食品中新兴真菌毒素检测技术及其污染现状研究进展

申慧婧[1,2], 张 弛[1,2], 周 爽[2], 吴永宁[1,2*]

(1. 北京工商大学食品与健康学院, 北京 100048; 2. 国家食品安全风险评估中心, 北京 100021)

摘 要: 真菌毒素是由曲霉菌、青霉菌和镰刀菌等丝状真菌在适当的环境条件下产生的有毒次生代谢产物, 是谷物、水果、坚果等食品中常见的污染物, 可引起广泛的毒性效应, 主要表现为致癌性、致突变性、肝毒性、肾毒性、免疫毒性、神经毒性、致畸性等, 对人类和动物的健康构成威胁。近些年来, 由于自然气候的改变及检测技术的创新发展, 一些新出现的真菌毒素逐渐引起大家的广泛关注, 如已报道的交链孢毒素、新兴镰刀菌毒素等。这些尚未得到监管, 并且如何产生、浓度水平和毒理数据有限的真菌毒素被定义为“新兴”真菌毒素。本文综述了两大类 12 种新兴毒素的结构性质、检测分析技术进展及在食品中的污染状况, 以期为真菌毒素污染的全面评估及防控提供思路。

关键词: 新兴真菌毒素; 检测技术; 污染状况

Research progress of emerging mycotoxin detection technology and its contamination status in food

SHEN Hui-Jing[1,2], ZHANG Chi[1,2], ZHOU Shuang[2], WU Yong-Ning[1,2*]

(1. *School of Food and Health*, *Beijing Technology and Business University*, *Beijing* 100048, *China*; 2. *China National Center for Food Safety Risk Assessment*, *Beijing* 100021, *China*)

ABSTRACT: Mycotoxins are toxic secondary metabolites produced by filamentous fungi such as *Aspergillus Penicillium* and *Fusarium* under appropriate environmental conditions. Mycotoxins are common contaminants in cereals, fruits, nuts and other foods. They can cause a wide range of toxicity, including carcinogenicity, mutagenicity, hepatotoxicity, nephrotoxicity, immunotoxicity, neurotoxicity and teratogenicity, which poses a threat to human and animal health. In recent years, due to the change of natural climate and the innovative development of detection technology, some new mycotoxins have gradually attracted widespread attention, such as *Alternaria* and *Fusarium* toxins. They have been recognized as “emerging” mycotoxins since no routine analysis or legislation is available and data on their production, contamination, and toxicity are limited. This paper reviewed the structural properties, detection and analysis techniques of 12 kinds of emerging toxins in two categories and their contamination status in food, in order to provide ideas for the comprehensive assessment and control strategies of mycotoxin contamination.

KEY WORDS: emerging mycotoxins; detection technology; contamination status

基金项目: 国家重点研发计划项目(2022YFF1100802)、国家自然科学基金项目(32272429、31871723)

Fund: Supported by the National Key Research and Development Program of China (2022YFF1100802), and the National Natural Science Foundation of China (32272429, 31871723)

***通信作者:** 吴永宁, 研究员, 主要研究方向为食品安全。E-mail: wuyongning@cfsa.net.cn

***Corresponding author:** WU Yong-Ning, Professor, China National Center for Food Safety Risk Assessment, Beijing 100021, China. E-mail: wuyongning@cfsa.net.cn

0 引 言

真菌毒素属于食品中的生物性污染，同时也是世界卫生组织(World Health Organization, WHO)公布的重要食源性致病因素[1]。真菌毒素在食品和饲料中十分常见，摄入后对人体和畜禽健康产生严重危害。目前已知的真菌毒素有 400 多种，主要包括黄曲霉毒素、单端孢菌烯毒素、玉米赤霉烯酮类毒素、赭曲霉毒素以及交链孢霉毒素等。随着全球气候变迁和检测技术的发展，一些新的真菌毒素逐渐引起人们的关注。这些毒素尚未得到限量监管，没有被标准检测方法覆盖，且其毒性研究和污染水平数据有限，因此被称为“新兴”真菌毒素。本文综述了检出率较高、污染浓度值得进一步关注的交链孢毒素[交链孢酚(alternariol, AOH)、交链孢酚单甲醚(alternariol monomethyl ether, AME)、细交链孢菌酮酸(tenuazonic acid, TeA)、腾毒素(tentoxin, TEN)、交链孢霉烯(altenuene, ALT)]和新兴镰刀菌毒素[如白僵菌素(beauvericin, BEA)、恩镰孢菌素(enniatins, ENNs)、串珠镰刀菌素(moniliformin, MON)、fusaproliferin (FUS)]共计两大类 12 种新兴真菌毒素的结构性质、检测技术、污染状况的研究进展，以期为真菌毒素污染风险全面评估及防控技术研发提供思路。

1 新兴真菌毒素的结构性质

1.1 交链孢毒素

链格孢霉菌是一种丝状腐败真菌，能够适应较宽的温度范围，对农作物(如苹果、番茄、梨、小麦等[1−3])造成一定危害，且可能产生多种有毒次生代谢产物，包括 AOH、AME、TeA、TEN、ALT 等[4]。AOH 在结构上是一种二苯并-α-吡喃酮，在 1 位有一个甲基，在 3、7 和 9 位有羟基(图 1a)，在谷物和水果等食品中均有一定程度的污染。AOH 对人类和动物不良影响的报道较少[5−6]。欧洲食品安全局(European Food Safety Authority, EFSA)制定的 AME 的毒理学关注阈值(threshold of toxicological concern, TTC)和 AOH 的 TTC 均为每天 2.5 ng/kg·bw[7]，AME 是 AOH 的甲基化修饰衍生物，其中 9 位的羟基已经转化为相应的单甲醚。ALT 是 AME 经羟基化、脱氢、环化过程后的产物，其主要存在于受到链格孢属真菌污染的农产品中，如谷物、蔬菜、水果等。在鸡胚胎中进行的体内研究表明，ALT 具有明显的毒性作用，超过了其他的交链孢毒素[8−9]。TEN 是由交链孢毒素产生的四环肽类毒素，水果、小麦、大麦和高粱等农产品中都能检出 TEN[10]。TeA 作为交链孢毒素中含量较高的代谢产物之一，本身性质较为活泼，可以在不同 pH、不同温度、不同溶液介质条件下发生构象变化生成异构体[11−12]，因此有时会利用 TeA 强螯合剂的性质转化为稳定的铜盐 $Cu(TeA)_2$ 来储存[13]。在缺乏完整毒理数据的情况下，EFSA 建议采用 TTC 来评价交链孢毒素对人体造成的潜在风险，AME 和 AOH 的 TTC 为每天 2.5 ng/kg· bw[14]，TEN 和 TeA 的 TTC 为每天 1500 ng/kg·bw[15]，该值可用作食品安全风险评估的一个参考指标，有助于制定合适的管理和防控措施。

