



超高效液相色谱-串联质谱法测定医用热塑性聚氨酯中33种芳香伯胺方法的建立及应用*

杨雅静^①, 杨剑², 肖宇¹, 胡丽², 成婕², 郭燕燕², 江燕², 赵代国^{②△}

1. 成都大学食品与生物工程学院(成都 610106); 2. 四川省药品检验研究院(四川省医疗器械检测中心 四川养麝研究所)(成都 611731)

【摘要】 目的 建立超高效液相色谱-串联质谱法(ultra-high performance liquid chromatography-tandem mass spectrometry, UPLC-MS/MS), 实现对医用热塑性聚氨酯(thermoplastic polyurethane, TPU) 中 33 种芳香伯胺含量的同时测定。方法 分别以80%甲醇和含10%乙醇的PBS溶液为溶剂提取目标化合物, 80%甲醇浸提液过滤后稀释至原浓度的1/5; PBS浸提液经HLB小柱(3 mL, 60 mg, 甲醇+水平衡)处理后, 5 mL甲醇洗脱, 过滤后甲醇定容至5 mL, 采用超高效液相色谱-串联质谱进行检测分析。色谱分离采用Agilent InfinityLab Poroshell 120 EC-C18色谱柱(150 mm×3.0 mm, 2.7 μm), 以甲醇(A)和含0.1%甲酸的去离子水(B)为流动相。梯度洗脱, 柱温为40 ℃; 流速为0.2 mL/min; 进样体积为1 μL。质谱检测选用电喷雾离子源(electro-spray ionization, ESI), 多反应监测(multiple reaction monitoring, MRM)正离子模式, 考察该方法在不同浸提条件下的标准曲线与定量限、精密度、回收率及基质效应。结果 33种芳香伯胺在2~100 ng/mL浓度范围内线性关系良好($r>0.998$), 检出限为0.1~0.5 ng/mL, 定量限为0.3~1.7 ng/mL; 80%甲醇样本中33种芳香伯胺的回收率为70.7%~116.0%; 含10%乙醇的PBS样本中31种芳香伯胺的回收率为74.9%~113.8%; 本方法在不同样本中的日内、日间精密度均<10%, 样品稳定性良好。采用本方法对样品浸提液中芳香伯胺含量进行分析, 结果表明, 在初始检测的6份样品中均检出MDA, 且在37 ℃模拟浸提及60 ℃加速浸提条件下, 共有3份样品持续或延迟释放出MDA; 2,4'-MDA在初始极限浸提阶段于2份样品中检出, 并在60 ℃加速老化条件下仍可在1份样品中检出, 但在37 ℃模拟生理环境中未见释放; 2,2'-MDA仅在初始极限浸提的2份样品中检出, 在后续模拟及加速浸提过程中均未释放。结论 该UPLC-MS/MS方法灵敏度高、准确度高, 不仅可满足医用TPU中33种芳香伯胺的精准检测需求, 更为该类材料及制品的芳香伯胺风险评估与质量控制提供了可靠技术支持。

【关键词】 超高效液相色谱-串联质谱法 医用热塑性聚氨酯 芳香伯胺 同时测定 浸提释放 风险评估

Development and Application of a Method for Determining 33 Aromatic Primary Amines in Medical-Grade Thermoplastic Polyurethane by Ultra-High Performance Liquid Chromatography-Tandem Mass Spectrometry

YANG Yajing^①, YANG Jian², XIAO Yu¹, HU Li², CHENG Jie², GUO Yanyan², JIANG Yan², ZHAO Daiguo^{②△}. 1. College of Food and Biological Engineering, Chengdu University, Chengdu 610106, China; 2. Sichuan Institute for Drug Control (Sichuan Testing Center of Medical Devices, Sichuan Institute of Musk Deer Breeding), Chengdu 611731, China

△ Corresponding author, E-mail: zhaodg@scidc.org.cn

This study was supported by the Sichuan Provincial Regional Innovation Cooperation Project (No. 2025YFHZ0299).

[Abstract] Objective To develop an ultra-high performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method for the simultaneous determination of 33 aromatic primary amines in medical-grade thermoplastic polyurethane (TPU). **Methods** The target compounds were extracted using 80% methanol and PBS solution containing 10% ethanol as the solvents. The 80% methanol extract was filtered through and diluted to one-fifth of the original concentration. The PBS extract was processed through an HLB solid-phase extraction column (3 mL, 60 mg, methanol and water equilibrium), eluted with 5 mL methanol, filtered, and diluted to 5 mL with methanol. Then, analysis was performed using UPLC-MS/MS. Chromatographic separation was performed using an Agilent InfinityLab Poroshell 120 EC-C18 column (150 mm × 3.0 mm, 2.7 μm) with methanol (A) and deionized water containing 0.1%

* 四川省区域创新合作项目(No. 2025YFHZ0299)资助

△ 通信作者, E-mail: zhaodg@scidc.org.cn

出版日期: 2026-05-20

formic acid (B) as the mobile phases. Gradient elution was conducted with a column temperature of 40 °C, a flow rate of 0.2 mL/min, and an injection volume of 1 µL. Mass spectrometry analysis was performed using an electro-spray ionization (ESI) source in multiple reaction monitoring (MRM) positive ion mode. The standard curves, quantification limits, precision, recovery rates, and matrix effects of the method under different extraction conditions were evaluated.

Results The 33 aromatic primary amines analyzed in the study showed good linearity ($r > 0.998$) within the 2-100 ng/mL concentration range. Detection limits ranged from 0.1 to 0.5 ng/mL, and quantification limits ranged from 0.3 to 1.7 ng/mL. Recovery rates for the 33 aromatic primary amines in 80% methanol samples ranged from 70.7% to 116.0%. Recovery rates for 31 aromatic primary amines in PBS samples containing 10% ethanol ranged from 74.9% to 113.8%. The intra-day and inter-day precision for different samples was both less than 10%, indicating good sample stability. Analysis of aromatic primary amine content in sample extracts using this method revealed that methylenedianiline (MDA) was detected in all 6 initially tested samples. Under simulated extraction at 37 °C and accelerated extraction at 60 °C, 3 samples exhibited continuous or delayed MDA release. 2,4'-MDA was detected in 2 samples during the initial limit extraction phase and remained detectable in 1 sample under 60 °C accelerated aging conditions, but no release was observed under the 37 °C simulated physiological environment. 2,2'-MDA was detected only in two samples during initial limit extraction and was not released in subsequent simulated or accelerated extraction processes. **Conclusion** The UPLC-MS/MS method demonstrates high sensitivity and accuracy, meeting the requirements for precise detection of 33 aromatic primary amines in medical-grade TPU and providing reliable technical support for risk assessment and quality control of aromatic primary amines in these materials and products.

