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多种样品前处理方法在高分辨质谱法检测农药残留中的应用

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摘　要: 食品、药品中的农药残留安全问题引起社会越来越多的关注，农药残留检测方法为食品、药品安全监管提供技术支撑。高分辨质谱法由于具有较高的分辨率和质量精确度，近年来在农药残留检测中的应用越来越多，尽管高分辨质谱法能在一定程度上降低基质干扰，但样品前处理仍然是必要的。样品前处理可以减少基质干扰成分，提取、富集目标检测物，对农药残留检测方法的准确度、灵敏度和重现性具有重要影响。本文对近年来高分辨质谱法检测农药残留所应用的前处理方法进行概述，主要包括 QuEChERS 法、固相萃取法、极性农药快速提取法、在线前处理法等，介绍了各前处理方法的原理和应用现状，对不同前处理方法的优缺点进行分析，并对高分辨质谱法检测农药残留所应用的样品前处理的发展趋势进行展望。

关键词: 农药残留；样品前处理；高分辨质谱法；QuEChERS；固相萃取；在线前处理

Application of various sample pretreatment methods in the detection of pesticide residues by high resolution mass spectrometry

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ABSTRACT: The safety problem of food and drug caused by pesticide residues has attracted more and more attention of the society. Pesticide residue detection methods provide technical support for food and drug safety supervision. High resolution mass spectrometry (HRMS) has been more and more applied in the detection of

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pesticide residues in recent years due to its high resolution and quality accuracy. Although HRMS can reduce matrix interference to a certain extent, sample pretreatment is still necessary. Sample pretreatment can reduce matrix interference as well as extract and enrich analytes, which has important influence on the accuracy, sensitivity and reproducibility of pesticide residue detection methods. This paper reviewed the pretreatment methods used in the detection of pesticide residues by HRMS in recent years, mainly including QuEChERS, solid phase extraction (SPE), quick polar pesticides extraction (QuPPe), on-line pretreatment and so on. This article also introduced the principle and application of each pretreatment method, analyzed the advantages and disadvantages of different pretreatment methods, and prospected the development trend of sample pretreatment in pesticide residue detection by HRMS.

KEY WORDS: pesticide residues; sample pretreatment; high resolution mass spectrometry; QuEChERS; solid phase extraction; on-line sample preparation

1 引言

目前我国和世界上商品化的农药超过1500种[1]，虽然农药有助于农产品增产稳产，但是不合理使用导致的农药残留会对人体健康造成危害[2,3]，解决食品、药品中农药残留的安全性问题需要农药残留检测技术的支持。农药残留检测的难点在于，相对于痕量的农药残留，被检测物中通常含有大量的淀粉、蛋白质、脂肪、色素以及有机酸等复杂的次级代谢产物，这些成分会对农药残留检测造成复杂的基质干扰。良好的样品前处理方法能在提取、富集目标检测物的同时最大程度地去除基质干扰成分，根据调查研究，前处理时间约占总实验时间的2/3，并产生1/3以上的误差[4]，因此样品前处理对农药残留检测方法的准确度、灵敏度和重现性具有重要影响，并能在一定程度上保护仪器。

目前农药残留检测技术主要有气相色谱法[5]、液相色谱法[6]、气相色谱串联质谱法[7]和液相色谱串联质谱法[8]等，近年来，高分辨质谱法逐渐应用于农药残留检测[9,10]。高分辨质谱法具有较高的分辨率和质量精确度，一定程度上能够降低复杂基质的干扰，同时筛查农药残留不依赖于农药对照品，为农药残留检测提供了新的解决方案，在农药残留检测中的应用越来越广泛。尽管高分辨质谱法能在一定程度上降低基质效应，但样品净化仍主要依赖于样品前处理，然而目前关于高分辨质谱法检测农药残留的样品前处理方法的综述性文献较少，因此本文对近年来高分辨质谱法检测农药残留所应用的前处理方法进行概述。

