保健食品中非法添加物检出限测定的概述

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摘 要: 近年来, 保健食品非法添加化学药的现象日趋严重, 非法添加化学药的种类也不断变化和增加, 严重地影响了保健食品的质量和信誉。不同的添加物有相应的检测方法。检出限是非法添加物检测方法的重要指标, 关系到结果的判定。已有研究中关于检出限的测定方法多种多样, 即使分析方法和分析物相同, 但由于检出限的测定方法没有统一, 导致结果相差甚远。本文通过对检出限定义的解读, 整理各种检出限测定方法的操作步骤, 对文献中的检出限测定方法进行归纳总结, 并提出改进建议, 以期为规范开展检出限测定提供参考。

关键词: 保健食品; 非法添加; 检出限

Overview of detection limit determination of illegal additives in health food

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ABSTRACT: In recent years, the use of illegal chemical additives in health food becomes more and more serious. The variety of illegally added chemical drugs is constantly changing and increasing, which seriously affects the quality and reputation of health food. Different additives have corresponding detection methods. Limit of detection is an important index of detection method of illegal additives, which is related to the determination of results. There are a variety of detection limit determination methods in existing studies. Although the analytical methods and analytes are the same, the results are far from each other due to the inconsistency of detection limit determination methods. Based on the interpretation of the definition of the limit of detection, this paper sorted out the operation steps of various detection limit determination methods, summarized the detection limit determination methods in the literatures, and put forward suggestions for improvement, in order to provide references for the standardization of detection limit determination.

KEY WORDS: health food; illegally added; limit of detection

1 引 言

保健食品是一种带有功能性的特殊食品, 对特定人群、特定年龄或者特殊病人, 有着辅助治疗作用的一种特殊食品。然而, 为了追求利益和虚假的疗效, 向保健食品中非法添加化学药物时有发生[1,2]。造成保健食品的安全风险增加, 给监管带来了更大压力。非法添加物从几十种增加到几百种, 长期大量服用此类保健食品, 可能造成严重的不良反应。检出限是非法添加物分析方法的基本性能参数之一, 无论是开发新方法, 制订标准, 以及实验室检测能力确认, 常规检测报告, 都涉及方法检出限的实验设计和评估[3]。由于检测分析者对检出限定义理解不

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同, 对相同的分析方法采用检出限的测定方法不一致, 导致检出限结果偏差较大。再者, 旧的检验标准没有制定方法检出限, 如国家食品药品监督管理局 2009 年~2014 年颁布的对非法添加物的药品补充检验方法[4-13]中均未给出方法检出限。在执行此类标准开展检测时, 检测人员对方法检出限的实验设计和评估方法选择各不相同, 导致检测结果没有可比性。因此, 本文综述了近年来保健食品中非法添加化学药物的分析方法。对文献中的分析方法及其检出限的确定方法进行了整理、分析和总结, 提出改进的建议, 以期为研究此类分析方法和日常检测工作提供参考。

2　非法添加物分析方法和检出限测定方法汇总

通过对相关文献的整理和和统计, 保健食品中非法添加的化学药按功效分为壮阳类、提高免疫力类、减肥类、调节血压类、调节血脂类、调节血糖类、镇静安神类、解热镇痛类等, 针对这些非法添加物, 主要的分析方法有: 理化分析法、薄层色谱法(thin layer chromatography, TLC)、高效液相色谱-二极管阵列检测法(high performance liquid chromatography-diode array detector, HPLC-DAD)、液相色谱-质谱联用法(liquid chromatography-tandem mass spectrometry, LC-MS/MS)、超高液相色谱-质谱联用法(ultrahigh performance liquid chromatography- tandem mass spectrometry, UPLC-MS/MS)、液相色谱-高分辨率四级杆飞行时间质谱(liquid chromatography-quadrupole-time of flight mass spectrometry, LC-Q-TOF)、超高效液相色谱-三重四极杆/复合线性离子阱质谱(high performance liquid chromatograph -triple quadrupole/composite linear ion trap mass spectrometry, UPLC-Qtrap-MS/MS)等。检出限的测定方法主要有: 直观法、信噪比法、基于标准偏差-曲线斜率法、目视评价法、数学模型法。现将近年来主要的分析方法及其检出限的测定综述如下, 见表 1。