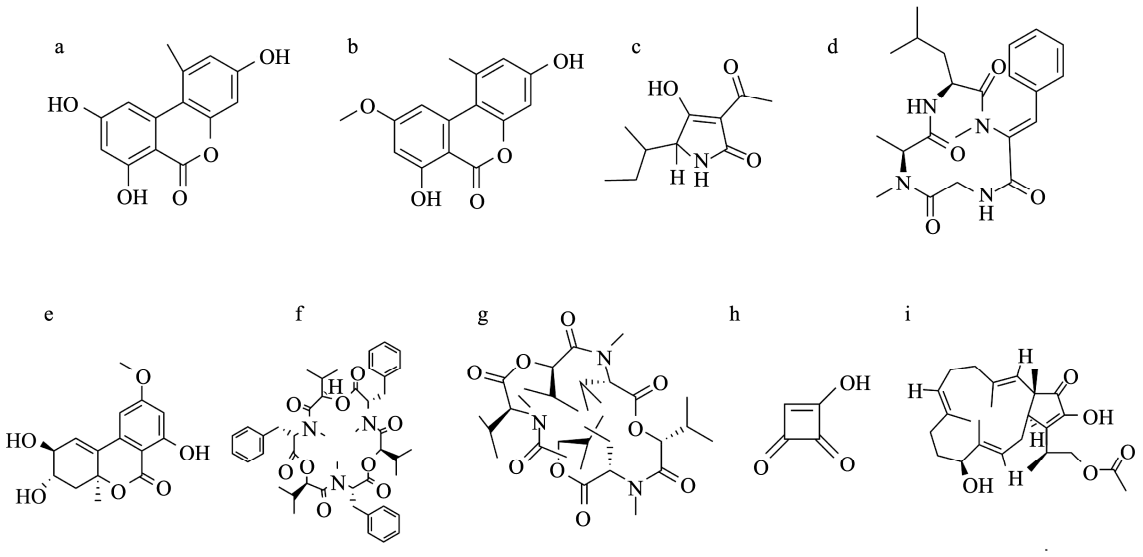
1.2 新兴镰刀菌毒素

镰刀菌是北温带地区最常见的真菌，它包括多个种类，是玉米和小粒作物的重要病原菌，可引起茎部和穗部腐烂，严重降低作物的产量。除了致病性外，一些镰刀菌菌株还能够产生真菌毒素，在收获前或储存的谷物中累积[16]，镰刀菌除能产生常见的玉米赤霉烯酮、脱氧雪腐镰刀菌烯醇、伏马菌素等毒素外，也能产生其他的有毒次生代谢产物，如 BEA、ENNs、MON、FUS 等。然而目前为止，关于新兴镰刀菌毒素的毒性、发生率和污染水平的研究依然有限。BEA 首先是在致病性真菌球孢白僵菌的培养物中发现的[5]，是一种三羧酸肽(图 1f)，其结构中无带电荷的基团，水溶性差，化学反应性较低，且容易在生物环境样本中积累[17−18]。ENNs(图 1g)的种类较多，最常见的为 ENNA、ENNA1、ENNB 和 ENNB1，由于分子量大、极性弱，ENNs 在水中溶解度很低，可溶于乙醇、甲醇、二甲基亚砜、二甲基甲酰胺等有机溶剂，也极易引起生物累积[19−20]。作为一种游离的强酸，MON(图 1h)在水和甲醇中都不太稳定，在自然界中以钠盐或钾盐的形式存在，且在环境中的持续污染较低[21]。FUS 最初是从培养的镰刀菌中分离出来的[22]，其毒性较强，对盐叶蒿、昆虫细胞和人 B 淋巴细胞均有毒性作用[23]，对鸡胚胎也会产生致畸作用[24]。FUS 的分解主要有两种不同的途径，分别为水解和热解。潮湿条件下更有利于 FUS 的水解，产生脱乙酰-FUS；热降解途径只发生在高温下，特别是在干燥条件下，可使 FUS 完全分解[25]。

这些真菌毒素不仅对公众健康构成威胁，而且对经济和环境也造成一定的危害。而多种真菌毒素在食品和环境中的共同存在，使污染情况变得更加复杂和严重。为明确新兴毒素的污染特征，预警食品中的新发风险隐患，需发展准确、全面、快速的筛查和确证技术。

2 新兴真菌毒素的检测技术

新兴真菌毒素的发现识别、污染特征和健康风险评估均需要准确可靠的分析方法，相较于已知常见的真菌毒素，新兴真菌毒素的检测方法相对较少，一些方法仍存在局限性，如灵敏度低、重复性差等问题[26−27]。由于食品样品基质复杂、真菌毒素结构性质差异较大且多为痕量污染等原因，快速高效的样品前处理方法是必不可少的。



注: a: AOH; b: AME; c: TeA; d: TEN; e: ALT; f: BEA; g: ENNs; h: MON; i: FUS。

图 1　部分新兴真菌毒素化学结构式

Fig.1　Chemical structural formula of some emerging mycotoxins

将目标毒素从样品基质中提取出来是分析实验的第一步。在综合考虑目标毒素理化性质、后续净化步骤、溶剂毒性、成本等多因素的基础上, 选用合适的提取溶剂, 有助于真菌毒素充分、高效地从基质中溶出。目前在提取食品真菌毒素过程中较常使用的溶剂为水、甲醇、乙腈、氯仿、乙酸乙酯、丙酮等溶剂[28–32]。提取过程可以采用涡旋振荡、高速均质以及超声等方式辅助加速提取。

同时, 为了减少对目标化合物的干扰、延长仪器使用寿命, 样品提取液在分析前通常需要进行净化, 将提取液中大量存在的干扰物质(脂肪、蛋白质、色素以及矿物质、纤维素等)除去。目前常用的净化手段包括利用待测物和杂质在不同溶剂中溶解度的差异进行萃取净化的液液萃取法(liquid-liquid extraction, LLE)[33]; 食品中真菌毒素检测常用到的固相萃取法(solid phase extraction, SPE)[34–35]; 利用生物分子(抗体、受体、核酸适配体等)与目标化合物间高度特异性结合作用保留目标毒素, 去除杂质, 而后实现分离和富集的免疫亲和层析法(immunoaffinity chromatography, IAC)[36]; 以及直接稀释法(dilute-and-shoot)[37]、分散液液微萃取法(dispersive liquid-liquid microextraction, DLLME)[38]、QuEChERS 法[39]等一系列常用的前处理方法。在实际应用中, 对不同待测样品的类型和目标真菌毒素的化学性质进行选择和组合, 根据实际情况对方法进行优化和调整, 以实现对不同类型食品样品中新兴真菌毒素的有效检测。

真菌毒素经过不同方法进行前处理后, 可采用一些方法进行分析, 目前已开发并运用了一些新兴真菌毒素的检测方法, 包括薄层色谱法(thin layer chromatography, TLC)、气相色谱-质谱法(gas chromatography-mass spectrometry, GC-MS)、液相色谱-质谱法(liquid chromatography-mass spectrometry, LC-MS)、酶联免疫吸附测定法(enzyme-linked immunosorbent assay, ELISA)等。

2.1　薄层色谱法

TLC 是早期使用的真菌毒素检测方法, 利用吸附剂固定相与移动相之间的相互作用, 实现对待测物质的分离和定性分析, 具有低成本、可以筛选大量样品等优点。TLC 可以结合紫外光谱进行食品中新兴真菌毒素的检测分析[40]: 筛查从红芸豆中分离得到的交链孢菌、青霉菌、曲霉菌等产生的青霉酸(penicillic acid)和 TeA[41]; 比对食管癌高、低发区食品中交链孢毒素 AME 和 AOH 的含量[42]。尽管 TLC 在新兴真菌毒素检测中具有操作简便、成本低廉等优点, 但其灵敏度与定性定量能力较差, 容易受到基质干扰。因此, 在实际应用中, TLC 作为早期一种快速筛查方法, 用于初步鉴定菌株产毒和样品污染。

2.2　气相色谱-质谱法

GC-MS 是一种将气相色谱法与质谱法相结合的高灵敏度和高选择性的分析技术。由于 GC-MS 具有较高的灵敏度, 使其可用于复杂基质中的化合物的检测, 挥发性、半挥发性、非极性和中等极性化合物可使用 GC-MS 检测[43]。然而, 新兴真菌毒素往往挥发性较弱, 在高温下可能会发生分解, 影响 GC-MS 检测的准确性和稳定性。并且大多新兴真菌毒素是极性化合物, 在分析过程中易与固定相发生相互作用, 导致分离效果不理想。因此, 在 GC-MS 分析之前, 通常需要衍生化, 通过化学衍生增强目标物的挥发性与非极性, 从而使其更适合气相色谱-质谱分析, 但这也可能会造成衍生反应不完全、基质干扰、重

复性差等问题[44–45]。尽管如此，在特定情况下，GC-MS 也可以作为新兴真菌毒素检测的一种有效方法。

2.3 液相色谱-质谱法

液相色谱法为新兴毒素的分离检测提供了更合适的选择。近年来，液相色谱法结合紫外检测[46]、蒸发光散射检测[47]、二极管阵列检测[48]和荧光检测[49–50]已被报道用于食品和饲料中新兴真菌毒素的检测。随着仪器革新和分析技术的发展，LC-MS 逐渐成为新兴毒素检测的主要手段。质谱技术基于目标化合物特异性的质荷比(m/z)进行检测，灵敏度高、特异性强、能够获得化学结构信息，且生成的特征碎片离子谱图为目标化合物的确证提供了理想的手段。同时，为多毒素同时测定和新毒素的发现识别提供了有力手段。