通过对近年来高分辨质谱检测农药残留的文献中所应用的前处理方法进行总结，发现主要包括QuEChERS方法、固相萃取法(solid phase extraction, SPE)、极性农药快速提取法(quick polar pesticides extraction, QuPPe)、在线样品前处理等，本文主要对这4部分展开叙述。QuEChERS方法是应用最为广泛的前处理方法，改进的提取溶剂、新型净化材料、新的净化方式的发展使QuEChERS方法不断完善，尤其适用于高通量农药残留检测；固相萃取法是经典的样品前处理方法之一，净化效果好，新的合成填料如磁性吸附材料的应用进一步发展了固相萃取方法，而在固相萃取基础上发展起来的固相微萃取技术操作更加简单，溶剂消耗少，样品用量少，在高分辨质谱法检测农药残留中也有较好地应用；常规样品制备方法不适用于高极性农药多残留分析，而极性农药快速提取法是用于高极性农药的前处理方法；在线样品前处理将样品前处理和分离检测在线联用，可以避免传统样品前处理方法的过程损失和人为误差，节省人力和时间，是前处理方法的新的发展；其他前处理方法如液液萃取法等在高分辨质谱法检测农药残留中也有应用，但应用较少。目前关于高分辨质谱法检测农药残留所应用的前处理方法方面几乎没有相关综述文献，本文对此方向的研究进行总结概述，以期为后续研究者提供参考。

2 QuEChERS方法

2.1 QuEChERS方法的发展历史

QuEChERS(quick, easy, cheap, effective, rugged, and safe)方法在2003年被Anastassiades等[11]首次提出，包括提取和净化2个部分，提取溶剂采用乙腈，净化采用分散固相萃取(dispersed solid phase extraction, d-SPE)，由于具有快速、简单、经济、高效、耐用、安全的诸多优点迅速得到推广应用。QuEChERS方法的引入是为了解决农药多残留检测方法在实际应用中的局限性，在应用中不断完善发展，出现了不同的改进方法。QuEChERS方法最初使用氯化钠作为促进相分离的盐析试剂，在应用过程中发现一些pH依赖型化合物不稳定导致回收率差，于是出现了能使pH维持在5左右的缓冲盐方法，分别为QuEChERS醋酸盐方法和柠檬酸盐方法，各自被美国分析化学家协会[12](Association of Official Analytical Chemists, AOAC)和欧洲标准委员会[13](European Committee for Standardization, CEN)作为官方方法。目前QuEChERS方法被广泛应用于不同基质中农药多残留检测的样品前处理[14–18]，该方法适用范围广，耐用性好，在有害物质多残留检测的样品制备中具有极好的发展潜力。

2.2　新的提取溶剂在 QuEChERS 方法中的应用

QuEChERS传统方法用乙腈作提取溶剂，但随着检测仪器的不同要求和待测物理化性质的多样性，QuEChERS 提取溶剂也越来越多样化。例如醋酸盐方法在乙腈中加入了 1%的乙酸；欧盟的乙酸乙酯方法[15]可以看作是对 QuEChERS 方法提取溶剂的改进。近年来 QuEChERS 方法非乙腈提取溶剂的应用如表 1 所示。乙酸乙酯方法适合气相色谱法相关检测分析[19]，但也可应用于液相色谱法相关检测技术，Besil 等[20]将乙酸乙酯前处理方法和液相色谱-四级杆串联飞行时间质谱法(liquid chromatography coupled to hybrid quadrupole-time-of-flight-mass spectrometry, LC-Q-TOF-MS)联用分析不同柑橘类水果中农药残留及共提取物的基质效应，用主成分分析法将样品提取液分为柑类、橘类、柠檬类，研究表明基质效应在属之间不同，在种之间相似，该实验将天然化合物鉴定、洗脱和农药洗脱相结合来表现基质效应，是在基质指纹图谱[18]之后评价基质效应的另一个新方向。