从汇总结果看, 对非法添加物的检测, 液相色谱配备各类质谱仪的联用, 具有快速、高效、定性准确、应用范围广等特点, 是常用的检测分析方法, 在检出限评估方法上, 信噪比法由于简便易行, 是检出限评估的常用方法。

表 1　非法添加物分析方法和检出限测定方法汇总

Table 1　Summary of methods for analysis and determination of detection limit of illegal additives

添加物类型	分析方法	检出限测定方法	检出限测量值	文献
壮阳类	UPLC-MS/MS	信噪比法	0.03~0.22 ng/mL	[14]
壮阳类	LC-MS/MS	目视评价法	0. 05 mg/kg	[15]
壮阳类	LC-MS/MS	信噪比法	0.1~5 ng	[16]
壮阳类	UPLC-DAD	信噪比法	0.3~0.6 μg/mL	[17]
壮阳类	UPLC-MS/MS	信噪比法	10.6 ng/mL	[18]
壮阳类	UPLC-Q-TOF-MS	目视评价法	0.1~50 mg/kg	[19]
减肥类	TLC	直视法	0.2 μg	[20]
减肥类	UPLC-DAD	信噪比法	0.10~4.1 ng	[21]
减肥类	LC-MS/MS	目视评价法	2~100 ng	[22]
减肥类	LC-MS/MS	信噪比法	0.95 μg/mL	[23]
减肥类	UPLC-MS/MS	信噪比法	0.0003~0.375 ng/g	[24]
减肥类	LC-MS/MS	信噪比法	5.0~15.6 ng	[25]
减肥类	毛细管电脉	信噪比法	0.16~0.65 μg/mL	[26]
降糖类	HPLC-Q-TOF	信噪比法	0.03~0.1 μg/g	[27]
降糖类	HPLC	信噪比法	0.02 μg/mL	[28]
镇静安神类	液相色谱-离子阱质谱法	信噪比法	0.1~5 ng	[29]
降血压类	HPLC-DAD	信噪比法	0.03~0.50 mg/g	[30]
抗炎镇痛类	UPLC-MS/MS	信噪比法	0.3~5.0 ng/g	[31]
尿酸调节类	液相色谱-串联质谱	定量离子对的信噪比	0.03~0.6 mg/kg	[32]
抗生素类	LC-MS/MS	目视评价法	0.001~205 ng	[33]

3 方法检出限的定义

有关检出限(limit of detection, LOD)的定义, 不同的标准中有不同的描述。

《中国药典》2010 年版一部[34]中药质量标准分析方法验证指导原则和《中国药典》2015 年版四部[35]药品质量标准分析方法验证指导原则中定义为: 检测限系指试样中被测物能被检测出的最低量。

GB/T 5009.1-2003[36]定义为: 把 3 倍空白值的标准偏差(测定次数 $n \geqslant 20$)相对应的质量或浓度称为检出限。

GB/T 27415-2013 分析方法检出限和定量限评估[37]中定义实验室间检出限(inter laboratory detection estimate, IDE)为: 能以较高概率检出的最小浓度, 即在 90%置信概率下, 浓度是 IDE 的样品被检出的实验室的比例为 95%, 浓度为 0 的样品不被检出的实验室的比例是 99%。

国际纯粹与应用化学联合会(International Union of Pure and Applied Chemistry, IUPAC)1998 年发表的《分析术语纲要》[38]中规定: 检出限以浓度(或质量)表示, 是指用特定的分析步骤能够合理地检测出的最小分析信号, 求得的最低浓度(或质量), 并规定应通过实验以足够多的测定次数求出。

4 测定方法[14,21,31,39-55]

4.1 直观法

用已知浓度的被测物, 实验得出能可靠地检测出的最低浓度或量。以薄层色谱法为例, 主要操作步骤如下:

(1)配制系列浓度的标准溶液(每个浓度水平可以是相差一个数量级), 或通过调节点样量作系列浓度, 按检验检测方法展开, 显色, 目测可检出斑点, 初定估计检出限浓度。