[Key words] Ultra-high performance liquid chromatography-tandem mass spectrometry Medical-grade thermoplastic polyurethane Aromatic primary amines Simultaneous determination Extraction and release Risk assessment

热塑性聚氨酯(thermoplastic polyurethanes, TPU)是聚氨酯的一个重要分支,兼具优异的机械性能、良好的生物相容性与加工适应性,在食品包装和医疗器械等领域得到广泛应用。通过改性优化,其性能可符合严格的医用及食品接触法规要求^[1]。在食品包装中,TPU薄膜因良好的透气、抗菌和可降解性能,有助于延长食品保质期^[2-3]。在医疗领域,TPU可通过流延、注塑和挤出等多种成型工艺,加工成诸如心脏泵、心血管系统及泌尿系统导管等结构复杂的医疗器械,为临床治疗提供了重要支持^[4]。

然而,在TPU合成过程中,残留的芳香族异氰酸酯单体,如二苯甲烷二异氰酸酯(diphenylmethane diisocyanate, MDI)和甲苯二异氰酸酯(toluene diisocyanate, TDI)中所含的异氰酸酯基团(-NCO)易水解成4,4'-二氨基二苯甲烷(4,4'-Methylenedianiline, MDA)、甲苯二胺(toluene diamine, TDA)等芳香伯胺类化合物^[5-7]。部分芳香伯胺具有明显的致癌性与遗传毒性^[8],并可能在材料使用过程中迁移至人体,构成潜在健康风险^[9]。因此,相关标准明确规定食品接触材料中不得检出芳香伯胺^[10],并在生物医用材料领域将其列为严格监控的风险物质。

目前,芳香伯胺的检测主要依赖色谱与质谱技术,包括气相色谱法^[11]、气相色谱-质谱联用法^[12-13]、高效液相色谱法^[14-15]、液相色谱-串联质谱法^[16]等。在食品和药品包装领域的检测方法已较为成熟^[17-18]。但针对生物医用材

料的相关研究仍显不足。医用材料的检测需模拟生理环境,其浸提基质与食品模拟液差异显著,且须结合长期接触下的释放行为进行安全性评估。尤其对于长期接触组织或体液的医用TPU,其在多模拟条件下芳香伯胺的系统迁移与释放规律,以及同时检测30余种目标物的高通量分析方法,目前仍缺乏系统研究。

因此,针对医用聚氨酯材料的实际应用场景,系统研究其在不同模拟生理环境中芳香伯胺迁移和释放规律具有重要意义。通过建立可同时检测33种芳香伯胺的超高效液相色谱-串联质谱法(ultra-performance liquid chromatography-tandem mass spectrometry, UPLC-MS/MS)方法,并基于释放数据开展科学的安全性评估,可为该类材料的实际应用提供重要支撑。

1 材料与方法

1.1 待测材料样品

本研究共收集市售医用TPU样品12批,其生产来源覆盖三个不同的厂家(同时包含国产品牌与进口品牌)。具体批次与生产厂家的对应关系如下:编号P1至P4的样品由厂家A生产;编号P5至P6的样品由厂家B生产;编号P7至P12的样品由厂家C生产,样品信息详见网络资源附件附表1。

1.2 主要试剂与仪器

甲酸(优级纯)、正己烷、二氯甲烷、乙腈、无水乙

醇、磷酸氢二钠、磷酸二氢钾、氯化钾和氯化钠均为分析纯,购自成都市科隆化学品有限公司;甲醇(质谱级),购自Fisher Chemical;33种芳香伯胺标准品详见网络资源附件附表2。5500Qtrap超高效液相色谱-质谱联用仪(UPLC系统:日本岛津;质谱系统:美国AB Sciex);AL-204-IC电子天平(Sartorius);恒温培养振荡器(上海智城分析仪器制造有限公司);Rotavapor旋转蒸发仪(BUCHI)。

1.3 对照品溶液制备

精密称取33种芳香伯胺标准品各10 mg(精确至0.1 mg),置于10 mL容量瓶中,甲醇溶解并定容,摇匀,制得各单标储备液。分别精密量取各单标储备液1 mL,置于同一50 mL容量瓶中,加甲醇稀释并定容,混匀,制得浓度约为20 $\mu\text{g/mL}$ 的混合对照品储备液。取适量该混合对照品储备液,用甲醇逐级稀释,配制成浓度为2~100 ng/mL的系列标准工作溶液。

1.4 样品浸提条件筛选

1.4.1 浸提条件选择

为全面评估目标物的最大可提取量并缩短模拟周期,本研究设定了不同浸提方案。在80%甲醇体系中,参考医用高分子材料加速老化试验的常用上限温度(60 $^{\circ}\text{C}$ 、6 d)条件模拟极限老化^[19]。在PBS模拟体液中,分别在37 $^{\circ}\text{C}$ (模拟体温)和60 $^{\circ}\text{C}$ (加速老化)条件下,于1、3、6、14、30 d取样,以模拟不同留置时间的释放行为。依据Arrhenius方程^[20],利用60 $^{\circ}\text{C}$ 加速试验外推预测长期释放趋势,系统评估约1~150 d应用周期内的释放行为。