QuEChERS 方法提取溶剂由单一的乙腈向多样化、复合型溶剂发展，使检测方式更加灵活，如乙酸乙酯提取法可用于气质联用检测；同时也有利于特殊待测物的提取，如季铵盐类农药[24]、阿维菌素类农药[26]等。

2.3　新型净化材料在 QuEChERS 方法中的应用

农药残留的样品基质具有多样性，QuEChERS 方法所用净化材料在传统的十八烷基硅烷(C_{18})[27]，N-丙基乙二胺(primary–secondary amine, PSA)[28]，石墨化碳黑(graphitized carbon black, GCB)[29]等基础上，增加了多种新材料的应用，包括增强型脂质去除材料(enhanced mtrix removal-lipid, EMR-Lipid)、二氧化锆、碳纳米管等。

EMR-Lipid 可以去除脂肪酸、甘油三酯等杂质，适合高油脂含量样品的净化。Moreno 等[30]用液相色谱-四级杆串联静电场轨道阱质谱法(liquid chromatography coupled to hybrid quadrupole-orbitrap mass spectrometry, LC-Q-Orbitrap-MS)检测橄榄油中农药残留量，采用 EMR-Lipid 做净化材料，对于正辛醇-水分配系数(octanol-water partition coefficient, K_{ow})在-2~7 之间的 162 种农药，检测限可达 0.5~50 μg/kg。

二氧化锆是过渡金属氧化物，表面同时具有酸性和碱性位点，具有路易斯酸-碱特性，对含有磺酸基、磷酸基、羧基的化合物具有强烈吸附性，对脂肪酸、磷酸、含有羧基的蛋白质等有较好的吸附效果。氧化锆包覆硅胶(a zirconia-coated silica, Z-Sep)和碳十八键合锆胶(a bonded C_{18} zirconia-coated silica, Z-Sep^{+})是以二氧化锆为基础的新型固相吸附材料[31,32]。Z-Sep 对脂肪酸、脂肪酸酯类和甾醇的去除效果较好，对杏仁和牛油果来说，Z-Sep 去除基质成分效果比 PSA 和 C_{18} 好，而且对回收率没有负面影响[33]。Palenikova 等[34,35]将 Z-Sep^{+}用于基质成分复杂的膳食补充剂和银杏叶营养制品的净化。

表 1　近年来 QuEChERS 方法新的提取溶剂在高分辨质谱法农药残留检测的应用

Table 1　Application of new extracting solvent of QuEChERS in pesticide residues detection by high resolution mass spectrometry in recent years

提取溶剂	基质	农药种类	检测方法	参考文献
乙酸乙酯	果蔬	70	GC-Q-TOF-MS*	19
乙腈-甲醇 (9:1, *V*:*V*)	果蔬	60	LC-TOF-MS#	21
乙酸乙酯	柑橘类水果	80	LC-Q-TOF-MS	20
乙酸乙酯	果蔬	45	GC-TOF-MS△	22
乙腈-乙酸乙酯 (25:75, , *V*:*V*)	芒果	68	LC-Q-TOF-MS	23
水-甲醇-甲酸(69.6:30:0.4, *V*:*V*:*V*)	食品、饮料	5(季铵盐农药)	LC-Q-Orbitrap-MS☆	24
正己烷-丙酮(9:1, *V*:*V*)	水、土壤	15(有机氯农药)	GC-Q-TOF-MS	25
乙腈 (含 0.5%氨水)	肉	6(阿维菌素类农药)	LC-Q-Orbitrap-MS	26

注: *: GC- Q-TOF-MS, gas chromatography coupled to hybrid quadrupole-time of flight mass spectrometry, 气相色谱四级杆串联飞行时间质谱法;

#: LC-TOF-MS, liquid chromatography coupled to time of flight mass spectrometry, 液相色谱飞行时间质谱法;

△ : GC-TOF-MS, gas chromatography coupled to time of flight mass spectrometry, 气相色谱飞行时间质谱法;