(2)取空白样品, 加入标准品使浓度达到估计检出限浓度, 依法操作, 检视, 验证检出限。

采用此法, 汪祺等[53]测得二甲双胍和苯乙双胍的检出限为 2 μg。张宏莲等[54]测得二甲双胍和苯乙双胍的检出限为 0.4 μg。

4.2 信噪比法

把已知低浓度试样测出的信号与空白样品测出的信号(基线噪声)进行比较, 计算其检出限。

采用此法, 倪赞等[14]测得氨基他达那非等被测物的检出限在 0.03~0.22 ng/mL。贾昌平等[21]测定比沙可啶等 17 种减肥类药的检出限为 0.10~4.1 ng。黄越燕等[31]取阴性样品按 0.5 mg/g 的添加量加入经适当稀释的混合对照品溶液, 进样, 测定, 以信噪比为 3 时, 各被测物的检出限为 0.3~5.0 ng/g。

4.3 基于响应值标准偏差和标准曲线斜率法。

根据仪器检出限或分析方法中标明的检出限, 制备空白样加标的工作曲线, 求得斜率 S, 再用最低浓度点重复进样测定, 求得 δ(δ 可以通过下列方法测得: ① 测定空白值的标准偏差; ② 标准曲线的剩余标准偏差或截距的标准偏差来代替)。孙晶等[55]用此法测得 54 种被测物的检出限为 0.1~16 ng/mL。

4.4 目视评价法

目视评价法是通过在样品空白中添加已知浓度的分析物, 然后确定能够可靠检测出分析物最低值的方法, 检出依据母离子和碎片的保留时间、质量数、离子丰度比等与标准品的匹配程度[1]。

于泓等[19]通过在 10 种基质中加入标准品, 加入浓度逐级递减, 直到能满足定性检出要求的浓度作为检出限。测得 98 种被测物在 10 种基质中的检出限在 0.1~50 mg/kg 或 0.1~50 mg/L。

4.5 数学模型法

GB/T 27415-2013[37]和美国 ASTM 标准[56]采用此法, 主要步骤是: 配制系列低水平浓度的空白样加标, 每个浓度水平重复实验 n 次, 依法测定, 作浓度与标准偏差的函数关系, 经“斜率为零”的 P 检验识别其关系是属于常数模型还是直线模型、如果是直线模型则进一步识别是同方差还是异方差, 同方差采用普通最小二乘法计算, 异方差用加权最小二乘法得到迭代计算式, 通过迭代计算进一步确定方法检出限。该法结果准确, 可靠性高, 但计算繁杂, 在所查阅的保健食品非法添加物检测的文献中, 未发现采用此法。

5 总 结

5.1 常见测定方法的应用特点

直观法主要用于理化分析法和薄层色谱法中检出限的测定。理化分析法和薄层色谱法属于快速筛查, 检出判定通过观察显色、沉淀等反应现象及薄层斑点清晰度等, 检出限值一般较高。信噪比法操作简单, 多用于能显示基线噪声的分析方法(如气相、液相色谱法), 信噪比法在仪器检出限与方法检出限应用上容易混淆, 应注意区分。对于液相质谱联用法, 信号峰有色谱峰、定量离子对峰、定性离子对峰之分, 在检出确定时, 应考察被测物母离子及碎片与标准品匹配度, 而不单以定量离子对的信噪比($S/N \geq 3$)确定, 因为一般定性离子对的响应较低而并未检出。基于标准偏差和标准曲线斜率法中, 斜率应通过在基质中加入系列低浓度求得, 而不是分析方法中的浓度对响应值标准曲线回归方程中的斜率。如果斜率使用浓度对标准偏差作的线性方程中的斜率, 则等效于 ISO 标准[57]中的同方差

法。目视评价法定性指标是以母离子及碎片的保留时间、相对分子量、离子丰度比等与标准品(或标准谱库)的匹配度来判定，定性指标多，定性准确度高。数学模型法中计算的数据来源于多家实验室，评估建立在严密的数理统计基础上，采用的数据量大，充分考虑低浓度区间目标物浓度与测量值标准偏差之间的函数关系，评定结果更客观、真实。在建立分析方法或建标时，应使用该法。