2.3.1 液相色谱-串联质谱法

液相色谱-串联质谱法(liquid chromatography-tandem mass spectrometry，LC-MS/MS)主要基于三重四极杆或离子阱低分辨质谱检测器，以保留时间和特征离子对实现目标化合物的定性，以质谱响应作为定量依据，已广泛应用于多种样品(农作物、水果、蔬菜及其副产品)中新兴真菌毒素的检测。超高效液相色谱-串联质谱法(ultra performance liquid chromatography-tandem mass spectrometry，UPLC-MS/MS)通过采用更小尺寸的均匀颗粒(1.5~1.8 μm)填充色谱柱，在更大的比表面积及更高的压力下，显著提高色谱柱的理论塔板数，从而缩短分析时间、减少溶剂消耗、提高分辨率、增强灵敏度、改善分析效率。同时，LC-MS/MS 不但能胜任单毒素或单一类别毒素的分析[51]，更能够实现多类别毒素的同时检测[52–54]。目前，结合直接稀释或 QuEChERS 等通用型前处理方案，已建立了涵盖交链孢毒素和新兴镰刀菌毒素的多目标物检测技术，成功应用于谷物及其制品、水果、果汁、番茄制品、葵花籽、烘焙产品和植物油等多种食品基质[55]以及烹饪后的膳食样本[56]。尽管 LC-MS/MS 具有缩短分析时间、减少溶剂消耗等优势，并且也成为毒素定量的主要选择，但要搭建液相色谱-串联质谱平台价值不菲且维修费用较高，对于酸性、中性物质的灵敏度还会存在差异，并且很少的 LC-MS/MS 关注样品清理的效率、参考物质和标准品数量的可用性，这些需要进一步的调查探索[57]。

2.3.2 液相色谱-高分辨质谱非靶向检测技术和新兴毒素的筛查识别

此外，随着新兴毒素的不断发现，一些基于液相色谱-高分辨质谱法(liquid chromatography-high resolution mass spectrometry，LC-HRMS)的筛查和非靶向检测技术也被用于新兴毒素衍生物的发现和鉴定[58]。高分辨质谱检测器，如飞行时间质谱仪(time of flight mass spectrometer)、静电场轨道阱(Orbitrap)质谱法等能够获得化合物的精确质量数(分辨率>20000，质量准确度误差<10 ppm)，结合全扫描、信息依赖采集、全离子碎裂、母离子扫描、子离子扫描、多级碎片等多种数据采集模式，不但能够实现多毒素同时检测，还能够依赖精确质量数和特征碎片信息，进行非靶向筛查，为新兴毒素的发现识别和结构鉴定提供了可能。

超高效液相色谱-四极杆飞行时间质谱法(ultra performance liquid chromatography-quadrupole-time of flight mass spectrometry，UPLC-Q-TOF MS)结合数据库筛查技术，从镰刀菌提取物中鉴定出包括 BEA、FUS、Fusarielin A 等 15 种镰刀菌代谢物[59]。新兴毒素在植物和动物体中，可以通过 I 相(氧化、还原、水解等)或 II 相代谢(与氨基酸、葡萄糖、硫酸基团和谷胱甘肽结合等)作用形成类似物或结合态。交链孢毒素的葡萄糖苷结合物及硫酸根结合物 AOH-3-G、AOH-9-G、AME-3-G、AOH-3-S、AME-3-S 在大麦、麦芽、番茄酱和啤酒等基质中相继被发现[60–62]，交链孢毒素的硫酸结合态 AOH-3-sulfate 和 AME-3-ulfate 还能进一步与血清白蛋白形成高度稳定的复合物[63]。此外，基于特异性的前处理技术，如酸水解等，将结合态毒素分解释放出游离态原型，可以实现毒素的类别总量测定，该思路已用于茄类蔬菜及其制品中交链孢毒素及其结合态的类别检测[64]。这些实验结果为未来新兴毒素的污染调查与风险评估提供更加全面的数据，也对农作物的监测提供了方向。与其他方法相比，LC-HRMS 显示出独特优势，有望应用于目前食品和环境中尚未充分评估的且具有潜在毒理学相关性的毒素新形态及代谢物的检测。

2.4 酶联免疫吸附测定法

色谱-质谱法为真菌毒素的精准检测提供了理想的解决方案，但考虑到仪器配备、操作复杂性、检测成本、样本量、以及现场检测需求等方面的因素，以免疫分析为代表的快速检测方法也有其广泛的应用空间，在食品生产、筛查抽检甚至民用领域发挥着重要作用。建立免疫分析法的关键在于获得高亲和性和高特异性的针对目标化合物的抗体。ELISA 在免疫分析原理基础上，利用酶标试剂催化底物反应进行定量，可分为直接法、间接法、竞争法、夹心法等多种模式[65–67]。在新兴真菌毒素检测方面，ELISA 既可以用于单一真菌毒素的测定[68–69]，也可用于多类真菌毒素的同时测定[70]。这些方法为靶向制备具有相似结构识别多重危害的抗体提供重要的策略，也在指导未来半抗原、全抗原的设计和抗体的改进上提供了一定的经验。免疫分析方法能够实现大量样本的同时检测，具有灵敏度高、速度快、操作简便等优点，但易出现假阳性和假阴性的实验结果，因此当进行大量样本检测时，免疫分析方法可作为筛选方法，但对可疑实验数据须进一步确证。

2.5 其他检测法

近年来，生物传感检测法因其快速、灵敏、简便的优势，逐渐受到人们青睐。生物传感器方法是一种新兴的检测技术，目前应用于新兴毒素检测的主要包括光学生物传感器[71–72]、免疫传感器[73–74]、电化学生物传感器[75]等，这些方法利用生物分子(如抗体、酶、适配体等)与新兴真菌

毒素的特异性结合, 可实现信号放大、灵敏度高等特点[76]。但是相应的检测设备在实际应用中也存在诸多方面的局限性, 如检测的稳定性、检测的便利性等[77]。另外, 随着检测技术的不断发展, 近红外光谱(near infrared spectroscopy, NIR)检测[78]、毛细管电泳(capillary electrophoresis, CE)[79]、傅立叶变换离子回旋共振质谱法(Fourier transform ion cyclotron resonance mass spectrometry, FTICR-MS)[80]也用于新兴真菌毒素的靶向和非靶向分析, 揭示了真菌提取物中次级代谢物的变化。这些新颖的检测方法为未来新兴真菌毒素的检测与分析提供了新思路, 简单、方便、高效、灵敏、特异、样品需求少、通用性强等特点使其在特定场景的新兴毒素检测中表现出独特优势。然而, 对于更广泛的食品基质, 这些方法仍然面临许多挑战, 例如食品中复杂成分是否干扰检测, 能否满足准确定量的需求, 以及实现多目标物的同时检测等问题值得进一步探索研究。表 1 列述了以上新兴真菌毒素的检测方法。