☆ : LC- Q-Orbitrap-MS, liquid chromatography coupled to hybrid quadrupole-orbitrap mass spectrometry, 超高液相色谱四级杆串联静电场轨道阱质谱法。

碳纳米管是碳元素同素异形体的一种，碳原子通过 SP^2 杂化与周围 3 个碳原子键合构成平面结构的石墨片，单层或多层石墨片绕同一中心轴卷曲形成了无缝纳米级管状结构，根据组成碳纳米管的石墨片层数分为单壁碳纳米管(single-walled carbon nanotubes, SWCNTs)和多壁碳纳米管(multi-walled carbon nanotubes, MWCNTs)，碳纳米管的吸附机理主要是疏水作用、π-π 作用、表面官能团的氢键作用以及表面带电形成的静电作用[36-39]。Chen 等[40]建立了 LC-Q-Orbitrap-MS 分析茶叶和菊花中氟虫腈及其代谢物的方法，前处理用 CNTs 做吸附材料，定量限 2 μg/kg。CNTs 也被应用于茶叶中 117 种农药残留测定的样品制备[41]。CNTs 也可以用来富集目标化合物，Deme 等[42]用 CNTs 提取富集葡萄和芒果汁中有机氯、有机磷、氨基甲酸酯、拟除虫菊酯等多种残留农药，甲醇-二氯甲烷(40:60, *V*:*V*)洗脱后进样分析，定量限 0.1~0.5 ng/mL。Su 等[43]等研制了一种含有多壁碳纳米管、硅藻土、中性氧化铝和无水硫酸镁的微型提取包，用于提取人参中的有机磷农药，提取和净化可以同时进行，一步完成。

在 QuEChERS 传统净化材料 C_{18}、PSA、GCB 等不能取得理想净化效果或者净化材料对待测物有吸附严重影响回收率的情况下，建议尝试应用新型净化材料。

2.4 新的提取净化方式在 QuEChERS 方法中的应用

为了简化样品制备，改善前处理效果，QuEChERS 的提取净化方法有新的改进，如注射器内分散固相萃取、一次性移液管提取、高通量平面固相萃取净化、分散液-液微萃取净化、固相萃取净化等。

Chen 等[41]对茶叶中 117 种农药残留进行测定，采用了注射器内分散固相萃取，与其他方法相比具有耗时少、溶剂消耗少、成本低、样品分析更加高通量的优点。Jia 等[44]测定绿茶提取物中 400 余种农药残留，将 QuEChERS 与一次性移液管提取(disposable pipet extraction, DPX)结合，更加简单省时。Oellig 等[45]则在 QuEChERS 提取之后采用高通量平面固相萃取(high-throughput planar solid phase extraction, HTpSPE)净化，几乎完全避免基质效应，可以用纯溶剂标准曲线定量，样品不经过色谱分离通过微流进样直接进入质谱分析，检测结果与传统的液相色谱串联质谱法一致。对于果蔬、肉类等食品中的多类农药残留，Amelin 等[46]将 QuEChERS 提取与分散液-液微萃取净化结合进行样品制备。传统的固相萃取(SPE)也可以作为 QuEChERS 的净化方法成为新的应用[21]，Goon 等[47]用 UPLC-Q-Orbitrap-MS 同时测定黑胡椒、豆蔻等 6 种香料中 199 种农药残留，基于 HLB 柱的 SPE 净化降低了假阴性率。测定茶叶中 146 种农药残留，Saito 等[48]在 QuEChERS 提取步骤用硅藻土助滤剂过滤，用磷酸盐缓冲液稳定 pH，依次通过 C_{18} 柱和 GCB/PSA 混合柱净化。