5.2　如何提高方法检出限的可靠性

(1)增加重复性实验次数，即增大自由度。(2)延长测量过程的时间跨度，一般要求在 3 天内进行不连续的测定。(3)在多台相同灵敏度级别的仪器上测定。(4)采用多家实验室数据计算评估。

在质谱分析方法中，应关注被测物子离子与标准品子离子是否一致，考查定性离子是否检出，因为检出限是定性概念。在多组分质谱分析中，几十种组分同时测定和单一组分测定相比较，后者灵敏度高，检出限低。为保持与分析方法同步，建议开展方法检出限测定时，采用多组分同时测定。

参考文献

[1] 国家食品药品监督管理局. 保健食品注册管理办法(试行)[Z].
China Food and Drug Administration. Measures for the administration of health food registration (trial) [Z].

[2] 李建辉, 张朝晖, 王琳, 等. 减肥保健食品中非法添加物检测方法研究进展[J]. 食品安全质量检测学报, 2017, 8(5): 1585−1595.
Li JH, Zhang ZH, Wang L, *et al*. Research progress of analysis of illegal additives in weight-reducing dietary supplements [J]. J Food Saf Qual, 2017, 8(5): 1585−1595.

[3] 李玉武, 任立军, 王婧瑞, 等. 方法检出限三个评估方法标准解读与比较[J]. 中国无机分析化学, 2015, 5(3): 24−33.
Li YW, Ren LJ, Wang JR, *et al*. Interpretation and comparison of three evaluation methods of method detection limit [J]. Chin J Inorg Anal Chem, 2015, 5(3): 24−33.

[4] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2009024 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2009024 [S].

[5] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2009029 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2009029 [Z].

[6] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2009030 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2009030 [Z].

[7] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2009032 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2009032 [Z].

[8] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2012004 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2012004 [Z].

[9] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2013001 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2013001 [Z].

[10] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2013002 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2013002 [Z].

[11] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 2014008 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval 2014008 [Z].

[12] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 BJS201701 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval BJS201701 [Z].

[13] 国家食品药品监督管理局. 药品检验补充检验方法和检验项目批准件 BJS201710 号[Z].
China Food and Drug Administration. Additional testing methods and projects document of approval BJS201710 [Z].

[14] 倪赞, 张崇生. UPLC-MS/MS 法测定补肾抗疲劳中成药及保健食品中非法添加的 9 种 PDE-5 抑制剂及其衍生物[J]. 中南药学, 2018, 16(9): 1295−1299.
Ni Z, Zhang CS. Determination of 9 phosphodiesterase-5 inhibitors and its derivative illegally added to invigorant herbal medicines and dietary supplements by UPLC-MS/MS [J]. Central South Pharm, 2018, 16(9): 1295−1299.

[15] 孙健, 胡青, 张甦, 等. 超高效液相色谱-三重四极杆质谱法测定保健食品中 30 种非法添加壮阳类化合物[J]. 分析测试学报, 2018, 37(4): 419−426.
Sun J, Hu Q, Zhang S, *et al*. Determination of 30 anti-impotence compounds illegally adulterated in health products by ultrahigh performance liquid chromatography-triplequadrupole mass spectrometry [J]. J Instrum Anal, 2018, 37(4): 419−426.

[16] 董宇, 姜鑫, 刘静, 等. 液质联用法同时检测保健食品中非法添加的 13 种壮阳类化学品[J]. 食品安全质量检测学报, 2018, 9(15): 4055−4060.
Dong Y, Jiang X, Liu J, *et al*. Simultaneous determination of aphrodisiac compounds illegally added into health food by liquid chromatography-mass spectrometry [J]. J Food Saf Qual, 2018, 9(15): 4055−4060.

[17] 程燕, 谭顺中, 姜登军. 超高效液相色谱法同时测定功能性饮品和抗疲劳类保健食品中非法添加的11种化学药物[J]. 食品安全质量检测学报, 2018, 9(15): 4078−4084.
Cheng Y, Tan SZ, Jiang DJ. Simultaneous determination of 11 kinds of illegally added chemical drugs in unctional drinks and anti-fatigue health foods by ultra performance liquid chromatography [J]. J Food Saf Qual, 2018, 9(15): 4078−4084.