1.4.2 极限浸提溶剂筛选

依据医疗器械生物学评价标准,极限浸提应选用能够最大化目标物释放的溶剂^[21]。参考既往研究,本研究分别选用水^[7]、正己烷^[22]、乙腈^[23]、二氯甲烷^[24]、乙醇-水混合溶液(密度为0.9373~0.9378 g/mL)^[25]及甲醇^[26]为候选浸提溶剂,以样品P2为测试对象进行筛选。浸提条件如下:水(70 $^{\circ}\text{C}$)、乙腈(70 $^{\circ}\text{C}$)、二氯甲烷(40 $^{\circ}\text{C}$)、正己烷(60 $^{\circ}\text{C}$)、乙醇-水混合溶液(60 $^{\circ}\text{C}$)以及体积比为20%、50%、80%、100%甲醇(60 $^{\circ}\text{C}$),均在相应温度下振摇浸提24 h,比较不同溶剂对芳香伯胺的提取效率。

1.5 样品浸提液制备

1.5.1 极限浸提

按1.4章节筛选所得最佳条件,精密称取各样品1 g(精确至0.001 g)于玻璃容器中,加入5 mL浸提溶剂^[27],密封后置恒温振荡箱中,60 $^{\circ}\text{C}$ 下振摇提取规定时间。取出冷却至室温,浸提液经0.45 μm 微孔滤膜过滤,滤液用甲醇稀释5倍,平行制备双份样品溶液,并同步制备空白对照。

1.5.2 模拟生理环境浸提

参照ISO 10993-12标准^[27],以含体积分数10%乙醇的PBS溶液(pH7.4)为模拟体液。精密称取P2、P5、P8样品各1 g(精确至0.001 g),分置于玻璃容器中,加入5 mL模拟体液,密封。分别在37 $^{\circ}\text{C}$ (模拟生理温度)及60 $^{\circ}\text{C}$ (加速老化温度)的恒温振荡箱中动态浸提,并于1、3、6、14、30 d取样。浸提液冷却后,通过预先用3 mL甲醇和3 mL水平衡的SWELL Chromclean HLB固相萃取小柱(3 mL, 60 mg)吸附5 min(弃初始流出液),用5 mL甲醇洗脱目标物。洗脱液经0.45 μm 滤膜过滤,并用甲醇定容至5 mL,平行制备双样,同时制备空白对照。

1.6 仪器条件

色谱分析采用Agilent Infinity Lab Poroshell 120 EC-C18色谱柱(150 mm $\times$ 3.0 mm, 2.7 μm),流动相为甲醇(A相)与含0.1%甲酸的水溶液(B相)。柱温保持40 $^{\circ}\text{C}$,流速为0.2 mL/min,进样体积为1 μL 。梯度洗脱程序如下:0~25 min, A相比例由5%上升至90%, B相应下降;25~33 min保持A相90%不变;33~35 min, A相比例由90%下降至10%, B相恢复上升为90%。

质谱检测采用三重四极杆质谱仪,电喷雾电离离子源(electron-spray ionization, ESI)正离子模式下运行,采用方式为多反应监测。离子源温度设定为500 $^{\circ}\text{C}$,碰撞气为氮气,碰撞气压力设置为Medium水平。33种目标芳香伯胺检测离子及对应的质谱参数详见网络资源附件附表2。

1.7 方法学验证

参考《中国药典》(2025版)9101分析方法验证指导原则^[28],对本方法的线性范围、检出限(limit of detection, LOD)、定量限(limit of quantification, LOQ)、回收率、精密度进行验证。

1.7.1 线性范围、检出限与定量限

取浓度为2~100 ng/mL的系列混合对照品溶液,在1.6设定的仪器条件下分析。以各目标物浓度(X, ng/mL)为横坐标,其对应的色谱峰面积(Y)为纵坐标,采用最小二乘法进行线性回归,建立校准曲线。另取2 ng/mL的混合对照品溶液用甲醇逐级稀释,制备0.1~1 ng/mL的标准溶液,同法进样分析。以各目标物响应信号强度(S)与背景噪声(N)的比值计算信噪比(S/N)。当S/N值为3时,对应的浓度定义为该化合物的LOD;当S/N值为10时,对应的浓度定义为该化合物的LOQ。

1.7.2 基质效应

精密量取适量混合标准溶液,分别用两种空白基质溶液(80%甲醇、含10%乙醇的PBS溶液)及纯溶剂(甲

醇), 配制成浓度为2、5、8、10、20、50、80、100 ng/mL的系列基质工作溶液与标准工作溶液。按既定方法进行测定, 分别绘制各目标物在两种基质及纯溶剂中的工作曲线。通过比较各基质工作曲线与纯溶剂工作曲线的斜率, 计算斜率比值。若该比值处于0.8~1.2范围内, 则表明基质效应可忽略或处于可接受水平^[29], 从而验证方法在相应基质中的适用性。

1.7.3 回收率(准确度)和精密度

为评估方法的准确度与精密度, 精密称取P10样品1 g, 分别按极限模拟条件(80%甲醇5 mL, 60 °C浸提6 d)和生理环境模拟条件(PBS 5 mL, 37 °C浸提6 d)平行制备12份供试品溶液, 并将同条件下所得溶液分别合并。取极限模拟合并溶液直接作为加标基质; 生理模拟合并溶液经固相萃取小柱(3 mL, 60 mg)处理、洗脱并定容至5 mL后作为加标基质。分别精密量取上述两种基质溶液各5 mL, 加入适量混合对照品溶液, 制备为5、10、15 ng/mL的加标回收溶液, 各浓度平行制备3份; 同法制备未加标的本底溶液各2份作对照。按1.6章节色谱-质谱条件测定, 扣除本底值后计算各浓度平均回收率及相对标准偏差(relative standard deviation, RSD)以评价准确度; 取10 ng/mL加标溶液, 分别考察日内精密度(同一天内连续进样6次)和日间精密度(连续3 d内6个不同时间点进样), 计算RSD进行评价。

2 结果

2.1 质谱条件的优化

本研究采用ESI正离子模式进行检测, 因芳香伯胺含

有氨基, 在该模式下易形成 $[M+H]^+$ 离子。通过流动注射泵连续进样标准溶液, 进行全扫描确定母离子, 随后对母离子进行子离子扫描, 获取相应的子离子谱图。选择响应强度高、干扰少的两对特征离子对作为监测离子对, 并优化碰撞能量以获得最佳响应。优化后的MRM参数见网络资源附件附表2。

