基于液相色谱法分析水环境中大环内酯类抗生素污染的研究进展

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摘 要 大环内酯抗生素广泛使用,在水环境中的残留越来越引起世界关注. 本文综述了国内外基于液相色谱技术分析水环境中大环内酯的方法,比较不同预处理法以及分析方法的灵敏度和检出限. 固相萃取法可以同时富集和净化,消耗试剂少,方便,野外操作可行,是理想的预处理技术. 液相色谱串联质谱技术选择性好、特异性高、灵敏度高,可以检测浓度低于 ng·L^{-1}的目标物,是一种可靠理想的分析方法. 最后对大环内酯分析研究进行了展望.

关键词 大环内酯类抗生素(MLs), 预处理, 高效液相色谱串联质谱法(HPLC-MS/MS).

20 世纪 40 年代开始,抗生素广泛用于疾病预防、治疗和动物生长促进剂[1]. 2000 年美国使用抗生素 16200 t,畜牧业用量占 70%,是医药品量的八倍[2]. 大环内酯类抗生素(Macrolides antibiotics,MLs)作为低浓度快速抑菌剂,广泛运用于医院临床和畜牧养殖业[3]. 1992—2003 年,澳大利亚使用大环内酯约 600 t,药用红霉素 397 t,农用泰乐霉素 109 t[4]. 2002 年,瑞士使用强力霉素 0.5 t,红霉素1.6 t[5]. 我国是抗生素生产和使用大国,据 1999 年化学医药工业统计大环内酯类原料药超过2500 t,2002 年的大环内酯类抗生素的产量已达到 72000 t,超过全球抗生素总产量 2/3[6]. 由于缺乏有效的法规和标准,我国抗生素滥用十分普遍,据统计治疗儿童普通感冒用抗生素频率超过 98%[7].

大环内酯经动物或者人体摄入后,一部分在生物体内代谢,一部分以原形或代谢产物形式随市政污水进入污水处理厂. Gao 等对北京市 8 个污水厂调查发现红霉素和罗红霉素最常检出,污水厂是抗生素的主要排放途径[5],然而污水厂仅去除部分大环内酯类抗生素(泥水分配系数 K_d < 500 L·kg^{-1}),去除效率为 17%—56%[8-9],在某些情况下甚至没有任何去除效果[10-11]. 污水厂出水、畜牧业场泥浆、粪便[12]等都可以将大环内酯引入环境,通过地表径流和地下渗透等方式污染地表水和地下水[13]. 近年来相继有从地表水、地下水、污泥、饮用水中检出大环内酯的报道[4,14-15]. 德国地表水和污水厂频繁检出红霉素及相关大环内酯,脱水红霉素达 6 μg·L^{-1}[16];瑞士污水厂和地表水中检测的大环内脂 1 μg·L^{-1}级[17];德国巴登-符腾堡州地下水中罗红霉素、脱水红霉素(49 ng·L^{-1})有所检出[18];美国自来水厂水检出罗红霉素、红霉素、泰乐霉素[19]. 玉河(Tamagawa River)、湄公河(Mekong River)、美国以及加拿大河流检出脱水红霉素、阿奇霉素、克拉霉素和罗红霉素[20-22]. 环境中的大环内酯含量与季节[23]、使用量、人口流动性有关,阿奇霉素冬季水平较高[24].

抗生素可能对非目标细菌存在毒性[25-26],长期暴露于低浓度抗生素的微生物会逐渐形成一定的耐药机制,优胜劣汰选择后,耐药性强的微生物生存和繁衍,微生物种群的组成改变,对生态系统和人类健康造成不可预知的危害[27-30]. Isidori[31]等通过商值法比较 6 种抗生素(红霉素、地灵霉素、磺胺甲恶唑、氧氟沙星、洁霉素和克拉霉素)对细菌、藻类、轮虫类和鱼类的急、慢毒性影响,结果红霉素、洁霉素和克拉霉素的风险值为 1、3.6 和 10,对水体生物有害. 因此分析水环境中大环内酯残留量对防止耐药微生物传播具有重要意义,然而目前国内并没有针对水环境中大环内酯类抗生素残留的系统分析方法.