[18] 舒展, 王帅. 液相色谱-高分辨率四级杆飞行时间质谱联用法测定保健食品中非法添加的 N – 去甲基他达拉非[J]. 中国药业, 2017, 26(4): 22−26.

Shu Z, Wang CS. Determination of N-desmethyltadalafil illegally added in dietary supplements by HPLC–QTOF [J]. China Pharm, 2017, 26(4): 22–26.

[19] 于泓, 胡青, 孙健, 等. 超高效液相色谱-四极杆-飞行时间质谱法定性筛查保健食品中西地那非及其相关功效类非法添加化合物[J]. 色谱, 2018, 36(10): 1005–1017.

Yu H, Hu Q, Sun J, *et al*. Qualitative analysis of illegally adulterated sildenafil and related compounds in dietary supplements by ultra-high performance Liquid chromatography-quadrupole-time-of-flight mass spectrometry [J]. Chin J Chromatogr, 2018, 36(10): 1005−1017.

[20] 许凤, 李莉, 张宏莲, 等. 薄层色谱扫描法对减肥保健食品中酚酞的定性定量分析[J]. 药物分析杂志, 2014, 34(9): 1634–1640.

Xu F, Li L, Zhao HL, *et al*. Identification and determination of phenolphthalein added intothe anti-obesity product and healthcare food by TLCS [J]. Chin J Pharm Anal, 2014, 34(9): 1634–1640.

[21] 贾昌平, 钱叶飞, 赵琪, 等. 减肥类保健食品中 25 种非法添加化学物质的 UPLC-DAD 快速筛查[J]. 中成药, 2018, 40(12): 2803–2808.

Jia CP, Qian YF, Zhao Q, *et al*. UPLC-DAD rapid screening of 25 illegal added chemicals in diet health food [J]. Chin Tradit Pat Med, 2018, 40(12): 2803−2808.

[22] 车宝泉, 张喆, 黄晓君, 等. 液质联用检查中药制剂及保健食品中减肥类药物[J]. 药物分析杂志, 2009, 29(4): 633−635.

Che BQ, Zhang Z, Huang XJ, *et al*. HPLC-MS/MS identification of antiobesities in traditional Chinese medicine and health foods [J]. Chin J Pharm Anal, 2009, 29(4): 633−635.

[23] 陈稚, 吴都督. HPLC/ESI-MS 测定减肥保健食品中的双去甲基西布曲明[J]. 中国食品卫生杂志, 2010, 22(1): 24–26.

Chen Z, Wu DD. Determination of N-di-desmethylsibutramine with HPLC/ESI-MS in slimming health food products [J]. Chin J Food Hyg, 2010, 22(1): 24–26.

[24] 欧贝丽, 张红伟, 徐宏祥. UPLC-MS/MS 法测定中成药及保健品中添加的 36 种化学药物[J]. 药物分析杂志 2013, 33(12): 2141–2147.

Ou BL, Zhang HW, Xu HX. Determination of 36 chemicals added into traditional Chinese medicines and health care products UPLC-MS/MS [J]. Chin J Pharm Anal, 2013, 33(12): 2141–2147.

[25] 颜红, 李晓瑜, 彭富全. HPLC-MS 同时检测减肥类保健食品中常见 4 种化学药物[J]. 现代食品与药品杂志, 2006, 16(5): 9–11.

Yan H, Li XY, Peng FQ. Simultaneous determination of 4 kinds of chemical drug in slimming foods by HPLC-mass spectrometry [J]. J Mod Food Pharm, 2006, 16(5): 9–11.

[26] 李阳, 薛丰, 王媛, 等. 高效毛细管电泳法同时测定减肥类功能食品中 7 种违禁成分[J]. 分析化学, 2011, 39(11): 1716–1720.

Li Y, Xue F, Wang Y, *et al.* Simultaneous determination of seven adulterants in slimming functional foods by high performance capillary electrophoresis [J]. Chin J Anal Chem, 2011, 39(11): 1716–1720.