表 1　新兴真菌毒素的主要检测方法

Table 1　Main detection methods of emerging mycotoxins

目标物	样品基质	检测方法	定量限	检出限	参考文献
TeA	番茄	TLC	-	0.7 μg/g	[40]
AOH、AME	番茄	TLC	-	0.1 μg/g	[40]
AME、AOH、TeA、ALT	苹果汁	GC-MS	-	-	[44]
FUS	小麦、大麦、黑麦、燕麦	GC-MS	50 μg/kg	100 μg/kg	[45]
AOH、TeA、ALT、AME	番茄酱、葵花籽油、小麦粉	LC-MS/MS	0.06~14 μg/kg	0.05~6.0 ng/g	[56]
AME、AOH、TEN、TeA、ALT	水果、蔬菜、蔬菜汁、蔬菜泥、果酱、蔬菜粉	LC-MS/MS	0.1~3 μg/L	0.03~0.9 μg/L	[81]
AOH、AME、ALT	谷物制品、番茄制品、葵花籽、柑橘类、苹果、橄榄、无花果、苹果汁、红酒	LC-MS/MS	1.0~5 μg/kg	-	[82]
MON	玉米、硬质小麦	LC-MS/MS	-	8~4811 μg/kg	[83]
FUS	玉米、小麦、大麦、燕麦粉、水稻	LC-MS/MS	0.6 mg/kg	0.21 mg/kg	[84]
AOH、AME、TeA、ALT	橘子	HPLC-MS/MS HPLC-MS/MS	0.03~9 μg/kg	0.6~18 μg/kg	[56]
ALT、AOH、AME、ENNB、BEA	玉米、小麦	HPLC-MS/MS	0.5~1 μg/kg	-	[85]
BEA、ENB	小麦粉	UPLC-MS/MS	-	1.5~3 μg/kg	[86]
BEA、ENNs	鸡蛋	UPLC-MS/MS	2~10 μg/kg	1~5 μg/kg	[87]
ENN A、ENN A1、ENN B、ENN B1、BEA	水稻、小麦、玉米、小麦粉、玉米粉	UPLC-MS/MS	0.06~0.51 μg/kg	0.02~0.17 μg/kg	[52]
MON	玉米、大麦、小麦、燕麦	HPLC-DAD	107~136 μg/kg	30~80 μg/kg	[88]
TeA、ALT	番茄产品、烘焙产品、葵花籽、果汁、植物油	HPLC-MS/MS	2.5~110 μg/kg	0.8~34 μg/kg	[89]
AOH、AME	柑橘	HPLC-MS/MS	<0.50 μg/kg	<0.13 μg/kg	[90]
ENNB、ENNB1、ENNA、ENNA1、AOH、AME、ALT、BEA	玉米	HPLC-MS/MS	0.25~5 ng/mL	0.07~1.5 ng/mL	[91]
BEA、ENNA、ENNA1、ENNB、ENNB1	辣椒粉	UPLC	9.5~9.90 μg/kg	2.8~3.0 μg/kg	[81]
ENN A、ENN A1、ENN B、ENN B1	玉米	MSPE-HPLC-MS/MS	0.07~0.17 μg/kg	0.02~0.05 μg/kg	[35]
AOH、AME、ALT、TeA	大米、燕麦片、大麦、番茄酱、番茄汁	UPLC-MS/MS	0.7~5.7 μg/kg	0.5~2.21 μg/kg	[82,91]
TeA	小麦啤酒、苹果汁、葡萄汁	ELISA	-	1.00 ng/mL	[67]
AOH、AME	小麦	ELISA	-	0.7~1.0 ng/mL	[69]
TeA	水稻	MIP	-	0.5 μg/mL	[75]
ENN A、ENNA1、ENNB、ENNB1	大麦	NIR	5 μg/kg	1.5 μg/kg	[78]
ENN A、ENNA1、ENNB、ENNB1、BEA	小麦	毛细管电泳	4.0~8.3 μg/kg	1.2~2.5 μg/kg	[79]

注: -代表未检出; 高效液相色谱-串联质谱法(high performance liquid chromatography-tandem mass spectrometry, HPLC-MS/MS); 高效液相色谱-二级线性阵列检测器法(high performance liquid chromatography-diode array detector, HPLC-DAD); 磁性固相萃取-高效液相色谱串联质谱法(micro solid phase extraction-high performance liquid chromatography-tandem mass spectrometry, MSPE-HPLC-MS/MS); 分子印迹聚合物(molecularly imprinted polymer, MIP)。

3 新兴真菌毒素在食品中污染现状

基于上述多种检测技术，初步解析了食品中新兴毒素污染分布特征。表 2 所示为交链孢毒素和新兴镰刀菌毒素在各类食品中的检出率及污染情况。对于交链孢毒素的 AOH，其在柑橘、玉米、小麦粉、葵花籽油中检出较少[56,92]，在番茄酱、番茄汁、干樱桃、樱桃酱等食品中较容易检出，污染浓度为 0.34~1787 μg/kg，其中，AOH 在番茄酱中的检出率为 100%[56,82]。同样，AME 在番茄酱中的检出率也是最高的，为 45.2%，在橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁、小麦、玉米中检出率为 5%~16.52%，在水稻、燕麦片和柑橘中检出较少[42,56,82]。TeA 在水稻、番茄酱、葵花籽油中的检出率较高(>50%)，最高可达 83.3%，番茄酱和无花果干中污染较严重，最高含量为 2345 μg/kg[82]。TEN 在果酱、柑橘类水果、草莓、葡萄、石榴等食品中几乎无检出[96]，但其在鲜、干、磨粉和油炸甜椒、烘焙产品的检出率可高达 100%，在腐烂苹果中的检出浓度范围较宽，为 0~1458.85 μg/kg[98]。ALT 在大部分食品中无检出，其最高检出率是在葵花籽油中，为 9.1%，在玉米中的检出率为 7.1%，表明 ALT 在食品中的污染相对较少[82]。综上，番茄及其制品中的交链孢毒素污染较为严重；TeA 污染最广泛，且含量最高，其次为 AOH，由于 AOH、AME 的 TTC 较低，即使低暴露也可能引发健康风险，应引起关注。

表 2 新兴真菌毒素在食品中的检出情况及污染情况

Table 2 Detection and contamination of emerging mycotoxins in food

目标物		样品基质	检出率/%	检出浓度/(μg/kg)#	参考文献
交链孢毒素	AOH	葵花籽油	42.9	0~0.5	[56]
		小麦粉	0	ND	[56]
		番茄酱	50~100	10.2~1787	[56,82]
		橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁	7	5.2~29	[82]
		柑橘	0	ND	[92]
		谷物(玉米、水稻、小麦)	2.4~38.4	1.83~32.3	[42,69,93–94]
		谷物(玉米、大麦、小麦、水稻、燕麦片)	4.33~16.52	5~432	[42,94–95]
	AME	番茄酱	41.7~50	3.8~4	[56,82]
		橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁	0~5	1.2~7.8	[82]
		葵花籽油	57.1	21~29	[56]
		小麦粉	0	ND	[56]
	TeA	番茄酱	83.3~100	202~322	[56,82]
		橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁	22~71	1.9~2345	[82]
		谷物(水稻、燕麦、大麦)	31~71	5~80	[95]
		番茄产品、葵花籽、植物油、小麦粉	9.1~91	6~800	[56,96]
		柑橘类水果、果酱、草莓、葡萄、石榴等	0	ND	[96]
	TEN	鲜、干、磨粉、油炸甜椒、烘焙产品	87~100	3.6~75.4	[96–97]
		腐烂苹果	0~6	0~1458.85	[98]
		果汁、樱桃、樱桃酱、樱桃罐头	0~48	0.21~236.58	[99]
		苹果、番茄酱、橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁	0	ND	[82]
		谷物(水稻、燕麦、大麦、玉米)	7.1~40	5~80	[94]
	ALT	苹果、番茄酱、橄榄、无花果干、葵花籽、葡萄酒、西红柿、柑橘、苹果汁	0	ND	[82]
		谷物(水稻、燕麦、大麦、玉米)	7.1~40	5~80	[95]
镰刀菌毒素	BEA	谷物(水稻、燕麦、大麦、玉米)	7.1~40	5~80	[95]
		谷物(水稻、小麦、玉米)	35.9~69.8	1.02~1016	[52,94]
		小麦粉	20	3.69~5.73	[86]
		鸡蛋	20	<2	[100]
		米糠	95~100	1459~2281	[101]

表 2(续)

目标物	样品基质	检出率/%	检出浓度/(μg/kg)[#]	参考文献
	谷物(水稻、小麦、玉米、无麸质面食)	0~78.2	0.17~322	[52,84,102]
	小麦粉	20	0.11~3.30	[52]
ENNA	玉米淀粉	28.3	0.63~68.2	[52]
	谷物(水稻、小麦、玉米、无麸质面食)	3.8~19.2	0.28~46	[52,102]
	小麦粉	6.3	0.3~1.78	[52]
ENNA1	玉米淀粉	<10	0.12~18.2	[52]
	玉米淀粉	<10	0.11~15.4	[52]
	小麦粉	10~43.2	0.23~18.2	[52,86]
ENNB	谷物(水稻、小麦、玉米、无麸质面食)	0~95	0.11~129	[52,102]
	米糠	100	0.11~15.36	[103]
	谷物(水稻、小麦、玉米)	22.4~95	0.19~880	[52]
	玉米淀粉		1.42~31.8	[52]
ENNB1	小麦粉	48.4	0.16~33.9	[52]
	辣椒粉	3.84	1.2±0.5	[89]
	米糠	100	0.53~14.70	[101]
	玉米、硬质小麦	45~95.1	15~41	[83,102]
	小麦、大麦、黑麦、燕麦	0	ND	[45]
	玉米	100	723~2162	[104]
MON	玉米、硬质小麦	45~95.1	15~41	[83,103]
FUS	小麦、大麦、黑麦、燕麦	0	ND	[45]
FUS	玉米	100	723~2162	[104]