2.2 色谱条件的优化

2.2.1 色谱柱的选择

33种目标芳香伯胺均含有极性伯胺基团($-NH_2$), 但其结构中含有一个或多个疏水性芳香环, 整体呈现弱极性。本研究评估了3种反相色谱柱的分离性能: Shim-pack GIST C8柱(100 mm×2.1 mm, 2 μ m)、Agilent InfinityLab Poroshell 120 EC-C18柱(150 mm×3.0 mm, 2.7 μ m)以及Phenomenon TitanK F5柱(150 mm×2.1 mm, 3 μ m)。结果显示, C8柱和C18柱对大部分化合物的保留与分离效果相近, 且均显著优于TitanK F5柱, 后者表现出最弱的保留能力和最差的峰形。

进一步考察5组关键同分异构体的分离能力时发现, C₈色谱柱无法有效分离其中的1组同分异构体(序号3-5)。而C18色谱柱对5组同分异构体(序号分别为1-2、3-5、10-12、11-16-26、19-21)均实现了基线分离, 且色谱峰形与灵敏度表现最优。图1展示了5组同分异构体在3种色谱柱上的分离色谱图, 分别为: 对苯二胺(1)与间苯二胺(2)、2,6-二氨基甲苯(3)与2,4-二氨基甲苯(5)、对甲氧基苯胺(10)与邻甲氧基苯胺(12)、4,4'-二氨基二苯甲烷(11)、2,4'-二氨基二苯甲烷(16)与2,2'-二氨基二苯甲烷(26)、2,4-二甲基苯胺(19)与2,6-二甲基苯胺(21)。

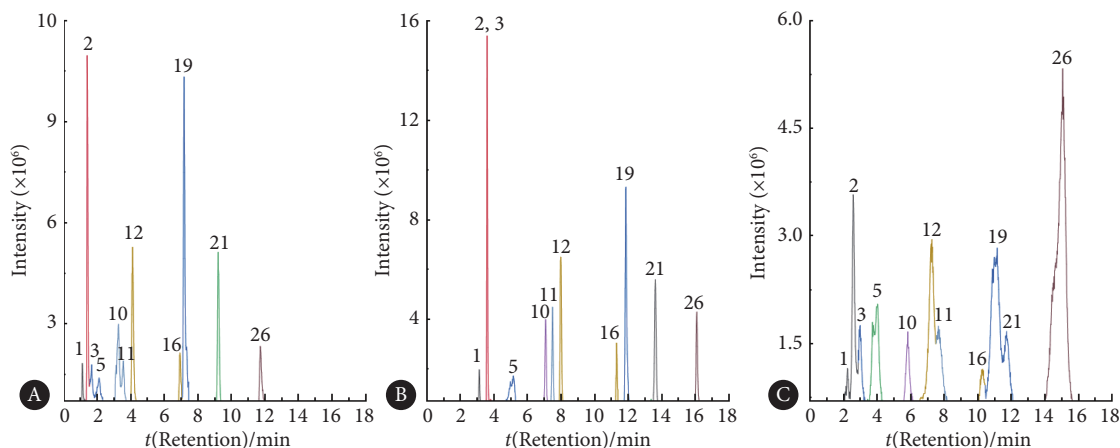


图1 5对同分异构体在3种色谱柱上的提取离子色谱图

Fig 1 Extracted ion chromatograms of 5 enantiomers separated on 3 chromatographic columns

A, Shim-pack GIST C8; B, agilent InfinityLab Poroshell 120 EC-C18; C,phenomenon TitanK F5. The five groups of isomers are: p-Phenylenediamine (1) and m-Phenylenediamine (2), 2,6-Diaminotoluene (3) and 2,4-Diaminotoluene (5), p-Anisidine (10) and o-Anisidine (12), 4,4'-Diaminodiphenylmethane (11), 2,4'-Diaminodiphenylmethane (16) and 2,2'-Diaminodiphenylmethane (26), 2,4-Dimethylaniline (19), and 2,6-Dimethylaniline (21).

2.2.2 流动相中甲酸浓度优化

研究对比了甲醇-水和乙腈-水两种流动相体系, 结果表明以甲醇为有机相时, 目标化合物在质谱检测中响应更佳。同时, 在考察水相中甲酸体积分数在0%~0.2%范围内变化对分离效果的影响时发现, 随着甲酸浓度从0%提高至0.1%, 目标化合物的分离效果得到显著改善, 且峰形更加尖锐对称, 减少了拖尾和前延现象; 当甲酸浓度提高至0.2%时, 峰形改善不明显。因此, 后续实验选择0.1%甲酸作为水相组成(图2)。

2.2.3 流动相流速优化

为确定最佳分离条件, 考察了0.1~0.4 mL/min范围内流动相流速对分离效果的影响。结果显示, 当流速为0.1 mL/min时, 色谱峰响应强度较高, 但分析时间显著延

长, 部分较早流出峰的峰形出现明显展宽; 当流速提高至0.3~0.4 mL/min时, 分析时间缩短, 但质谱响应强度降低, 灵敏度下降。相比之下, 0.2 mL/min的流速综合性能更优: 相邻色谱峰之间的分离度改善, 峰谷高度降低, 有效避免了低流速下的峰展宽与高流速下可能出现的共洗脱现象, 各目标物均实现基线分离(图3)。经系统优化后的梯度洗脱程序可在30 min内完成33种目标芳香伯胺的分离, 并保障色谱柱在每次进样间实现快速平衡。在最终优化的色谱-质谱条件下, 33种目标化合物的总离子流色谱图见图4, 图中各峰序号见网络资源附件附表2。

2.3 待测样品浸提条件筛选

结果显示, 样品中共检出3种芳香伯胺——MDA、2,4'-二氨基二苯甲烷(2,4'-diaminodiphenylmethane, 2,4'-MDA)