本文综述了国内外关于水环境中大环内酯类抗生素残留的预处理和分析检测方法,便于其风险评价和环境管理服务.

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1 大环内酯类抗生素的理化性质

大环内酯是由链霉菌产生的一类弱碱性抗生素,具有 14—16 元大环内酯环的基本化学结构. 通过作用于细菌细胞核糖蛋白体 50s 亚单位,抑制细菌蛋白质合成,从而快速抑制革兰氏阳性菌和某些革兰氏阴性菌、支原体的生长[32]. 不同类型大环内酯的生物活性存在差异,十六元环生物活性最强. 大环内酯具有亲脂性,易溶于甲醇、乙腈、乙酸乙酯等有机溶剂,不易溶于水;因显示弱碱性,在酸性环境不稳定,具有水解性[33];溶解性、稳定性与 pH 有关,大部分 MLs 随着溶剂极性的增加而溶解度增加,随着温度升高溶解度降低. 泰乐霉素在酸、碱性环境中不稳定,中性条件(pH 7)相对稳定;pH = 6—8 水溶液中,红霉素稳定性较差;pH 值小于 6 时,形成脱水红霉素,抗菌活性降低[34];pH 值小于 2.3 时,红霉素稳定性急剧下降. 酸性环境中,罗红霉素比红霉素更加稳定;克拉霉素和阿奇霉素生物利用效率较其它 MLs 高[35]. 酸性环境中,克拉霉素和红霉素分解服从假一级动力学方程[36]. Tong 等[37]发现阿奇霉素在人造光源下降解遵从一级动力学方程,加入含硝酸盐(5 $mg\cdot L^{-1}$)和腐植酸(0.5 $mg\cdot L^{-1}$)的混合溶液加快阿奇霉素降解. 低剂量臭氧条件下,克拉霉素迅速氧化为对应的 N-氧化物(N-oxides),从而不具有生物特性[38]. 人工湿地对克林霉素去除效率低,洁霉素甚至没有去除效果[39]. 某些大环内酯在污水厂进水未检出,而在出水中检出. Gracia-Lor 等[40]发现红霉素和罗红霉素在污水厂出水中检出而进水中未检出,Göbel 等[8]认为这可能是 MLs 从粪便等排泄物释放到水体造成.

大环内酯代谢能力弱,主要通过尿液和粪便等以原型方式排出体外,排出总量百分比:克拉霉素 10%—20%,罗红霉素 30%,螺旋霉素 10%—20%,阿奇霉素 6%—12%,红霉素 5%—10%[41]. 除罗红霉素 pK_a值为 9.2 外,其它物质 pK_a(酸度系数)为 7.4(泰乐菌素)—8.9(红霉素);红霉素和罗红霉素 lgK_{ow}(正辛醇-水分配系数)分别为 3.06 和 2.75;红霉素的污泥-水分配系数(K_d)为 164.76 $L\cdot kg^{-1}$;泰乐霉素的土壤-水分配系数(K_d):8.3—128 $L\cdot kg^{-1}$[42]. 环境中大环内酯抗生素的滞留时间长,距离污水厂出口 100 m 处仍可检出克林霉素[43];土壤中红霉素生物转化半衰期为 11.5 d[44],竹桃霉素半衰期 27 d,泰乐菌素 8 d,泰妙菌素 16 d,沙利霉素 5 d. 在 35 d 内罗红霉素残留基本无变化,持久性强[45];地表水中的泰乐霉素好氧降解半衰期为 9.5—40 d[46].