注: ND 代表未检出, [#]表示检出浓度范围。

对于新兴镰刀菌毒素, BEA 污染水平较高, 在水稻、米糠、小麦、小麦面粉和玉米粉中均有检出, 在米糠中的含量高达 2281 μg/kg[56,82,101]。恩链孢菌素在谷物原粮中的污染较普遍, 污染水平也相对较高; 而在加工后的小麦粉和玉米淀粉中, 检出率与污染水平均有明显下降, 可能是由于脱壳、研磨和干燥等过程可有效去除部分毒素[56]。同时, 95%以上的米糠样本中都可检测到 ENNB 和 ENNB1[103], 这也佐证了新兴镰刀菌毒素的污染主要发生在谷物皮壳, 脱壳加工可以有效脱毒。ENNA 和 ENNA1 在小麦中的含量较低, 玉米是污染最严重的谷物, 玉米中最常见的真菌毒素是 ENNA 和 ENNB1, 其次是 BEA、ENNB 和 ENNA1。MON 在玉米和硬质小麦中均有检出, 最高检出率为 95.1%, 污染浓度为 15~41 μg/kg[83,102]。FUS 在玉米中的检出率高达 100%, 受污染程度较高, 污染浓度为 723~2162 μg/kg[104], 但在小麦、大麦、黑麦和燕麦中均未检出[45]。新兴镰刀菌毒素污染广泛, 特别是 BEA、ENNB 和 FUS 污染水平较高, 应进一步关注。

4　总结与展望

新兴真菌毒素的发生风险、污染情况和毒理学效应的研究数据尚不完善, 目前未被列入常规监管, 但国内外围绕新兴毒素的检测及污染情况已开展了相关研究。本文综述了近年来交链孢毒素和新兴镰刀菌毒素的 TLC、GC-MS、HPLC、LC-MS/MS、LC-HRMS、生物传感器等多种检测技术研究进展及发展过程, 总体呈现以下趋势: (1)由单毒素向多毒素发展。涵盖新兴毒素的真菌毒素多组分检测技术, 甚至包含真菌毒素在内的多类型污染物同步检测技术迅速发展, 这类方法大多基于色谱-质谱技术, 实现了样品的“一针式”检测, 大大节约了时间和成本, 这是食品分析领域的一个显著变化, 也将持续成为该领域的未来发展趋势。(2)由靶向检测向非靶向筛查发展。传统的靶向检测技术适用于已知毒素的精准检测, 但在缺乏标准品和参考物质的情况下难以识别新毒素和新形态, 导致毒素总量和风险被低估。液相色谱-质谱法, 特别是高分辨质谱的应用, 为毒素新形态和类别筛查提供了新的技术手段。(3)多种快速检测技术和设备的研发。为实现便捷快速的低成本检测, 光学生物传感器、免疫传感器、电化学生物传感器以及传感技术与电化学发光、表面等离子体共振、环介导等温扩增技术和智能手机等相结合, 开发出新的多模式传感检测方法, 正越来越多地应用于新兴毒素检测, 显示出广阔的应用前景。食品基质的复杂性、毒素痕量污染对于检测灵敏度的要求、多毒素同时检测、数字化智慧化

等仍是快检技术面临的挑战。多种检测方法共同发展，优势互补，为新兴毒素的发现鉴定、污染状况及健康风险研究提供了技术保障。

同时，现有的新兴毒素污染水平调查主要集中于谷类和水果，新兴镰刀菌毒素和交链孢毒素在食品中的污染较为普遍，其中，番茄及其制品中的交链孢毒素 TeA、AOH 和 AME，谷类中的 BEA 和 FUS 尤为值得关注。未来可进一步扩展相关食品类别的调查，充分考虑新兴毒素通过食品加工和食物链迁移传递产生的食品污染和健康风险。

综上，未来有必要进一步开展新兴毒素毒性评价、检测技术研发和污染水平调查，在此基础上实现全面的风险评估，提出符合中国国情的新兴真菌毒素污染控制措施，为食品中新污染物的防控提供支持和依据。

参考文献

[1] THOMMA BPHJ. *Alternaria* spp.: From general saprophyte to specific parasite [J]. Mol Plant Pathol, 2003, 4(4): 225–236.

[2] ALAM K, MAZUMDER A, SIKDAR S, *et al*. Streptomyces: The biofactory of secondary metabolites [J]. Front Microbiol, 2022, 13(5): 39530.

[3] MUKESH M, ANDLEEB Z, DUBEY MK, *et al*. Comparative evaluation of biochemical changes in tomato (*Lycopersicon esculentum* Mill.) infected by *Alternaria alternata* and its toxic metabolites (TeA, AOH, and AME) [J]. Front Plant, 2016, 7(53): 1408.

[4] EFSA Panel on Contaminants in the Food Chain. Scientific opinion on the risks for animal and public health related to the presence of phomopsins in feed and food [J]. EFSA J, 2012, 10(2): 2567.

[5] SÁ SVM, MONTEIRO C, FERNANDES JO, *et al*. Emerging mycotoxins in infant and children foods: A review [J]. Crit Rev Food Sci, 2021, 5(4): 1–15.

[6] SCOTT PM, LAWRENCE GA, LAU BPY. Analysis of wines, grape juices and cranberry juices for *Alternaria* toxins [J]. Mycotoxin Res, 2006, 22: 142–147.

[7] GAMBACORTA L, DARRA N, FAKHOURY R, *et al*. Incidence and levels of *Alternaria* mycotoxins in spices and herbs produced worldwide and commercialized in Lebanon [J]. Food Control, 2019, 106: 106724.

[8] SCHRADER TJ, CHERRY W, SOPER K, *et al*. Examination of *Alternaria alternata* mutagenicity and effects of nitrosylation using the Ames *Salmonella* test [J]. Teratog Carcinog Mutagen, 2010, 21(4): 261–274.

[9] XING L, ZOU L, LUO R, *et al*. Determination of five *Alternaria* toxins in wolfberry using modified QuEChERS and ultra-high performance liquid chromatography-tandem mass spectrometry [J]. Food Chem, 2020, 311: 125975.

[10] YELKO RC, JORDI M, HOUDA B, *et al*. Development and validation of a LC-ESI-MS/MS method for the determination of *Alternaria* toxins alternariol, alternariol methyl-ether and tentoxin in tomato and tomato-based products [J]. Toxins, 2016, 8(11): 328.

[11] ZHOU H, PAN S, TAN H, *et al*. A novel high-sensitive indirect competitive chemiluminescence enzyme immunoassay based on monoclonal antibody for tenuazonic acid (TeA) detection [J]. Eur Food Res Technol, 2022. DOI: 10.1007/s00217-021-03905-9

[12] 孙帆, 曹雪强, 余佃贞, 等. 食品中新兴真菌毒素链格孢毒素的生物合成调控研究进展[J]. 未来食品科学, 2022, 2(3): 73–84.
SUN F, CAO XQ, YU DZ, *et al*. Research progress in biosynthetic regulation of *Alternaria* toxins, an emerging mycotoxin in food [J]. Future Food Sci, 2022, 2(3): 73–84.

[13] 吴春生, 马良, 江涛, 等. 链格孢霉毒素细交链格孢菌酮酸的研究进展[J]. 食品科学, 2014, 19(11): 7.
WU CS, MA L, JIANG T, *et al*. A review on tenuazonic acid, a toxic produced by *Alternaria* [J]. Food Sci, 2014, 19(11): 7.

[14] SCHEIBENZUBER S, DICK F, ASAM S, *et al*. Analysis of 13 *Alternaria* mycotoxins including modified forms in beer [J]. Mycotox Res, 2021, 37: 149–159.

[15] EFSA Scientific Committee. Scientific opinion on exploring options for providing advice about possible human health risks based on the concept of threshold of toxicological concern (TTC) [J]. EFSA J, 2012, 10(7): 2750.