[27] 姜春来, 邢俊波, 靳守东. HPLC-Q-TOF 法测定降糖类中成药及保健食品中 14 种非法添加药物[J]. 解放军药学学报, 2016, 32(6): 514–517.

Jiang CL, Xing JB, Jin SD. Determination of 14 illegally added antidiabetics in traditional chinese medicines and health care products by performance liquid chromatography-quadrupole/time of flight mass spectrometer [J]. Pharm J Chin PLA, 2016, 32(6): 514–517.

[28] 黄佳佳, 江东文, 杨昭, 等. 多壁碳纳米管分散型固相萃取-高效液相色谱测定降糖保健食品中非法添加药物罗格列酮[J]. 食品工业科技, 2017, 38(2): 53–58.

Huang JJ, Jiang DW, Yang Z, *et al*. Determination of illegal added rosiglitazone in dietary supplementby multi-walled carbon nanotubes dispersive solid-phaseextraction combined with high performance liquid chromatography [J]. Sci Technol Food Ind, 2017, 38(2): 53−58.

[29] 董宇, 矫晓蔓, 王晓黎, 等. 液质联用法检测镇静安神类中药制剂及保健品中非法掺入的化学品[J]. 中国药品标准, 2012, 13(6): 454−457.

Dong Y, Jiao XM, Wang XL, *et al*. Determination of compounds illegally added into sedative traditional chinese medicine and health food by liquid chromatography-mass spectrometry [J]. Drug Stand China, 2012, 13(6): 454−457.

[30] 陈林, 温家欣, 齐春艳, 等. 降压类中成药及保健食品中 21 种非法添加化学药物的快速检测与确证方法研究[J]. 分析测试学报, 2016, 35(8): 937−942.

Chen L, Wen JX, Qi CY, *et al*. Rapid detection and conformation of 21 illegal chemical drugs in antihyertension traditional Chinese medicine and healthy food [J]. J Instrum Anal, 2016, 35(8): 937−942.

[31] 黄越燕, 屠婕红, 徐宏祥, 等. UPLC-MS/MS 法快速测定中药及保健食品中非法添加 17 种抗炎镇痛类化学药的研究[J]. 中草药, 2016, 47(2): 246−254.

Huang YY, Tu JH, Xu HX, *et al*. Rapid determination of 17 anti-inflammatory and analgesic chemicals illegally added into Chinese patent medicine and health foods by UPLC-MS/MS [J]. Chin Tradit Herb Drug, 2016, 47(2): 246−254.

[32] 张秋炎, 罗辉泰, 黄晓兰, 等. 液相色谱-串联质谱同时快速测定中成药和保健食品中 9 种非法添加尿酸调节类药物[J]. 分析测试学报, 2018, 37(9): 989−994.

Zhang QY, Luo HT, Huang XL, *et al*. Determination of nine uric acid regulation drugs illegally added in chinese traditional patent medicine and health-care food by liquid chromatography-tandem mass spectrometry [J]. J Instrum Anal, 2018, 37(9): 989−994.

[33] 张甦, 胡青, 孙健, 等. 液质联用检测中成药和保健食品中非法添加的 48 种抗生素类成分[J]. 中成药, 2015, 37(3): 542−548.

Zhang S, Hu Q, Sun J, *et al*. Simultaneous determination of 48 antibiotics in Chinese patent medicines and health foods by LC-ITMS [J]. Chin Tradit Pat Med, 2015, 37(3): 542−548.

[34] 中国药典. 2010 年版. 一部. 2010. 附录 130[Z].

Chinese pharmacopoeia. 2010 edition. Part I. 2010. Appendix 130 [Z].

[35] 中国药典. 2015 年版. 四部. 2015. 通则 9101.376[Z].

Chinese pharmacopoeia. 2015 edition. Four parts. 2015. General rules 9101.376 [Z].

[36] GB/T 5009.1-2003 食品卫生检验方法理化部分[S].

GB/T 5009.1-2003 Food hygiene inspection method physical and chemical part [S].

[37] GB/T 27415-2013 分析方法检出限和定量限评估[S].

GB/T 27415-2013 The detection limit and quantitative limit of the analytical method were evaluated [S]

[38] IUPAC compendium of analytical nomenclature [S].