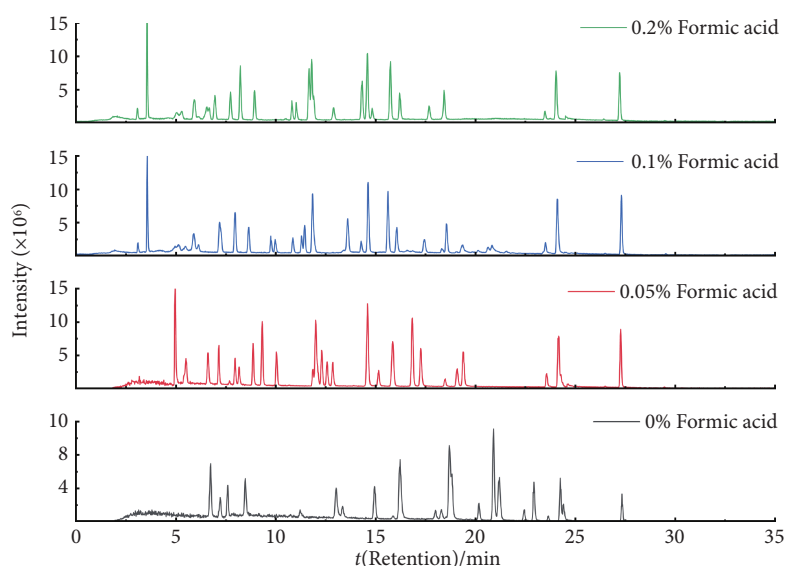


图2 不同甲酸添加量下33种芳香伯胺的提取离子色谱图

Fig 2 Extracted ion chromatograms of 33 aromatic primary amines at different concentrations of formic acid

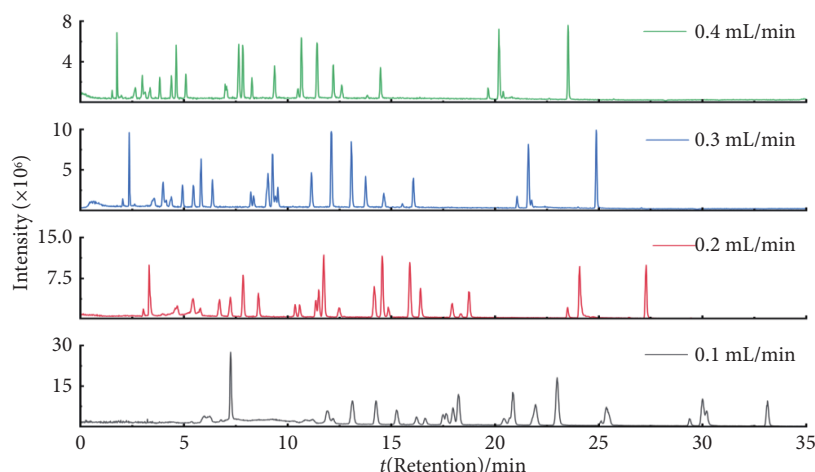


图3 不同流速下33种芳香伯胺的提取离子色谱图

Fig 3 Extracted ion chromatograms of 33 aromatic primary amines at different flow rates

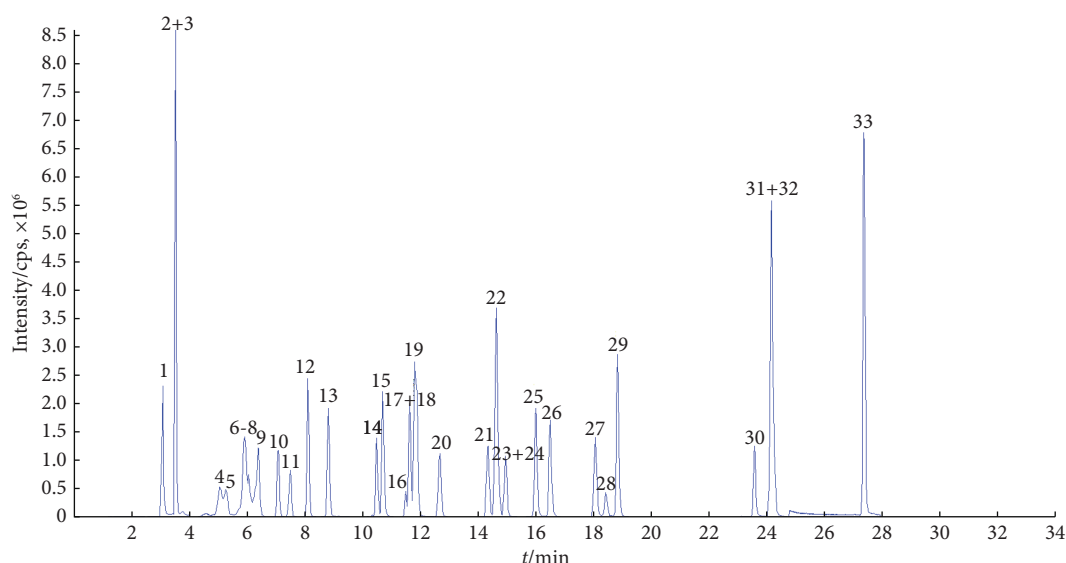


图 4 33种芳香伯胺的总离子流图谱

Fig 4 Total ion current spectra of 33 aromatic primary amines

The peak numbers in the figure correspond to the order of the compounds listed in Appendix 2.