2 预处理

水环境中大环内酯浓度相对较低,检测前需要多个处理步骤,建立快速、科学、高效的预处理方法是前提. 针对环境样品如废水、环境水体、土壤、污泥、沉积物,预处理一般包括取样、富集、萃取、净化[47]. 消除基质干扰和高效提取目标物是前处理的关键. 固体索氏提取法、加压溶剂萃取(Accelerated solvent extraction,ASE)和超声波辅助萃取(Ultrasound-assisted extraction,UAE)[48]是萃取固体样品(污泥、土壤)目标物的常用方法. Jacobsen 等[49]采用加压溶剂萃取法从土壤中提取金霉素、氧四环素、磺胺嘧啶、红霉素和泰乐菌素,以柠檬酸和甲醇为萃取溶剂,采用 SAX + HLB 柱串联富集净化,SAX 柱去除腐植酸类物质、HLB 富集目标物,MLs 回收率为 60%—100%,检出限为 2.4—5.5 $\mu g\cdot kg^{-1}$. Löffler 等采用超声波提取结合固相萃取(SPE)净化法,成功从土壤和沉积物中提取大环内酯,采用甲醇、丙酮、乙酸乙酯超声波提取两次后进行 LC-ESI-MS 分析,定量限为 20 $ng\cdot g^{-1}$[50].

对于水环境样品,预处理方法包括:液液萃取法(liquid-liquid extraction,LLE)、固相萃取法(solid-phase extraction,SPE)、固相微萃取方法(Solid-phase microextraction,SPME)等,其中固相萃取法最常用.

2.1 液液萃取法

Hammel[51]采用 4 步 LLE 法,以 1 mL 乙腈、0.5 mL 10% 三氯乙酸水溶液(trichloroacetic acid,TCA) + 1 mL 乙腈、40 μL 九氟戊酸(nonafluoropentanoic acid,NFPA) + 1 mL 乙腈、1 mL 乙腈为提取溶剂,从蜂蜜中成功提取 42 种抗生素,包括 7 种大环内酯(红霉素、竹桃霉素、替米考星、罗红霉素、螺旋霉素、泰乐菌素、脱藻糖泰洛星),LC-ESI-MS/MS 分析,方法回收率为 28%(泰乐菌素,10 $\mu g\cdot kg^{-1}$)—104%(螺旋霉素,20 $\mu g\cdot g^{-1}$),其中替米考星最难提取. LLE 法萃取水样中的 MLs 运用较少.

2.2 固相萃取法

固相萃取法通过吸附柱选择性地保留和洗脱目标物从而实现复杂样品中目标物的富集、分离和纯化. 应根据基质(水溶液或者有机溶剂)和目标物质性质(极性、非极性、离子态)选择萃取柱,以求最好

回收率. 当样品基质复杂,如含腐殖酸和金属离子,MLs 会与二、三价阳离子(Ca^{2+}、Mg^{2+}、Al^{3+}等)结合,降低萃取效率. EDTA 具有广泛的配位性能,几乎能与所有金属离子形成配合物,预处理时常加入 EDTA[52-54],加入比例 0.5%(g·L^{-1},*W*/*V*). 大多抗生素物质是偏酸性,pH 值影响化合物的化学结构、稳定性,调整 pH 值有助于改善萃取效率. 水样过滤后通常加入柠檬酸、甲酸、硫酸等调 pH 值到 3—5[14,52-53,55-56]. 某些分析溶液 pH 值调为 6[12]或者大于 6[57]. 但徐维海等发现河水 pH 值(pH 3—9)对 MLs 回收率影响不大[58]. C18 和 Oasis HLB 柱具有较好的稳定性和 pH 适用性,操作性稳定,广泛用于大环内酯类抗生素及其代谢物[14,52,54,56]的检测. 对于 Oasis HLB 柱富集目标物质,甲醇[52, 55]、乙腈[59]以及超纯水均可活化 HLB 柱;富集后,加入一定量的超纯水(3—5 mL)、缓冲盐或 5% 甲醇水溶液去除柱上的蛋白质、无机盐以及其它水溶性干扰物[60],使用甲醇或甲醇和氨混合溶液洗脱可以得到较好的回收率[61]. 将洗脱的溶剂蒸干或氮气吹干,再用合适的溶剂重新溶解有利于仪器分析. 除 HLB 柱富集外,Strata™ X 固相萃取柱[62]、Oasis MCX 柱[54]、LiChrolute EN 柱和 Lichrolute C18[14]等萃取污水厂和河水中 MLs 的回收率为 60%—80%. 因富集目标物的同时可能富集大量共存干扰物,可以选用硅胶柱(Silica)[63]、强阳离子交换柱(SCX)[64-65]等进一步净化. Schlüsener 等[66]使用 DVB-phobic Speedisk cartridges 萃取污水厂进出水的目标物,首先甲醇和色谱级水活化 SPE 柱,富集水样后用色谱级水淋洗离子化合物,用甲基叔丁基醚(MTBE)和甲醇洗脱类固醇激素、克拉霉素、红霉素和罗红霉素,使用体积排斥色谱法(size-exclusion chromatography,SEC)净化. 目标物质采用 HPLC-MS/MS 进行定量分析,以 Phenosphere-Next RP18 柱分离,以 0.1 mol·L^{-1}乙酸铵和乙腈做流动相,MLs 回收率为 79%—100%,检出限为 2—6 ng·L^{-1}.