QuEChERS 净化的吸附材料可能会降低某些待测物的回收率，在实际应用中会对净化材料进行优化或者去掉净化步骤。灭菌丹是碱性 pH 敏感农药并且容易在前处理过程中降解，Badoud 等[49]在前处理做出 2 个改进：一是用 1%甲酸冰水溶液和乙腈提取，二是在净化步骤去掉了会使 pH 升高至 7~9 的净化材料 PSA。Albert 等[50]考察了有无净化步骤情况下，水果中 4 种农药的方法学参数和检出结果，二者基本一致。高分辨质谱法可以无需净化过程对复杂基质婴儿食品中的农药残留进行检测[51–53]，净化步骤也可以采用多变量曲线解析的化学计量学清除来代替[54]。

QuEChERS 方法传统采用 d-SPE 净化方式，但净化方式是灵活多变的，在不影响检测目的情况下，甚至前处理可以不采用净化步骤。与 d-SPE 相比，注射器内分散固相萃取、一次性移液管提取、高通量平面固相萃取优势在于更加简单、省时、高效，但需要特定的实验耗材；分散液-液微萃取净化、固相萃取净化优势在于净化效果更好，但相对操作复杂，耗时较长。实际检验或方法开发中，可根据不同检测需求灵活选择净化方案。

2.5 QuEChERS 方法的不足

QuEChERS方法被提出以后，以其独特的优势迅速得到广泛应用，但 QuEChERS 方法不是完美的，作为一种通用的前处理方法，更倾向于兼顾多种农药的整体提取效果，对于特定基质或待测物，其他前处理方法可能会有更好的效果。例如对于蜂蜜中的新烟碱类杀虫剂，Valverde 等[55]考察了 SPE 和 QuEChERS 2 种前处理方法，QuEChERS 法(无净化步骤)适合分析浅色蜂蜜，SPE 适合分析深色蜂蜜。说明 SPE 净化效果优于 QuEChERS 法；王慧君等[56]用 LC-Q-TOF-MS 检测苹果和番茄中 282 种农药残留时比较了 SPE 和 QuEChERS 法，得出一致结论，认为 2 种前处理方法与高分辨质谱结合均能满足农药残留日常检测，SPE 净化效果更好，定量更为准确，但步骤繁琐，操作费时，QuEChERS 法更加简单高效，检测时应根据不同目的选择合适的前处理方法。Meghesan 等[57] 对蔬菜中 10 种农药代谢产物进行分析，发现 Mini-Luke 法的回收率普遍明显高于 QuEChERS 法。Meghesan 等[58]针对葡萄和土豆基质比较了 5 种前处理方法：QuEChERS 醋酸盐法、QuEChERS 氯化钠法、Mini-Luke 法、乙酸乙酯方法和 DIN EN 1567 方法，最终选择改进的 Mini-Luke 法。高分辨质谱测定大豆和大豆异黄酮补充剂中 257 种农药和真菌毒素[59]的实验结果表明，稀释注射法(dilute and shoot)比 QuEChERS 提取效果好。

QuEChERS法虽应用较广，但实际检测时应根据特定的农药残留检测需求充分调研多种前处理方法，考察后选择最合适的前处理方法。

3　固相萃取法

3.1　固相萃取简介及应用

固相萃取利用了色谱分离原理，以固定相做吸附剂，对样品或样品提取液中的目标分析物选择性吸附富集，再通过合适的有机溶剂洗脱后用于检测分析。SPE 是应用最广泛的样品提取净化方法之一，因为溶剂消耗少、经济实惠，成为了液液萃取法的替代方法[60]。根据吸附剂类型和适用范围，SPE 柱可分为键合硅胶 C_{18}、C_8SPE 柱，多孔苯乙烯-二乙烯基苯共聚物 SPE 柱，石墨碳 SPE 柱，离子交换树脂 SPE 柱和金属配合物吸附剂 SPE 柱等[61]，可以根据待测化合物或基质成分的理化性质选择合适的 SPE 柱，因此 SPE 方法专属性较好，去除基质干扰作用较强。