和2,2'-二氨基二苯甲烷(2,2'-diaminodiphenylmethane, 2,2'-MDA)。对比不同浸提溶剂的提取效果发现,甲醇对这3种芳香伯胺的提取效率最高,其检出浓度均显著高于其他5种溶剂。考虑到目标物主要源于异氰酸酯的水解,因此进一步系统考察了甲醇含量(20%、50%、80%及100%甲醇)对其提取效率的影响。通过对样品P2在60℃振荡浸提24 h后的分析,结果显示,与其他3种甲醇浓度相比,80%甲醇对上述芳香伯胺的检出量最高。因此,后续实验选择80%甲醇作为待测样品的浸提溶剂(图5)。

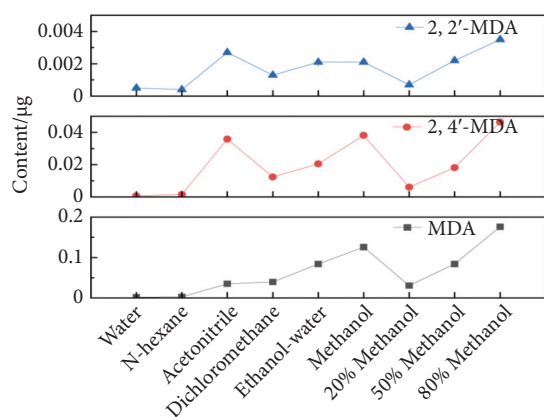


图 5 不同溶剂对三种芳香伯胺的提取结果

Fig 5 Extraction results of 3 aromatic primary amines by different solvents

2.4 方法学评价

2.4.1 线性范围、检出限与定量限

33种目标芳香伯胺在2~100 ng/mL浓度范围内线性关系良好,相关系数(r)均大于0.998。LODs为

0.1~0.5 ng/mL、LOQs为0.3~1.7 ng/mL(表1)。

2.4.2 基质效应

在80%甲醇与含10%乙醇的PBS两种模拟基质中,各待测物的基质效应值范围分别为0.82~1.12与0.84~1.16。经样品前处理后,基质干扰得到了有效控制。因此,本方法采用标准工作溶液进行定量分析(表1)。

2.4.3 回收率(准确度)和精密度

在80%甲醇浸提体系中,33种目标物的平均回收率为70.7%~116.0%,相对标准偏差(RSD, $n=9$)为1.5%~6.0%;日内精密度(RSD, $n=6$)为0.6%~6.4%,日间精密度(RSD, $n=6$)为2.2%~8.0%。

在含10%乙醇的PBS浸提体系中,31种目标物的平均回收率为74.9%~113.8%,RSD($n=9$)为1.7%~8.4%;日内精密度(RSD, $n=6$)为0.6%~5.1%,日间精密度(RSD, $n=6$)为0.9%~6.2%。其中,两种芳香伯胺在该体系中的回收率偏低,可能与其结构的不稳定性有关:氨基偶氮甲苯中的偶氮键易发生分解^[30],而对苯二胺在水环境中易发生光降解^[31]。

2.5 方法学应用

采用所建立的方法检测12批待测样品的极限浸提液,以外标法定量分析33种芳香伯胺的含量。结果显示,共有6批样品检出了芳香伯胺,涉及MDA、2,4'-MDA和2,2'-MDA三种目标物。其中,厂家A生产的样品P1(分别为0.339、0.075、0.017 $\mu\text{g/g}$)和P2(分别为0.659、0.114、0.003 $\mu\text{g/g}$)均检出上述三种物质;厂家B的样品P5、P6及厂家C的样品P8和P9仅检出痕量MDA,含量分别为0.059 $\mu\text{g/g}$ 和0.036 $\mu\text{g/g}$ 。选取各厂家检出水平较高的代

表 1 方法学考察结果
Table 1 Results of methodological investigation

Compound	<i>r</i>	LOD/ (ng/mL)	LOQ/ (ng/mL)	80% Methanol			PBS (10% Ethanol)		
				Matrix effect	Extraction recovery/%	RSD/%	Matrix effect	Extraction recovery/%	RSD/%
						A, B, C			A, B, C
p-Phenylenediamine	0.998 7	0.2	0.7	0.86	70.7	1.7, 2.6, 4.0	0.90	2.9	7.3, 5.1, 6.2
m-Phenylenediamine	0.998 7	0.2	0.7	0.90	99.9	5.3, 2.1, 5.4	1.04	94.3	3.6, 3.1, 3.3
2,6-Diaminotoluene	0.998 5	0.5	1.7	0.82	93.5	5.4, 2.1, 5.6	1.14	103.3	1.7, 2.1, 3.0
2,4-Diaminoanisole	0.998 7	0.5	1.7	1.06	89.0	3.3, 3.5, 5.3	1.12	74.9	2.7, 3.4, 1.9
2,4-Diaminotoluene	0.999 0	0.5	1.7	0.85	106.8	6.0, 3.3, 4.8	0.89	94.8	1.7, 1.7, 3.3
Aniline	0.998 1	0.2	0.7	0.87	103.3	5.8, 1.7, 2.5	1.12	105	4.1, 2.2, 5.4
1,5-Diaminonaphthalene	0.998 2	0.5	1.7	1.12	99.6	5.8, 2.8, 4.6	1.16	87.2	4.0, 1.8, 3.4
Benzidine	0.999 5	0.2	0.7	1.10	116.0	2.0, 1.9, 3.1	0.88	113.8	3.6, 0.6, 1.0
4,4'-Diaminodiphenylether	0.998 8	0.1	0.3	0.95	96.9	4.4, 6.4, 6.5	0.84	112	4.4, 0.9, 2.1
p-Anisidine	0.999 1	0.1	0.3	1.02	104.1	3.7, 1.5, 5.9	0.94	104.8	5.1, 1.5, 2.9
4,4'-Diaminodiphenylmethane	0.999 2	0.2	0.7	0.99	114.3	1.9, 2.0, 3.5	0.86	101.1	4.6, 2.6, 3.9
o-Anisidine	0.999 1	0.2	0.7	0.93	106.2	3.5, 0.6, 7.6	0.87	106.4	5.2, 1.0, 1.1
o-Toluidine	0.998 3	0.5	1.7	0.97	105.8	4.7, 1.3, 7.5	0.92	105.9	6.3, 2.6, 2.1
3,3'-Dimethoxybenzidine	0.999 4	0.1	0.3	0.92	105.9	1.5, 2.0, 5.5	1.04	103.7	4.3, 1.7, 2.3
3,3'-Dimethylbenzidine	0.999 0	0.1	0.3	1.00	104.8	2.5, 2.1, 5.8	0.95	103.1	6.2, 1.2, 1.2
2,4'-Diaminodiphenylmethane	0.999 4	0.1	0.3	1.06	108.9	3.9, 1.1, 3.5	1.03	103.3	4.8, 1.3, 3.4
2-Methoxy-5-methylaniline	0.999 2	0.1	0.3	1.00	106.0	3.1, 1.6, 6.2	1.09	100.4	5.9, 1.8, 2.7
3,3'-Dimethyl-4,4'-diaminodiphenylmethane	0.999 4	0.2	0.7	1.06	100.0	3.8, 3.0, 3.5	1.00	101.5	3.4, 1.7, 1.5
2,4-Dimethylaniline	0.997 8	0.2	0.7	1.01	106.0	4.7, 5.2, 6.2	1.05	104.5	6.7, 4.4, 1.4
4-Chloroaniline	0.999 1	0.1	0.3	0.95	106.1	4.1, 1.0, 6.1	1.08	102.1	4.8, 1.4, 4.3
2,6-Dimethylaniline	0.998 8	0.5	1.7	1.01	104.3	5.5, 1.4, 8.0	0.98	102.9	8.4, 3.4, 2.9
2,4,5-Trimethylaniline	0.998 8	0.2	0.7	1.02	99.8	3.7, 1.3, 2.6	0.99	99.1	5.5, 2.2, 0.9
4,4'-Diaminodiphenyl sulfide	0.999 3	0.2	0.7	1.05	103.3	3.2, 1.2, 2.2	1.08	99.9	6.3, 1.8, 1.0
2-Naphthylamine	0.999 3	0.2	0.7	0.99	105.8	3.1, 2.6, 3.4	1.10	100.2	5.8, 2.8, 1.8
2,4,6-Trimethylaniline	0.999 2	0.2	0.7	0.98	108.7	3.0, 1.5, 3.8	1.10	101.1	7.7, 1.9, 3.2
2,2'-Diaminodiphenylmethane	0.999 3	0.1	0.3	1.05	108.8	3.1, 1.7, 3.7	1.13	102.4	4.2, 1.4, 1.7
4-Chloro-o-toluidine	0.999 3	0.1	0.3	0.98	107.1	3.7, 1.6, 6.7	0.92	99.5	3.3, 1.7, 1.8
2-Amino-4-nitrotoluene	0.998 4	0.5	1.7	1.06	96.0	4.3, 5.5, 6.8	0.94	104.1	2.8, 3.1, 5.2
4-Aminobiphenyl	0.999 3	0.2	0.7	0.99	101.3	2.7, 2.1, 6.1	0.94	96.2	2.3, 1.7, 4.5
3,3'-Dichlorobenzidine	0.999 5	0.2	0.7	1.03	107.2	5.6, 2.1, 2.7	1.02	84.7	2.5, 1.7, 3.9
4-Aminoazobenzene	0.998 7	0.2	0.7	0.97	104.5	2.1, 2.1, 6.7	1.12	86.9	2.5, 2.1, 3.2
3,3'-Dichloro-4,4'-diaminodiphenylmethane	0.999 5	0.1	0.3	0.99	101.7	2.0, 2.2, 3.9	1.05	95.3	4.3, 0.9, 3.2
o-Aminoazotoluene	0.999 1	0.2	0.7	0.99	106.1	4.5, 2.0, 4.4	0.95	53.2	6.8, 3.2, 3.5