2.3　固相微萃取法

固相微萃取技术(SPME)基于萃取涂层与样品之间的吸附/溶解-解吸平衡而建立的集进样、萃取、浓缩功能于一体的样品前处理与富集技术,属于非溶剂型选择性萃取法,由 Pawliszyn 提出[67]. SPME 有 3 种基本的萃取模式:直接萃取(Direct Ectraction SPME)、顶空萃取(Headspace SPME)和膜保护萃取(membrane-protected SPME). SPME 法主要萃取空气和水中的挥发或半挥发物质[68]. 对样品组分进行选择性富集和采集,然后将吸附组分热脱附或淋洗脱附后对样品进行气相色谱(GC)、液相色谱(LC)及毛细管电泳(CE)等分离分析. SPME-GC 联用技术较为完善、运用广泛,但对于极性、非挥发性物质需要衍生化. 衍生化加长预处理的时间,甚至可能出现目标物不完全衍生化现象,影响定量效果. Mcclure 等[69]采用 SPME-HPLC-MS-MS 分析废水中的大环内酯、磺胺、甲氧苄氨嘧啶,进出水中的定量限(LOD)分别为 16—1380 ng·L^{-1}和 35—260 ng·L^{-1},相比之下,SPE 前处理的 LOD 分别为 4.7—15 ng·L^{-1}和 0.86—6.1 ng·L^{-1}. Volmer 等[70]采用纤维从水中提出红霉素 A 及其降解产物,纤维头在水中浸泡 15 min 后,再浸入解吸池中用甲醇/水(50/50)溶剂解吸;C8 色谱柱分离,用 LC-ESI-MS 分析. SPME 主要用于生物样品如:牛奶、尿液、血浆中药物的提取,环境样品运用较少[71].

LLE 萃取容易出现乳化现象,需要大量溶剂. SPME 法简单,快速,无毒害,不需要或需要少量有机溶剂,适用性强,可现场采样,但是易出现鬼峰,精密度较差,重复性差. SPE 通常需要购买 SPE 小柱,成本较高. 然而 SPE 较 SPME、LLE 重现性好、回收率高,便于现场处理和批量处理,节约时间,可以自动化操作,实际运用广泛,是主流的萃取方法.

3　分析测定

微量污染物的分析高度依赖于仪器和检测技术的发展,目前抗生素的分析方法有微生物法(Microbiological bioassay)、薄层色谱法(thin-layer chromatography)、纸色谱分析法(paper chromatography)、气相色谱法(gas chromatography)、高效液相色谱法(high-performance liquid chromatography)、毛细管区带电泳法(capillary zone electrophoresis,CZE)[72]、液相色谱联合紫外光法(LC-UV),液相色谱联合荧光法(LC-FL),液相色谱化学发光法(LC-CL),液相色谱电化学法(LC-ED)等方法[73].

3.1　微生物法和毛细管区带电泳法

微生物学方法是传统的大环内酯分析方法[74],由于微生物法采用的菌种不同,不同厂家的组分比

例存在差异,微生物法缺乏特异性和灵敏性,很难达到准确的定性定量目的,特别是复杂介质(如废水和沉积物)中抗生素的分析要求. 毛细管电泳法是近年来发展最快的分析方法之一. Zhou 等[75]利用毛细管电解法串联快速还原伏安检测法成功测定水体中红霉素、螺旋霉素、竹桃霉素,但用于分析 MLs 的运用较少.