高分辨质谱检测农药残留前处理常用的 SPE 柱主要有 C_{18} 柱、亲水亲脂平衡(HLB)柱、石墨化碳黑-氨基(Carbon-NH_2)混合柱和 Florisil 柱等。Ares 等[62]用 C_{18} 柱前处理结合 LC-Q-TOF MS 对蜂蜜中痕量氟虫胺进行检测，定量限 0.4~0.6 mg/kg。米糠蛋白粉成分复杂，Wu 等[63]在同位素稀释高分辨质谱检测之前，用简易溶剂萃取和 HLB 柱处理样品，检测稻瘟灵、戊唑醇、丙环唑、三环唑 4 种农药，具有较低的定量限(0.2~1 μg/kg)。Pang 的研究团队建立高分辨飞行时间质谱快速筛选果蔬中几百余种农药残留方法时均采用 Carbon-NH_2 混合柱进行样品制备[10,64-65]。Zhang 等[66]建立对映选择性测定顺-氟环唑和茚虫威的高分辨质谱方法，对新鲜茶叶、炮制茶叶、土壤等样品用 GCB-Florisil 混合柱处理，茶汤用 C_{18} 柱处理。大气压化学电离源(atmospheric pressure chemical ionization source, APCI)的 GC-Q-TOF MS 检测肉类等脂肪基质中 50 种农药残留[67]，样品经过乙酸乙酯提取，无水硫酸镁过滤后 Florisil 柱净化，定量限 50 μg/kg。

SPE 作为经典的样品制备方法，净化效果好，有利于检测方法灵敏度的提高；而根据上述 Pang 等对几百余种农药多残留检测的研究经验，SPE 在农药多残留检测的基质净化方面仍具有应用潜力。

3.2　新填料在固相萃取中的应用

新合成吸附材料的应用使 SPE 方法得到进一步的发展，可以改善方法性能，降低成本，节约时间。二乙烯三胺-功能磁芯壳聚合物改性氧化石墨烯(diethylenetriamine-functional magnetic core-shell polymer modified graphene oxide, DETA-MPs-GO)是一种新的磁性吸附材料，具有氢键和 π-π 叠加的协同吸附作用，被应用于磁性固相萃取(magnetic solid-phase extraction, MSPE)中[68]，结合高分辨质谱测定水果中 9 种杀菌剂，具有基质干扰小、回收率高、精密度高的优点，所测化合物定量限 0.01~0.30 μg/kg。Zhang 等[69]采用了一种基于聚合物阳离子交换材料(polymer cation exchange material, PCX)的分散微固相萃取(dispersive micro-solid phase extraction, DMSPE)方法对蜂蜜进行前处理，测定 5 种三嗪类农药，此方法净化一个样品所需时间总约 5 min，并且成本是 SPE 柱的 1/10，在蜂蜜中三嗪类化合物检测方面有良好应用前景。

新净化材料在 SPE 中的应用使传统 SPE 方法具有了新的发展潜力，但目前商品化的 SPE 新净化材料较少，文献中多为自制 SPE 净化材料，距离广泛应用还需要一些时间。

3.3　固相微萃取法

固相微萃取法(solid phase micro-extraction, SPME)是在固相萃取原理的基础上，通过包被纤维涂层的特殊组件直接与样品接触或悬浮在样品顶空，将采样、分离、吸附、富集一步完成的样品制备方法。SPME 免去了溶剂消耗、简化了样品前处理步骤、减少了样品用量，并且萃取物相对更加干净、富集程度更好[70]。

Souza 等[71]自制了一种改性涂层纤维，应用于固相微萃取中，通过直接浸渍即可提取葡萄中农药残留，但是此方法不适用高极性农药和高疏水性农药。Chen 等[72]首次把聚合物阳离子交换吸附剂(polymer cation exchange, PCX)作为分散微固相萃取(dispersive micro-solid-phase extraction, DMSPE)吸附材料提取柑橘和苹果中的吗啉，研究认为 PCX 在碱性物质痕量检测中有良好应用前景。Obuseng 等[73]提取延药睡莲中的农药残留，考察了 QuEChERS 和 SPME 2 种方法，认为二者均是植物中农药残留痕量检测的良好前处理方法。测定水果中三唑类杀菌剂，Souza 等[74]比较了 QuEChERS 醋酸盐方法和 SPME 方法，SPME 的定量限比 QuEChERS 方法至少低了一个数量级，准确度和精密度 2 个方法相当。