表性样品(P2、P5、P8), 在37 ℃下进行多时间点模拟浸提, 以考察其在模拟生理环境中目标芳香伯胺的释放行为。结果表明, 仅厂家A的样品P2检出MDA, 其含量随时间呈缓慢上升趋势, 而厂家B和C的样品均未检出目标物(表2)。

进一步对上述样品进行60 ℃加速浸提实验, 通过温

度提升模拟约1 ~ 150 d的临床应用周期。结果显示, 随浸提时间延长, 厂家B的样品P5和厂家C的样品P8中开始有少量MDA检出; 厂家A的样品P2除MDA外, 亦检出少量2,4'-MDA。该结果表明, 在加速老化条件下, 部分医用TPU材料中长期潜在的芳香伯胺释放风险可能随接触时间延长而逐渐显现(表2)。

表 2 医用TPU 模拟生理环境浸提和加速浸提结果
Table 2 Results of simulated extraction under physiological environment and accelerated extraction of medical-grade TPU

Condition		Sample	Compounds/(μg/g)			
Temperature	Time		MDA	2, 4'-MDA	2, 2'-MDA	
37 °C	1 d	P2	N.D	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
	3 d	P2	0.003	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
	6 d	P2	0.006	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
	14 d	P2	0.008	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
	30 d	P2	0.009	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
	60 °C	1 d	P2	0.010	N.D	N.D
			P5	N.D	N.D	N.D
			P8	N.D	N.D	N.D
3 d		P2	0.018	N.D	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
6 d		P2	0.025	0.004	N.D	
		P5	N.D	N.D	N.D	
		P8	N.D	N.D	N.D	
14 d		P2	0.040	0.005	N.D	
		P5	0.003	N.D	N.D	
		P8	N.D	N.D	N.D	
30 d		P2	0.078	0.013	N.D	
		P5	0.014	N.D	N.D	
		P8	0.005	N.D	N.D	

N.D indicates not detected.

3 讨论

本研究成功建立了用于高效、灵敏检测医用TPU中33种芳香伯胺的UPLC-MS/MS方法。通过结合极限浸提(80%甲醇)与模拟生理环境浸提(含10%乙醇的PBS溶液,分别于37 ℃和60 ℃加速条件下进行),系统评估了材料中芳香伯胺的潜在总含量及其在不同条件下的迁移释放行为。

本研究结果表明,80%甲醇极限浸提结果可作为评估材料中潜在芳香伯胺风险的重要指标,有助于识别需重点监控的目标物。在模拟临床使用环境的PBS浸提体系中,部分样品中检出MDA,其迁移量随温度升高和浸提时间延长而显著增加。例如,样品P2在60 ℃、浸提30 d条件下的MDA迁移量(0.078 μg/g)远高于其在37 ℃、浸提3 d的结果(0.003 μg/g),且在该条件下同时检出2,4'-MDA,这一现象提示,材料在长期使用过程中可能存在风险物质的“延迟释放”。