3.2 液相色谱法

1906 年茨维特将植物色素提取液加到装有碳酸钙微粒的玻璃柱子上部,以石油醚淋洗柱子,使不同色素得到分离,这是最早的色谱分离方法. 根据所用流动性的不同,色谱法又分为气相色谱法和液相色谱法[76]. 20 世纪 50 年代,分离手段与检测系统的结合使色谱分析法在环境分析中得到高度的运用. GC-MS用于分析极性、半极性、挥发性或者半挥发性有机物,抗生素极性强、水溶性好、不易挥发,不适合 GC-MS 分析[26]. 液相色谱对大分子量、溶解性有机化合物具备高分离能力,是环境中抗生素主要分析方法[77]. 液相色谱最常用的检测器有紫外检测器(UVD,DAD)[78]、荧光检测器(FD)、有示差折光检测器(RID)和电导检测器(ECD)等.

早在 1973 年就有运用色谱法分析红霉素 A、红霉素 B 和柱晶白霉素的研究报道[79]. 1978 年 Tsuji 等利用 HPLC、Bondapak C_{18}反相柱、流动相为乙腈∶甲醇∶乙酸铵(pH 6.2)∶水 (45∶10∶10∶35)分离出红霉素 A、B、C 以及至少 9 种红霉素同分异构体和降解产物,相对标准偏差为 0.6%,检测结果与微生物检测法十分吻合[80]. 同样,有文献报道乙腈、甲醇、乙酸铵缓冲液(pH 7.0)测定红霉素、琥乙红霉素,可同时分离红霉素 A、红霉素 B、红霉素 C[81].

1980 年,Lin 等[82]采用 LLE-HPLC-UV 法测定血清中的罗沙米星,样品经碳酸钾碱化、乙醚两步萃取,乙腈-醋酸缓冲混合物为流动相,C18 柱分离目标物质,254 nm 波长检测,回收率约 86%,检出限为 10 $mg\cdot L^{-1}$.

1985 年 Dow 等采用全自动 HPLC-UV(230 nm)法测定血浆中的螺旋霉素,回收率为 71%—96%[83]. 螺旋霉素、泰乐霉素、替米考星的共轭双键具有发色团,可采用 UV 检测器在 232 nm 或者 287 nm测定吸光度,改善仪器条件、衍生化等方法可提高 UV 检测效果. 相比微生物法,HPLC-UV 具有更好的灵敏度,然而大部分大环内脂缺少合适的发色团,对某些没有特征紫外吸收的大环内酯类抗生素如红霉素及其半合成衍生物(如克拉霉素、阿奇霉素、罗红霉素、竹桃霉素等)的内酯环上无共轭双键,摩尔吸光系数低,即使 210 nm 和 215 nm 也很难实现高灵敏度的分析[73, 84]. 同时 UV 检测红霉素时要求低波长,高浓度,选择性和灵敏度低,很难实现复杂介质中低浓度大环内酯的检测. Wilms 等[85]以克拉霉素为内标物,使用酰氯(9-fluorenylmetoxycarbonyl-chloride,FMOC-Cl)柱前衍生化,C18 色谱柱、乙腈-磷酸盐缓冲液作流动性的高效液相色谱分离,267 nm 激发波长、317 nm 发射波长下荧光检测血浆、血液、水体中的阿奇霉素,血浆、血液、水体中的检出限为(0.042 ± 0.017) $mg\cdot L^{-1}$、(0.119 ± 0.065) $mg\cdot L^{-1}$、(0.072 ± 0.036) $mg\cdot L^{-1}$,血浆和血液的线性范围为 0—1.5 $mg\cdot L^{-1}$,水体中为 0—9 $mg\cdot L^{-1}$,此方法成功用于阿奇霉素药代动力学研究. 荧光衍生化易导致某些大环内酯的分解如红霉素,限制了荧光检测器的应用. González de la Huebra 等[86]采用 LLE-HPLC-ECD 法成功检测尿液中的 10 种大环内酯类抗生素(红霉素、地红霉素、泰乐霉素、替米考星、螺旋霉素、交沙霉素、北里霉素、罗沙米星、罗红霉素和竹桃霉素),尿液经过 0.45 μm 和 0.22 μm 孔径醋酸纤维素薄膜过滤器过滤,滤液于 −28 ℃保存待使用;饱和磷酸氢二钠碱化尿液,甲基叔丁基醚(MTBE)为萃取剂两次离心分离出目标物,以罗红霉素为内标,C8 色谱柱,HPLC 梯度分离,电化学检测器检测,检出限和定量限分别为:0.04 $mg\cdot L^{-1}$和 0.21 $mg\cdot L^{-1}$. 高效液相色谱-电化学法(HPLC-ECD)需要进行衍生,耗时、步骤繁琐[87];与色谱的梯度洗脱兼容性差,一般用于单个大环内酯的分析[88]. UVD、FD、ECD 只能选择性地检测某些物质.