固相微萃取法需要特定的实验耗材，目前文献中的应用较少，方法的稳定性、耐用性需要更多研究来证明。

4　极性农药快速提取法

极性农药快速提取法[75]是欧盟农药残留标准体系的组成部分，于 2011 年首次公布，是为了解决不适用于 QuEChERS 等常规样品制备方法的高极性农药多残留分析问题。该方法用水和酸化甲醇萃取，混合物离心、过滤后通过检测仪器分析，通常采用同位素内标补偿体积偏差、样品制备过程中的分析物损失和测量过程中的基质效应。提取溶剂酸化甲醇主要包括 2 种，对于百草枯、敌草快等极性农药推荐使用 1%甲酸酸化的甲醇，对于二季铵盐类农药推荐使用 1:1(*V*:*V*)的甲醇-盐酸水溶液(0.1 mol/L)。

Nortes 等[76]用 1%甲酸甲醇对橄榄油和橄榄中的百草枯、缩节胺、三乙膦酸铝等 7 种极性农药进行提取，通过亲水相互作用液相色谱-高分辨质谱法分析检测，大多数化合物定量限<5 μg/kg。QuPPe 官方方法没有净化步骤，Lara 等[77]对 QuPPe 方法进行改进，用 PSA 对蔬菜提取液

净化后用于 APCI 源的高分辨质谱实时直接测定，测定环丙氨嗪、霜霉威、三乙醇胺、1,2,4-三氮唑等 7 种高极性农药，检测限 20~60 μg/kg，该方法结合了高分辨质谱法实时直接测定，样品制备和仪器分析的速度都非常快，适合高极性农药的多残留快速筛选。季铵类强极性农药需要用到极性更强的提取溶剂，Nardin 等[24]对 QuPPe 方法进行改进，用水-甲醇-甲酸(69.6: 30:0.4, *V*:*V*:*V*)提取矮壮素、缩节胺等 5 种农药，检测限≤3 μg/L。

QuPPe 主要应用于常规样品制备方法无法解决的高极性农药残留前处理，专属性较强，当待测物仅含有极性农药时适合采用此方法，但当待测物极性差异较大时建议考察后选用。

5 在线样品前处理

在线样品前处理将前处理和分离检测在线联用，实现自动化前处理和分离检测，可以避免传统样品前处理的过程损失和人为误差，同时节省人力和时间，提高了色谱分析方法的准确度、精密度和分析速度，已经成为分析化学的研究热点[78]。Andrade 等[79]对玉米中莠去津、西马嗪、特丁利、西咪替林和阿米替林 5 种农药进行分析，采用了在线分子印迹固相萃取法对目标化合物进行自动在线富集，定量限 5~10 μg/kg。Cotton 等[80]建立 LC-Q-Orbitrap-MS 法测定水中 300 余种农药残留，通过 HLB 柱进行在线富集净化，36 min 即可完成样品净化和分析检测全部流程，大多数化合物检测限 0.1 μg/L。测定水果软饮料中尿嘧啶类农药，Ivanova 等[81]采用 C_{18} 柱在线纯化样品用于紫外-基质辅助激光解析电离-静电场轨道阱质谱法分析，检测限 0.011 ng/g。

在线样品前处理是分析检测前处理方法的发展方向，具有良好发展前景，但是对仪器设备和实验操作都有一定要求，由于目前发展还不够成熟，方法相对缺少灵活性。相信随着仪器设备、实验耗材的进步，在线样品前处理将会在农药残留检测中得到更多应用。

