_6O_4S$	9.78	489.227 85	489.228 27	0.86	169.097,151.086 5

4.3 快速定性筛查数据库的建立

利用四级杆静电场轨道阱串联质谱技术,直接收集了中药保健品中 11 类共 114 种常见化学药物的一级全扫描和二级质谱数据,建立定性、定量筛查方法数据库。在实际样品测定时,可在不使用对照品情况下,直接利用数据库中的一级离子和二级离子的精确质量数及谱图进行初步确证和初步定量,节省检验成本。

结果表明,本实验建立基于高效液相色谱与四级杆静电场轨道阱串联质谱联用技术的分析方法,可同时在 25 min 内对 114 种非法添加成分进行筛查,消除基质干扰,具有快速、准确,专属性高,覆盖面广的特点,可应用于日常中药保健品监管工作中,针对层出不穷的添加手段,严厉打击不法犯罪行为,提供有力支撑。

REFERENCES

［1］ GONG L P, TIAN Z Y, GUO C C, et al. Rapid screening and quantitative detection of 24 illegally added anti-inflammatory painkillers in traditiongal Chinese mediciones and health foods by ultra performance liquid chromatography-quadruple/electrostaticfield orbitrap high resolution mass spectrometry［J］. Chin Pharm J(中国药学杂志), 2015, 50(24):2154-2159.

［2］ ZHANG Y, YANG Z, ZHU R J, et al. Determination of thirty antihypertensive chemical medicines adulterateds in traditional Chinese patent medicines and health foods by UPLC-MS /MS ［J］. Chin Pharm J(中国药学杂志), 2012, 47(2):141-145.

［3］ LIU Y W, ZOU Y H, YIN H M, et al. Identification of a tadalafil analogue based on Q-TOF-MS［J］. Chin Pharm J(中国药学杂志), 2016, 51(23):2059-2062.

［4］ WANG Q, SU J, TAN H, et al. Determination of eleven antidiabetics illegally adulterated into Chinese patent drugs and health foods by TLC［J］. Chin Pharm Aff(中国药事), 2010, 24(7):647.

［5］ XU J H, ZHANG R L, SONG X Y, et al. The determination of 11 chemical antidiabetic material in antidiabetics of Chinese traditional medicine by HPLC［J］. Drug Stand China(中国药品标准), 2010, 11(5):335.

［6］ YU H, HU Q, SUN J, et al. Qualitative analysis of illegally adulterated sidenafil and related compounds in dietary supplements by ultra-high performance liquid chromatography-quadrupole-time-of-flight mass spectrometry［J］. Chin J Chromatogr(色谱), 2018, 36(10):1005-1017.

［7］ SUN J, HU Q, FENG R, et al. Determination of 30 antiimpotence compounds illegally adulterated in health products by ultra-high performance liquid chromatography-triple quadrupole mass spectrometry［J］. J Instrum Anal(分析测试学报), 2018, 37(4):419-426.

［8］ GONG X, LU L, FENG Y L, et al. Fast screening of 25 illegally added chemical drugs in weight-reducing, lipid-lowering and hypoglycemic health foods by HPLC-IT-TOF-MS［J］. China Pharm(中国药师), 2018, 21(8):1463-1468.

［9］ ZHAO J L, OU B L, ZHOU Y. Simultaneous determination of 11 chemicals added in itching agents traditional Chinese edicines by UPLC-MS/MS［J］. Chin J Mod Appl Pharm(中国现代应用药学), 2016, 33(12):1558-1562.

［10］ ZHENG W Y, LI Z, CHEN M, et al. LC-MS/MS Detection of illegally added drugs for weight loss and glucose reduction in Chinese patent medicine and health products［J］. J Shenyang Pharm Univ(沈阳药科大学学报), 2018, 35(1):58-66.

［11］ LI X L, CHEN J, YANG C F, et al. Determination of six antilipemic chemicals illegally added in antilipemic functional foods by UPLC-MS/MS［J］. Food Sci(食品科学), 2018, 39(18):320-324.

［12］ LIU Y, DING T, LIAO X Q, et al. Direct determination of 42 chemical drugs illegally added in herbal medicines and dietary supplement by high performance liquid chromatography-quadrurpole/electrostatic field orbitrap high resolution mass spectrometry［J］. Chin J Anal Chem(分析化学), 2016, 44(3):423-429.

［13］ GUO C C, SUN H, SHI F, et al. Highthroughput screening of 13 digestive drugs adulterated illegally in biochemical drugs, chinese patent medicines and dietary supplements by orbitrap high-resolution mass spectrometry［J］. J Instrum Anal(分析测试学报), 2018, 37(3):300-306.

［14］ JIANG S G, GUO C C, SHI F, et al. Application of Q-orbitrap high resolution mass spectrometry to the detection of illegal adulterated antihyperlipidemics in herbal medicines and dietary supplements［J］. Chin J Pharm Anal(药物分析杂志), 2015, 35(8):1447-1452.

（收稿日期:2019-06-30）