3.3 液相色谱质谱法

液相色谱-质谱联用技术始于 1970 年,液相色谱质谱法可以鉴别和分析痕量水平的物质,并定量微量物质. 质谱(MS)尤其是串联质谱(MS/MS)通过碰撞诱导解离(CID)和选择离子模式(SIM),选择性好,灵敏度高,所得质谱图对每一种物质都具有专一性. 电喷雾电离(ESI)和大气压化学电离(APCI)是 LC-MS 通常采用的离子化方式. 大气压光电离(Atmospheric pressure photo-ionization,APPI)较前两种电离模式不容易产生信号抑制,有利于分析复杂样品的目标物质,例如 Takino 利用 LC-MS 分析时采用

APPI 检测水果和蔬菜中的氨基甲酸脂农药,然而并未见 MS/MS 中的运用报道[89]. 电喷雾电离(ESI)对极性、弱非极性、离子化、高分子以及热不稳定性物质良好的适用性,是抗生素分析中最频繁使用的离子化方式[90]. HPLC 的分离能力与质谱检测器的丰富信息与高灵敏度,使得 HPLC-MS 联用技术成为当前复杂基质中痕量大环内酯残留检测发展最快的分析手段之一. Abuin 等[12]以北里霉素(Kitasamycin)为内标,使用 SPE 预处理,富集 250 倍,用 LC-MS 和 LC-MS/MS 法检测出河水中 ng·L^{-1}级多种大环内酯类抗生素,串联质谱精确度、检出限优于质谱检测(高 1 个数量级).

反相 C18 柱分离目标物质,效能高、不易拖尾、选择性好、高疏水性以及高硅醇基活性,色谱分离效果好,广泛运用于 MLs 分离[15,53,55,57,59];另外,Synergi Hydro RP[4]、RP-18 [66] 和 phenylhexyl 柱[91]分离 MLs 也较常用. 甲醇、乙腈或者两者的混合物作流动相,得到的保留时间短、分辨率高. 为改善灵敏度和分析物的离子化,可采用低浓度的甲酸、乙酸、乙酸铵作为流动相改良剂[4, 14, 56, 59],进行梯度洗脱得到最佳的分离条件.

不同样品的基质效应不同,选择合适的内标物或替代内标物可以补偿损耗和干扰,替代内标物与分析物具有相似的物化性质,其保留时间与分析物几乎相同,能补偿共萃取产生的干扰基质效应[92-95]. 通常泰乐霉素、克拉霉素[96]、红霉素-^{13}C,D_3或者交沙霉素为内标物[97-98]. Miao 等[99]采用 6 mL 丙酮、6 mL 甲醇、6 mL 超纯水(pH 6.0)活化 HLB 柱,富集 1 L 污水厂出水,氮吹后用 3 ×2 mL 甲醇洗脱;研究采用 LC-ESI-MS/MS法分析、Genesis C18 柱分离、乙腈和乙酸铵(0.05% 甲酸,pH 5)为流动相梯度洗脱分离,成功分析加拿大 5 个城市 8 大污水厂出水中包括大环内酯类(脱水红霉素、罗红霉素、克拉霉素)在内的多种抗菌剂,回收率为 73%—87%,检出限(MDL)均为 1 ng·L^{-1}. Gros[100]采用离线固相萃取法预处理、LC-MS/MS分析地表水和污水中的药物残留,经 RP-18 柱同时分离出止痛药、非甾体类抗炎药、精神药品、抗生素和 β-阻断剂等,其中 LOD 和 LOQ 分别为 1—43 ng·L^{-1}和 3—120 ng·L^{-1}. 液相色谱串联质谱(LC-MS/MS)分离和检测抗生素选择性好、灵敏度高、重现性好,是目前分析磺胺、四环素、喹诺酮、大环内酯等抗生素的主要方法[101-102].