6 其他前处理方法

除以上应用较多的几种前处理方法之外，其他前处理方法在高分辨质谱法检测农药残留中也有应用，例如 Amelin 等[82]测定牛奶、肉、鸡蛋等食品中农药残留，采用了液液萃取法。Goscinny 等[83]建立筛选果蔬中 100 种农药残留的离子淌度飞行时间质谱法，采用果蔬农残甲醇提取法[84]制备样品。Saito 等[85]用 LC-Q-TOF-MS 测定果蔬中 149 种农药残留，采用了日本官方方法，乙腈提取后加入氯化钠和 pH 7.0 的磷酸盐缓冲液，再经过 C_{18} 柱和 GCB/PSA 串联柱 2 次净化。

农药残留的前处理方法多种多样，各有优缺点和适用范围，在样品制备过程中，根据样品特征、仪器条件等同时应用多种前处理方法或将不同的前处理方法优势组合是新的发展趋势。Cladiere 等[86]用 LC-TOF -MS 对茶叶和茶汤中包括农药残留在内的理化性质差异较大的 4 类食品污染物进行检测时，使用了多种前处理方法：茶汤用液液萃取(liquid-liquid extraction, LLE)和稀射法(dilute and shoot, D&S)简单处理后进样分析；茶叶用无净化步骤的 QuEChERS 方法制备。Sanchez 等[87]用 LC-Q-TOF-MS 测定拌种作物的花粉和蜂蜜中新烟碱类农药及其代谢物残留，蜂蜜用反相聚合物 SPE 柱前处理，花粉用固液萃取法处理。LC-Q-Orbitrap-MS 分析果蔬和茶叶中农药残留，QuEChERS 柠檬酸盐法提取后，果蔬用硫酸镁、PSA、C_{18} 净化，茶叶用硫酸镁、Z-Sep 净化[88]。测定银杏营养制品中农药残留，研究者用稀射法结合 QuEChERS 净化进行样品制备[89]。

农药品种繁多，理化性质迥异，因此农药多残留检测对前处理具有较高要求，面对多种多样的样品前处理方法，在实际检测或方法开发过程中，不必拘泥于传统方法、主流方法或限制于一种方法，可在充分调研的基础上，考察多种前处理方法，根据检测目的对传统方法进行创新，或将多种方法优势互补组合成新的方法以满足检测需求。

7 结论与展望

目前，高分辨质谱法检测农药残留应用最多的前处理方法是 QuEChERS 法，该方法操作简单，成本低，效率高，通用性强，适用于农药多残留高通量检测分析，提取溶剂、净化材料和提取净化方式的改进使 QuEChERS 方法得到了进一步发展，仍将在农药残留检测中具有广泛应用；SPE 方法相对操作复杂，耗时较长，在农药残留高通量检测应用中不具有优势，在高分辨质谱检测农药残留中的应用较少，但作为一种经典前处理方法，SPE 仍具有较好的净化效果，将 SPE 净化与 QuEChERS 提取结合是前处理方法的一种新发展；常规样品制备方法无法满足高极性农药残留检测分析要求，而 QuPPe 正是适用于高极性农药残留检测的样品前处理方法；在线前处理可以避免样品前处理的过程损失和人为误差，并节省人力和时间，由于对仪器设备有一定要求，目前应用较少。

高分辨质谱法检测农药残留的前处理方法的发展趋势主要表现在 3 个方面：(1) 新型提取净化材料在前处理中的应用，如 EMR-Lipid、Z-Sep$^+$等在 QuEChERS 中的应用，磁性吸附材料在 SPE 方法中的应用；(2) 在线前处理，在线前处理可以实现自动化样品前处理，避免人为误差和过程损失，在农药残留样品前处理中有良好应用前景；(3) 组合型前处理方法，如 QuEChERS 提取结合 SPE 净化，根据基质和待测物性质选择不同前处理方法等。不断发展进步的前处理方法与高分辨质谱技术的结合将使农药残留检测技术更加成熟，为食品、药品安全监管提供强有力的技术支撑，从而更好地保障食品、药品安全。

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