[16] NIELSEN LK, JENSEN JD, NIELSEN GC, *et al*. Fusarium head blight of cereals in denmark: Species complex and related mycotoxins [J]. Phytopathology, 2011, 101(8): 960–969.

[17] BÜCHTER C, KOCH K, FREYER M, *et al*. The mycotoxin beauvericin impairs development, fertility and life span in the nematode *Caenorhabditis elegans* accompanied by increased germ cell apoptosis and lipofuscin accumulation [J]. Toxicol Lett, 2020, 334: 102–109.

[18] BERTERO A, FOSSATI P, TEDESCO DEA, *et al*. Beauvericin and enniatins: *In vitro* intestinal effects [J]. Toxins, 2020, 12(11): 686.

[19] GRUBER-DORNINGER C, NOVAK B, NAGL V, *et al*. Emerging mycotoxins: Beyond traditionally determined food contaminants [J]. J Agric Food Chem, 2017, 65(33): 7052–7070.

[20] NÁCHER-MESTRE J, BELTRÁN E, STRACHAN F, *et al*. No transfer of the non-regulated mycotoxins, beauvericin and enniatins, from feeds to farmed fish reared on plant-based diets [J]. Food Chem, 2020, 323: 126773.

[21] SCARPINO V, BLANDINO M. Effects of durum wheat cultivars with different degrees of FHB susceptibility grown under different meteorological conditions on the contamination of regulated, modified and emerging mycotoxins [J]. Microorganisms, 2021, 9(2): 408.

[22] GAUTIER C, PINSON-GADAIS L, RICHARD-FORGET F. Fusarium mycotoxins enniatins: An updated review of their occurrence, the producing *Fusarium* species, and the abiotic determinants of their accumulation in crop harvests [J]. J Agric Food Chem, 2020, 68(17): 4788–4798.

[23] ĆERANIĆ A, SVOBODA T, BERTHILLER F, *et al*. Identification and functional characterization of the gene cluster responsible for fusaproliferin biosynthesis in *Fusarium proliferatum* [J]. Toxins, 2021, 13(7): 468.

[24] MASI M, ZONNO MC, BOARI A, *et al*. Terpestacin, a toxin produced by *Phoma exigua* var. heteromorpha, the causal agent of a severe foliar disease of oleander (*Nerium oleander* L.) [J]. Nat Prod Res, 2022, 36(5): 1253–1259.

[25] JAJIĆ I, DUDAŠ T, KRSTOVIĆ S, *et al*. Emerging *Fusarium* mycotoxins fusaproliferin, beauvericin, enniatins, and moniliformin in Serbian maize [J]. Toxins, 2019, 11(6): 357.

[26] LAGO LO, NIEVIEROWSKI TH, MALLMANN LP, *et al*. QuEChERS-LC-Q TOF MS for the simultaneous determination of legislated and emerging mycotoxins in malted barley and beer using matrix-matched calibration as a solution to the commercial unavailability of internal standards for some mycotoxins [J]. Food Chem, 2021, 345: 128744.

[27] SOARES MAR, BARROS S, PENA A, *et al*. Mycotoxins in pistachios (*Pistacia vera* L.): Methods for determination, occurrence, decontamination [J]. Toxins, 2021, 13(10): 682.

[28] OZER Z, CARIKCI S, YILMAZ H, *et al*. Determination of secondary metabolites of *Origanum vulgare* subsp. hirtum and *O. vulgare* subsp. vulgare by LC-MS/MS [J]. J Chem Metrol, 2020, 14(1): 25–34.

[29] 潘晨, 许勇, 韩晶, 等. 睫毛精华类化妆品中 5 种前列腺素类似物的高效液相色谱法测定及质谱验证[J]. 药物分析杂志, 2021, 41(6): 6.
PAN C, XU Y, HAN J, *et al*. Determination of five prostaglandin analogues in eyelash essence cosmetics by high performance liquid chromatography and mass spectrometry verification [J]. J Pharm Anal, 2021, 41(6): 6.

[30] ZERROUKI S, MEZHOUD S, YILMAZ MA, *et al*. LC/MS-MS Analyses and *in vitro* anticancer activity of *Tourneuxia variifolia* extracts [J]. Nat Prod Res, 2022, 36(17): 4500–4504.

[31] CHANG FC, CHEN CY, LIN CY, *et al*. A combined analytical method for biological monitoring of arsenic, benzene and polycyclic aromatic hydrocarbons in human urine by liquid chromatography tandem mass spectrometry [J]. Talanta, 2019, 198: 137–145.

[32] TAKEWAKI Y, OKABE R, NEMOTO S, *et al*. Determination of quinclorac in livestock products by LC-MS/MS [J]. Shokuhin Eiseigaku Zasshi, 2022, 63(5): 177–181.

[33] PENG R, LE J, YANG SL, *et al*. Cold-induced phase separation for the simple and reliable extraction of sex hormones for subsequent LC-MS/MS analysis [J]. J Lipid Res, 2022, 63(1): 357–359.

[34] NAKHJAVAN B, BLAND J, KHOSRAVIFARD M. Optimization of a multiresidue analysis of 65 pesticides in surface water using solid-phase extraction by LC-MS/MS [J]. Molecules, 2021, 26(21): 6627.

[35] WEI D, PAN A, ZHANG C, *et al*. Fast extraction of aflatoxins, ochratoxins and enniatins from maize with magnetic covalent organic framework prior to HPLC-MS/MS detection [J]. Food Chem, 2023, 404: 134464.

[36] DONG L, BEBRIN N, PIATKOV K, *et al*. An automated multicycle immunoaffinity enrichment approach developed for sensitive mouse IgG1 antibody drug analysis in mouse plasma using LC/MS/MS [J]. Anal Chem, 2021, 93(16): 6348–6354.

[37] ZHAO B, BIAN J, RAO M, *et al*. A dilute-and-shoot liquid chromatography-tandem mass spectrometry method for urinary 18-hydroxycortisol quantification and its application in establishing reference intervals [J]. J Clin Lab Anal, 2022, 36(8): e24580.

[38] VELA-SORIA F, GARCÍA-VILLANOVA J, MUSTIELES V, *et al*. Assessment of perfluoroalkyl substances in placenta by coupling salt assisted liquid-liquid extraction with dispersive liquid-liquid microextraction prior to liquid chromatography-tandem mass spectrometry [J]. Talanta, 2021, 221: 121577.

[39] SONG JG, CAO C, LI J, *et al*. Development and validation of a QuEChERS-LC-MS/MS method for the analysis of phenolic compounds in rapeseed oil [J]. J Agric Food Chem, 2019, 67(14): 4105–4112.

[40] HASAN HAH. *Alternaria* mycotoxins in black rot lesion of tomato fruit: Conditions and regulation of their production [J]. Mycopathologia, 1995, 130: 171–177.

[41] SANCHIS V, SCOTT PM, FARBER JM. Mycotoxin-producing potential of fungi isolated from red kidney beans [J]. Mycopathologia, 1988, 104(3): 157–162.

[42] 娄振岭, 张惠芳, 马丽萍, 等. 食管癌高低发区有关粮食与食品中互隔交链孢霉毒素的测定[J]. 河南肿瘤学杂志, 1995, (4): 251–253.
LOU ZL, ZHANG HF, MA LP, *et al*. Determination of interseptal cross-streptotoxin in grain and food in high and low incidence area of esophageal carcinoma [J]. Henan J Oncol, 1995, (4): 251–253.

[43] KPPEN R, KOCH M, SIEGEL D, *et al*. Determination of mycotoxins in foods: Current state of analytical methods and limitations [J]. Appl Microbiol Biot, 2010, 86(6): 1595–1612.

[44] ERARPAT S, BODUR S, ÖZTÜRK ER E, *et al*. Combination of ultrasound-assisted ethyl chloroformate derivatization and switchable solvent liquid-phase microextraction for the sensitive determination of l-methionine in human plasma by GC-MS [J]. J Sep Sci, 2020, 43(6): 1100–1106.

[45] MIYAGAWA H, BAMBA T. Comparison of sequential derivatization with concurrent methods for GC/MS-based metabolomics [J]. J Biosci Bioeng, 2019, 127(2): 160–168.

[46] ZHU K, CHEN Y, YU L, *et al*. Determination of neotame in various foods by high-performance liquid chromatography coupled with ultraviolet and mass spectrometric detection [J]. Food Chem, 2023, 416: 135863.