在液相色谱方法中,采用小粒径的填料如亚 2 μm 填料,可以得到更高的柱效及更快的分离速度. 超高压液相色谱仪(UPLC)采用亚 2 μm 填料,运行压力一般超过 40 MPa. 与传统高效液相色谱(HPLC)相比,UPLC 具有以下优势:高效、高速、高分辨率[103]. Q-TOF-MS 是高分辨串联质谱,灵敏度高并且能够确定精确的质量数,从而确定化合物的分子式. 采用超高效液相色谱与串联四极杆飞行时间质谱联用技术(UPLC-Q-TOF-MS)分析环境中的抗生素,分离度高、速度快、灵敏度好,可获得准确的质量数、高分辨率和全扫描质谱,对痕量物质定性和定量更准确. 随着小粒度色谱柱、仪器耐压、检测等技术进一步完善,高效前处理以及特异性的检测方法如 UPLC-Q-TOF-MS 将是未来环境化学分析的趋势.

4　结论

大环内酯抗生素污染物在环境中频繁检出,会促进微生物耐药性以及抗生素抗性基因产生,影响生态系统、威胁人类健康. 针对水环境中大环内酯类抗生素的分析,高效液相色谱质谱(HPLC-MS)特别是串联质谱(MS/MS)是目前分析方法的主流,采用固相萃取(SPE)前处理技术,特别是 Oasis HLB 柱富集、甲醇洗脱可获得理想的效果. 分离多采用反相色谱柱 C18 柱,流动相为甲醇、乙腈或者两者的混合物,低浓度甲酸、乙酸、乙酸铵能够改善灵敏度和峰形. 液相色谱质谱联用技术灵敏度高、选择性大、检出限优越,是分析 MLs 理想的方法. 环境样品复杂,为了更加准确快速定性和定量低浓度目标物,未来应该加强样品的净化技术以及开发出更具有特异性的仪器,如:四极杆飞行时间质谱(Q-TOF-MS)技术. 目前,我国对大环内酯类抗生素的环境污染以及可能造成的生态风险尚缺乏系统研究数据,未来有待加强研究.

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Determination of macrolide antibiotic residues in water environment based on the liquid chromatography: A review

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ABSTRACT

Macrolide antibiotic is widespread used throughout the world as one kind of typical antibiotics. Because of its huge usage, there is high residue in environment. Macrolide antibiotic leads to microbial resistance and does harm to organisms in water by producing acute and chronic toxicity. It is necessary to strengthen analysis and research of the risk from macrolide antibiotics. This article reviewed the analysis methods for determining macrolide antibiotics using high performance liquid chromatography-mass spectrometry in water environment. At the same time, different pretreatments and detection methods were compared in terms of their sensitivity and detection limits, and detection of macrolide antibiotics in water environment was prospected in the future.

Keywords: macrolides antibiotics (MLs), pretreatment, high performance liquid chromatography-tandem mass spectrometry(HPLC-MS/MS).

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UPC² 的主要流动相"压缩二氧化碳(CO_2)"与液相色谱和气相色谱使用的液体流动相或载气相比表现出众多显著优点. 和 HPLC 所用的液体相比,CO_2 在单独使用或与一种共溶剂联用时,可达到更高扩散速率并具有更强质量转移能力的低粘度流动相. 与气相色谱相比,单用 CO_2 作为流动相,可以在低得多的温度下进行分离. 沃特世 ACQUITY UPC² 系统的另一优点是使用便宜且无毒的压缩 CO_2 作为主要流动相,可以替代价格极其昂贵且销毁成本高昂的有毒挥发溶剂.

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