[39] 张晓丹, 傅小英, 陈静, 等. HPLC-DAD 数据库快速筛查减肥类中药制剂及保健食品中的 10 种非法添加化学药物[J]. 中国新药杂志, 2012, 21(2): 195–201.

Zhang XD, Fu XY, Chen J, *et al*. A HPLC-DAD spectrum library for rapidly detecting 10 anti-obesity chemicals illegally adulterated in traditional Chinese medicines and healthy foods [J]. Chin J New Drugs, 2012, 21(2): 195–201.

[40] 孙鑫贵, 赵榕, 张正, 等. 减肥、缓解体力疲劳和辅助降血糖类保健食品违法添加药物状况调查[J]. 中国食品卫生杂志, 2010, 22(5): 450–452.
Sun XG, Zhao R, Zhang Z, *et al*. Survey on the illegal drugs added in health food with losing weight, relieving physical fatigue and assist-reducing glycemia functions [J]. Chin J Food Hyg, 2010, 22(5): 450–452.

[41] 徐文峰, 金鹏飞. 降糖类中成药和保健食品中非法添加化学药物检测技术的研究进展[J]. 中南药学, 2016, 14(11): 1233–1237.
Xu WF, Jin PF. Advances in determination of illegally adulterated chemical substances in antidiabetic traditional Chinese medicines and dietary supplements [J]. Central South Pharm, 2016, 14(11): 1233–1237.

[42] Guo C, Shi F, Jiang S, *et al*. Simultaneous identification, confirmation and quantitation of illegal adulterated antidiabetics in herbal med icines and dietary supplements using high-resolution benchtop quadru-pole-orbitrap mass spectrometry [J]. J Chromatogr B, 2014, 967: 174–182.

[43] Zhou Z, Zhang J, Zhang W, *et al*. Rapid screening for synthetic an-tidiabetic drug adulteration in herbal dietary supplements using direct analysis in real time mass spectrometry [J]. Analyst, 2011, 136(12): 2613–2618.

[44] 张玉婷, 孔璇, 吴燕. 辅助降血糖类保健食品中 18 种非法添加物的 HPLC-MS 定性定量检测法[J]. 职业与健康, 2017, 33(19): 2644–2651.
Zhang YT, Kong X, Wu Y. Qualitative and quantitative determination of 18 illegally added anti-diabetic chemical components in auxiliary hypoglycemic health foods by HPLC-MS [J]. Occup Health, 2017, 33(19): 2644–2651.

[45] 胡青, 孙健, 于泓, 等. 超高效液相色谱-三重四极杆质谱法测定保健食品中 28 种降糖类非法添加化合物[J]. 食品安全质量检测学报, 2018, 9(1): 93−102.
Hu Q, Sun J, Yu H, *et al*. Determination of 28 anti-diabetic compounds in health foods by ultra performance liquid chromatography-triple quadrupole mass spectrometry [J]. J Food Saf Qual, 2018, 9(1): 93−102.

[46] 邓鸣, 朱斌, 尹利辉. 中成药及保健食品中非法添加调血脂类药物的 HPLC 快速检测方法研究[J]. 药物分析杂志, 2016, 36(9): 1639−1647.
Deng M, Zhu B, Yin LH. Rapid HPLC testing method for lipid-regulating drugs illegally added in traditional Chinese medicines and health food [J]. Chin J Pharm Anal, 2016, 36(9): 1639−1647.

[47] 孙亮, 张蓉, 邬国庆, 等. 高效液相色谱法同时测定保健食品中 9 种非法添加降脂类药物[J]. 食品安全质量检测学报, 2016, 7(8): 3098−3102.
Zhang L, Zhang R, Wu GQ, *et al*. Simultaneous determination of 9 kinds of lipid lowering drugs illegally added in health food by high performance liquid chromatography [J]. J Food Saf Qual, 2016, 7(8): 3098−3102.