[47] GRACEFFA O, KIM E, BROWELEIT R, *et al*. Choice of buffer in mobile phase can substantially alter peak areas in quantification of lipids by HPLC-ELSD [J]. J Chromatogr B, 2022, 1209: 123417.

[48] HOLLÁ M, BÍLKOVÁ A, JAKUBEC P, *et al*. Benefits and pitfalls of HPLC coupled to diode-array, charged aerosol, and coulometric detections: Effect of detection on screening of bioactive compounds in apples [J]. 2021, 26(11): 3246.

[49] HAMEEDAT F, HAWAMDEH S, ALNABULSI S, *et al*. High performance liquid chromatography (HPLC) with fluorescence detection for quantification of steroids in clinical, pharmaceutical, and environmental samples: A review [J]. Molecules, 2022, 27(6): 1807.

[50] FLISZÁR-NYÚL E, LEMLI B, KUNSÁGI-MÁTÉ S, *et al*. Effects of microenvironmental changes on the fluorescence signal of alternariol: Magnesium induces strong enhancement in the fluorescence of the mycotoxin [J]. Int J Mol Sci, 2021, 22(16): 8692.

[51] QIN Q, FAN Y, JIA Q, *et al*. The potential of *Alternaria* toxins production by *A. alternata* in processing tomatoes [J]. Toxins, 2022, 14(12): 827.

[52] LIN X, ZHANG Q, ZHANG Y, *et al*. Further data on the levels of emerging *Fusarium* mycotoxins in cereals collected from Tianjin, China [J]. Food Addit Contam B, 2021, 14(1): 74–80.

[53] GONZÁLEZ-JARTÍN JM, RODRIGUEZ-CANAS I, ALFONSO A, *et al*. Multianalyte method for the determination of regulated, emerging and modified mycotoxins in milk: QuEChERS extraction followed by UHPLC-MS/MS analysis [J]. Food Chem, 2021, 356: 129647.

[54] RADIĆ B, KOS J, JANIĆ HE, *et al*. Fusarium metabolites in maize from regions of Northern Serbia in 2016—2017 [J]. Food Addit Contam B, 2021, 14(4): 295–305.

[55] PUNTSCHER H, ML KÜTT, SKRINJAR P, *et al*. Tracking emerging mycotoxins in food: Development of an LC-MS/MS method for free and modified *Alternaria* toxins [J]. Anal Bioanal Chem, 2018, 410(18): 4481–4494.

[56] QIU N, SUN D, ZHOU S, *et al*. Rapid and sensitive UHPLC-MS/MS methods for dietary sample analysis of 43 mycotoxins in China total diet study [J]. J Adv Res, 2022, 39: 15–47.

[57] CHEN A, MAO X, LI Y, *et al*. *Alternaria* mycotoxins: An overview of toxicity, metabolism, and analysis in food [J]. J Agric Food Chem. 2021, 69(28): 7817–7830.

[58] SCARPINO V, VANARA F, SULYOK M, *et al*. Fate of regulated, masked, emerging mycotoxins and secondary fungal metabolites during different

large-scale maize dry-milling processes [J]. Food Res Int, 2021, 140: 109861.

[59] VIEIRA NC, CORTELO PC, CASTRO-GAMBOA I. Rapid qualitative profiling of metabolites present in *Fusarium solani*, a rhizospheric fungus derived from *Senna spectabilis*, using GC/MS and UPLC-QTOF/MS^{E} techniques assisted by UNIFI information system [J]. Eur J Mass Spectrom, 2020, 26(4): 281–291.

[60] PUNTSCHER H, COBANKOVIC I, MARKO D, *et al*. Quantitation of free and modified *Alternaria* mycotoxins in European food products by LC-MS/MS [J]. Food Control, 2019, 102: 157–165.

[61] SCHEIBENZUBER S, DICK F, ASAM S, *et al*. Analysis of 13 *Alternaria* mycotoxins including modified forms in beer [J]. Mycotoxin Res, 2021, 37: 149–159.

[62] SCHEIBENZUBER S, DICK F, BRETTRÄGER M, *et al*. Development of analytical methods to study the effect of malting on levels of free and modified forms of *Alternaria* mycotoxins in barley [J]. Mycotoxin Res, 2022, 38(2): 137–146.

[63] LEMLI B, VILMÁNYI P, FLISZÁR-NYÚL E, *et al*. Testing serum albumins and cyclodextrins as potential binders of the mycotoxin metabolites alternariol-3-sulfate, alternariol-9-monomethylether and alternariol-9-monomethylether-3-sulfate [J]. Int J Mol Sci, 2022, 23(22): 14353.

[64] TANG H, HAN W, FEI S, *et al*. Development of acid hydrolysis-based UPLC-MS/MS method for determination of *Alternaria* toxins and its application in the occurrence assessment in solanaceous vegetables and their products [J]. Toxins, 2023, 15(3): 201.

[65] LIANG Y, WANG Y, WANG F, *et al*. An enhanced open sandwich immunoassay by molecular evolution for noncompetitive detection of *Alternaria* mycotoxin tenuazonic acid [J]. Food Chem, 2021, 361: 130103.

[66] WANG J, PENG T, ZHANG X, *et al*. Application of quantitative structure-activity relationship analysis on an antibody and alternariol-like compounds interaction study [J]. J Mol Recognit, 2019, 32(6): e2776.

[67] LIANG YF, ZHOU XW, WANG F, *et al*. Development of a monoclonal antibody-based ELISA for the detection of *Alternaria* mycotoxin tenuazonic acid in food samples [J]. Food Anal Method, 2020, 13(8): 1594–1602.

[68] WANG Z, CHEN L, ZHENG P, *et al*. Recombinant antibody-based and computer-aided comprehensive analysis of antibody's equivalent recognition mechanism of alternariol and alternariol monomethyl ether [J]. Front Chem, 2022, 10: 12–17.

[69] WANG J, PENG T, ZHANG X, *et al*. A novel hapten and monoclonal antibody-based indirect competitive ELISA for simultaneous analysis of alternariol and alternariol monomethyl ether in wheat [J]. Food Control, 2018, 94: 65–70.

[70] NGUYEN NT, VARGA E, MARAGOS C, *et al*. Cross-reactivity of commercial and non-commercial deoxynivalenol-antibodies to emerging trichothecenes and common deoxynivalenol-derivatives [J]. World Mycotoxin J, 2019, 12(1): 45–53.

[71] CAO FJ, CHENG HH, MA SX, *et al*. Three-channel smartphone-based aptamer sensor for multiplexed detecting antibiotics in water through resonance light scattering [J]. Sens Bio-Sens Res, 2022, 38: 100533.

[72] QUÍLEZ-ALBURQUERQUE J, GARCÍA-IRIEPA C, MARAZZI M, *et al*. Interaction of a 1,3-dicarbonyl toxin with Ru (II)-biimidazole complexes for luminescence sensing: A spectroscopic and photochemical experimental study rationalized by time-dependent density functional theory calculations [J]. Inorg Chem, 2021, 61(1): 328–337.

[73] WANG S, GAO H, WEI Z, *et al*. Shortened and multivalent aptamers for ultrasensitive and rapid detection of alternariol in wheat using optical waveguide sensors [J]. Biosens Bioelectron, 2022, 196: 113702.

[74] QUILEZ-ALBURQUERQUE J, DESCALZO AB, MORENO-BONDI MC, *et al*. Luminescent molecularly imprinted polymer nanocomposites for emission intensity and lifetime rapid sensing of tenuazonic acid mycotoxin [J]. Polymer, 2021, 230: 124041.

[75] SOHRABI H, ARBABZADEH O, KHAAKI P, *et al*. Emerging electrochemical sensing and biosensing approaches for detection of fumonisins in food samples [J]. Crit Rev Food Sci, 2022, 62(31): 8761–8776.

[76] MAN Y, LI A, LI B, *et al*. A microfluidic colorimetric immunoassay for sensitive detection of altenariol monomethyl ether by UV spectroscopy and smart phone imaging [J]. Anal Chim Acta, 2019, 1092: 75–84.

[77] 陈瑞鹏, 高志贤, 梁俊. 农产品中真菌毒素检测方法研究进展[J]. 食品安全质量检测学报, 2021, 12(6): 2283–2291.
CHEN RP, GAO ZX, LIANG J. Research progress on detection methods of mycotoxins in agricultural products [J]. J Food Saf Qual, 2021, 12(6): 2283–2291.

[78] SANTOS CET, PIACENTINI KC, ALMEIDA NA, *et al*. Rapid assessment of enniatins in barley grains using near infrared spectroscopy and chemometric tools [J]. Food Res Int, 2022, 161: 111759.

[79] DELGADO-POVEDANO MD, LARA FJ, GÁMIZ-GRACIA L, *et al*. Non-aqueous capillary electrophoresis-time of flight mass spectrometry method to determine emerging mycotoxins [J]. Talanta, 2023, 253: 123946.

[80] GOTTHARDT M, KANAWATI B, SCHMIDT F, *et al*. Comprehensive analysis of the *Alternaria* mycobolome using mass spectrometry based metabolomics [J]. Mol Nutr Food Res, 2020, 64(3): 1900558.

[81] JI XF, DENG T, XIAO YP, *et al*. Evaluation of *Alternaria* toxins in fruits, vegetables and their derivatives marketed in China using a QuEChERS method coupled with ultra-high performance liquid chromatography-tandem mass spectrometry: Analytical methods and occurrence [J]. Food Control, 2023, 147(3): 11.

[82] LÓPEZ P, VENEMA D, DE RIJK T, *et al*. Occurrence of *Alternaria* toxins in food products in the Netherlands [J]. Food Control, 2016, 60: 196–204.

[83] BERTUZZI T, GIORNI P, RASTELLI S, *et al*. Co-occurrence of moniliformin and regulated *Fusarium* toxins in maize and wheat grown in Italy [J]. Molecules, 2020, 25(10): 25–29.

[84] MECA G, ZINEDINE A, BLESA J, *et al*. Further data on the presence of *Fusarium* emerging mycotoxins enniatins, fusaproliferin and beauvericin in cereals available on the Spanish markets [J]. Food Chem Toxicol, 2010, 48(5): 1412–1416.

[85] HEREBIAN D, SEBASTIAN ZÜHLKE, LAMSHFT M, *et al*. Multi-mycotoxin analysis in complex biological matrices using LC-ESI/MS: Experimental study using triple stage quadrupole and LTQ-Orbitrap [J]. J Sep Sci, 2015, 32(7): 939–948.

[86] 周贻兵, 李磊, 吴玉田, 等. 小麦粉中 2 种新型真菌毒素含量测定方法[J]. 现代面粉工业, 2021, 35(4): 53–54.
ZHOU YB, LI L, WU YT, *et al*. Determination of two novel mycotoxins in wheat flour [J]. Mode Flour Ind, 2021, 35(4): 53–54.

[87] FRENICH AG, ROMERO-GONZÁLEZ R, GÓMEZ-PÉREZ ML, *et al*. Multi-mycotoxin analysis in eggs using a QuEChERS-based extraction procedure and ultra-high-pressure liquid chromatography coupled to triple quadrupole mass spectrometry [J]. J Chromatogr A, 2011, 1218(28): 4349–4356.

[88] RADIC B, HAJNAL EJ, MANDIC A, *et al*. Development and validation of an HPLC-DAD method for the determination of moniliformin in maize [J]. J Food Process Pres, 2022, 46(10): 33–38.

[89] HICKERT S, BERGMANN M, ERSEN S, *et al*. Survey of *Alternaria* toxin contamination in food from the German market, using a rapid HPLC-MS/MS approach [J]. Mycotoxin Res, 2016, 32(1): 1–12.

[90] MAGNANI RF, SOUZA GD, RODRIGUES-FILHO E. Analysis of alternariol and alternariol monomethyl ether on flavedo and albedo tissues of tangerines (*Citrus reticulata*) with symptoms of *Alternaria* brown spot [J]. J Agric Food Chem, 2007, 55(13): 4980–4986.

[91] RAUSCH AK, BROCKMEYER R, SCHWERDTLE T. Development and validation of a QuEChERS-based liquid chromatography tandem mass spectrometry multi-method for the determination of 38 native and modified mycotoxins in cereals [J]. J Agric Food Chem, 2020, 68(16): 4657–4669.

[92] HICKERT S, GERDING J, NCUBE E, *et al*. A new approach using micro HPLC-MS/MS for multi-mycotoxin analysis in maize samples [J]. Mycotoxin Res, 2015, 31(2): 109–115.

[93] MAGNANI RF, SOUZA GD, RODRIGUES-FILHO E. Analysis of alternariol and alternariol monomethyl ether on flavedo and albedo tissues of tangerines (*Citrus reticulata*) with symptoms of *Alternaria* brown spot [J]. J Agric Food Chem, 2007, 55(13): 4980–4986.

[94] HICKERT S, GERDING J, NCUBE E. A new approach using micro HPLC-MS/MS for multi-mycotoxin analysis in maize samples [J]. Mycotoxin Res, 2015, 31(2): 109–115.

[95] WALRAVENS J, MIKULA H, RYCHLIK M, *et al*. Development and validation of an ultra-high-performance liquid chromatography tandem mass spectrometric method for the simultaneous determination of free and conjugated *Alternaria* toxins in cereal-based foodstuffs [J]. J Chromatogr A, 2014, 1372: 91–101.

[96] WALRAVENS J, MIKULA H, RYCHLIK M, *et al*. Development and validation of an ultra-high-performance liquid chromatography tandem mass spectrometric method for the simultaneous determination of free and conjugated *Alternaria* toxins in cereal-based foodstuffs [J]. J Chromatogr A, 2014, 1372: 91–101.

[97] GAMBACORTA LD, MAGISTÀ, PERRONE G, *et al*. Co-occurrence of toxigenic moulds, aflatoxins, ochratoxin A, *Fusarium* and *Alternaria* mycotoxins in fresh sweet peppers (*Capsicum annuum*) and their processed products [J]. World Mycotox J, 2018, 11(1): 159–173.

[98] LI Y, ZHANG X, NIE J, *et al*. Occurrence and co-occurrence of mycotoxins in apple and apple products from China [J]. Food Control, 2020, 118: 107354.

[99] QIAO X, YIN J, YANG Y, *et al*. Determination of *Alternaria* mycotoxins in fresh sweet cherries and cherry-based products: Method validation and occurrence [J]. J Agric Food Chem, 2018, 66(44): 11846–11853.

[100] FRENICH AG, ROMERO-GONZÁLEZ R, GÓMEZ-PÉREZ ML, *et al*. Multi-mycotoxin analysis in eggs using a QuEChERS-based extraction procedure and ultra-high-pressure liquid chromatography coupled to triple quadrupole mass spectrometry [J]. J Chromatogr A, 2011, 1218(28): 4349–4356.

[101] SIRI-ANUSORNSAK W, KOLAWOLE O, MAHAKARNCHANAKUL W, *et al*. The occurrence and co-occurrence of regulated, emerging, and masked mycotoxins in rice bran and maize from Southeast Asia [J]. Toxins, 2022, 14(8): 567.

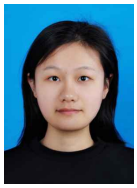
[102] SIRI-ANUSORNSAK W, KOLAWOLE O, MAHAKARNCHANAKUL W, *et al*. The occurrence and co-occurrence of regulated, emerging, and masked mycotoxins in rice bran and maize from Southeast Asia [J]. Toxins, 2022, 14(8): 567.

[103] TOLOSA J, RODRIGUEZ-CARRASCO Y, GRAZIANI G, *et al*. Mycotoxin occurrence and risk assessment in gluten-free pasta through UHPLC-Q-exactive Orbitrap MS [J]. Toxins, 2021, 13(5): 21–26.

[104] GARCÍA-NICOLÁS M, ARROYO-MANZANARES N, CAMPILLO N, *et al*. Cellulose-ferrite nanocomposite for monitoring enniatins and beauvericins in paprika by liquid chromatography and high-resolution mass spectrometry [J]. Talanta, 2021, 226(4): 12214.

(责任编辑：张晓寒　郑　丽)

作者简介



申慧婧，博士研究生，主要研究方向为食品安全。
E-mail: huijings001@163.com

吴永宁，研究员，主要研究方向为食品安全。
E-mail: wuyongning@cfsa.net.cn