[48] 曲晓宇, 董雷, 张四喜, 等. HPLC-MS/MS 法同时检测抗疲劳药物及保健品中非法添加的 7 种壮阳类化学药物[J]. 中国药房, 2013, 24(33): 3129−3130.
Qu XY, Dong L, Zhang SX, *et al*. Simultaneous detection of 7 illegal added anti-impotence medicines in anti-fatigue preparations and health care products by HPLC-MS/MS [J]. China Pharm, 2013, 24(33): 3129−3130.

[49] 黄芳, 吴惠勤, 黄晓兰, 等. 高效液相色谱-串联质谱法同时测定保健品及中成药中非法添加的 17 种壮阳类化学药[J]. 色谱, 2016, 34(3): 270−278.
Huang F, Wu HQ, Huang XL, *et al*. Simultaneous determination of 17 aphrodisiac chemical drugs illegally added in health products and Chinese patent medicines by high performance liquid chromatography-tandem mass spectrometry [J]. Chin J Chromatogr, 2016, 34(3): 270−278.

[50] 李杨杰, 欧国灯, 李泳雪, 等. HPLC-MS-MS 法测定降压类中成药和保健食品中非法添加氨氯地平和乐卡地平的研究[J]. 中成药, 2013, 35(5): 956−960.
Li YJ, Ou GD, Li YX, *et al*. Detection of amlodipine and lercanidipine adulterated into antihypertensive traditional Chinese patent medicines and health-care foods by HPLC-MS-MS [J]. Chin Tradit Pat Med, 2013, 35(5): 956−960.

[51] 徐硕, 金鹏飞, 徐文峰, 等. 补肾壮阳类药品中非法添加化学药物检测技术的研究进展[J]. 西北药学, 2017, 32(5): 677−680.
Xu S, Jin PF, Xu WF, *et al*. Research advances on analytical technologies of illegally adulterated chemical sub-stances in medicines for invigorants [J]. Northwest Pharm J, 2017, 32(5): 677−680.

[52] 庄航, 葛雪松, 卓静, 等. 超高效液相色谱法同时检测抗风湿类保健品及中成药非法添加的解热镇痛抗炎药和激素类成分[J]. 中国药业, 2016, 25(17): 71−74.
Zhuang H, Ge XS, Zhuo J, *et al*. Simultaneous determination of antipyretic analgesic and anti-inflammatory, and hormone components illegally added in anti-rheumatism health products and Chinese patent medicine by UPLC [J]. Chin Pharm, 2016, 25(17): 71−74.

[53] 汪祺, 苏晶, 覃红萍, 等. TLC 快速筛查降糖类中成药及保健食品中添加的化学药品[J]. 中国药事, 2010, 24(7): 647−649.
Wang Q, Su J, Qin HP, *et al*. Determination of eleven antidiabetics illegally adulterated into Chinese patent drugs and health foods by TLC [J]. Chin Pharm Aff, 2010, 24(7): 647−649.

[54] 张宏莲, 李莉, 刘吉成, 等. TLC 法快速检测降糖类中药及保健品中的双胍类成分[J]. 齐齐哈尔医学院学报. 2013, 34(5): 720−721.
Zhang HL, Li L, Liu JC, *et al.* Determination of biguanideadulterated into Chinese patent drugs and health foods by TLC [J]. J Qiqihar Univ Med, 2013, 34(5): 720−721.

[55] 孙晶, 曹玲, 冯有龙, 等. 液质联用法筛查降压类中成药和保健食品中添加的 54 种化学药物[J]. 药物分析杂志, 2018, 38(11): 1981−1993.
Sun J, Cao L, Feng YL, *et al.* Screening of 54 illegally added chemical drugs in anti-hypertensive Chinese traditional patent medicine and health foods by liquid chromatography tandem mass spectrometry [J]. Chin J Pharm Anal, 2018, 38(11): 1981−1993.

[56] ASTM committee DI9 on water and ASTM of subcommittee DI9.02 on general specifications, technical resources, and statistical methods. ASTM D6091-2007, standard practice for 99%/95% inter-laboratory detection estimate (IDE) for analytical methods with negligible calibration error [S].

[57] Technical committee ISO/TC 69, applications of statistical methods, subcommittee SC 6, measurement methods and results. ISO 11843.2-2000, capability of detection-part 2; methodology in the linear calibration case [S].

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