实验结果显示,检出的芳香伯胺以MDA为主,其来源一方面可归因于TPU合成过程中残留异氰酸酯单体的水解,另一方面也可能源于材料中氨基甲酸酯基团的水解或醇解反应^[32],这与不同厂家的配方与工艺密切相关。此外,三个厂家的硫酸钡显影料在两种浸提体系中均检出MDA,提示硫酸钡的加入可能促进氨基甲酸酯键的降解,从而产生MDA。不同厂家同类产品中MDA检出水平存在差异。在80%甲醇极限浸提体系中,聚醚显影料样品P2的MDA检出量显著高于P5和P8;聚碳酸酯显影料样品P1的MDA检出量显著高于P9;芳香族(P10)与聚醚脂肪族(P12)样品中未检出芳香伯胺;三个厂家的透明料中,仅厂家B的产品P6检出MDA。上述结果表明,不同来源TPU原料中芳香伯胺的残留水平及其在模拟生理环境下的释放动力学存在明显差异,这可能直接影响由其制成的长期植入器械的生物相容性风险。

医用TPU广泛用于制造各类植介入器械,其接触时间涵盖短期(< 30 d)至长期(> 90 d)。对于此类持久接触(C类)医疗器械,需采用较严格的评价策略^[33]。参照欧洲化学品管理局(ECHA)数据库^[34]MDA的口服重复剂量毒性数据[LOAEL= 9 mg/(kg·d)],并依据药品每日允许暴露量(PDE)评估方法进行计算^[35],得到MDA的口服PDE值为0.3 mg/d,进而推导出其注射途径的PDE值为0.03 mg/d。假设患者每日使用一支质量为1 g(如中心静脉导管)或5 g(如外周中心静脉导管)的TPU器械,可推算出相应的MDA安全性阈值。结构类似的2,4'-MDA和2,2'-MDA可参照该阈值进行评价。

本研究中所有样品在模拟浸提条件下检出的MDA及2,4'-MDA含量(范围0.003 ~ 0.078 μg/g)均远低于上述安全性阈值,提示在单一使用条件下其迁移风险较低。然而,考虑到医疗器械临床使用的复杂性(如多器械同时使用)以及材料在长期服役过程中释放行为的动态变化,其安全性评价仍面临挑战。田晨旭等^[36]在动物实验中采用组织学动态变化评价,对PU薄膜材料的安全性进行了探索,提示未来的安全性评价中需采取更保守的策略,并

建立动态风险评估体系。

本研究建立了一种系统性的分析策略,将极限浸提与模拟长期生理环境的动态浸提相结合,弥补了现有食品接触材料标准(通常浸提条件单一且侧重于短期迁移)在评价长期植入医用材料生物安全性方面的不足。在方法学层面,所建立的UPLC-MS/MS方法实现了33种目标物的良好分离与高灵敏检测,其LOD(0.1~0.5 ng/mL)优于部分已有报道^[13, 18]。通过多温度、多时间点的浸提设计,在医用TPU材料中观测到MDA等物质的“延迟释放”现象,这对于全面评估长期植入器械的安全性具有关键价值。

综上所述,本研究建立的方法为医用TPU材料及其制品的生产质量控制提供了可靠的分析手段,也为相关医疗器械的临床前生物安全性评估与监管决策提供了重要的科学依据。

* * *

作者贡献声明 杨雅静负责数据编、正式分析、调查研究、验证、可视化和初稿写作,杨剑负责论文构思、研究方法、监督指导、可视化、初稿写作和审读与编辑写作,肖宇负责研究方法、监督指导、初稿写作和审读与编辑写作,胡丽、成婕和郭燕燕负责研究方法、验证、初稿写作和审读与编辑写作,江燕负责研究项目管理、提供资源、监督指导和审读与编辑写作,赵代国负责论文构思、经费获取、研究方法、监督指导、可视化和审读与编辑写作。所有作者已经同意将文章提交给本刊,且对将要发表的版本进行最终定稿,并同意对工作的所有方面负责。

Author Contribution YANG Yajing is responsible for data curation, formal analysis, investigation, validation, visualization, and writing--original draft. YANG Jian is responsible for conceptualization, methodology, supervision, visualization, writing--original draft, and writing--review and editing. XIAO Yu is responsible for methodology, supervision, writing--original draft, and writing--review and editing. HU Li, CHENG Jie, and GUO Yanyan are responsible for methodology, validation, writing--original draft, and writing--review and editing. JIANG Yan is responsible for project administration, resources, supervision, and writing--review and editing. ZHAO Daiguo is responsible for conceptualization, funding acquisition, methodology, supervision, visualization, and writing--review and editing. All authors consented to the submission of the article to the journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

利益冲突 所有作者声明不存在利益冲突

Declaration of Conflicting Interests All authors declare no competing interests.

参 考 文 献

- [1] SRIVASTAVA A, MAITY S, DAS R B. A review on multi-functional polyurethane (PU) coatings for fabric applications: materials, processes and recent developments. *Prog Org Coat*, 2025, 207: 109377. doi: 10.1016/J.PORGCOAT.2025.109377.
- [2] BO C, ZHIJIA Z, WENJUN Z, *et al*. Review: Application status of antibacterial polyurethane. *J Polym Res*, 2024, 31(9): 275. doi: 10.1007/S10965-024-04092-3.
- [3] SAROJINI S K, INDUMATHI M, RAJARAJESWARI G. Mahua oil-based polyurethane/chitosan/nano ZnO composite films for biodegradable food packaging applications. *Int J Biol Macromol*, 2018, 124: 163-174. doi: 10.1016/j.ijbiomac.2018.11.195.
- [4] 赵代国, 张明杰, 李震, 等. 医用聚氨酯合成所用有机催化剂及其生物毒性研究进展. *四川大学学报(医学版)*, 2024, 55(4): 807-812. doi: 10.12182/20240760401.
- [5] ZHAO D G, ZHANG M J, LI Z, *et al*. Research progress in organocatalysts used in the synthesis of medical polyurethanes and their biotoxicity. *J Sichuan Univ (Med Sci)*, 2024, 55(4): 807-812. doi: 10.12182/20240760401.
- [6] 任平, 赵洁, 居莹, 等. 食品接触材料中初级芳香胺的迁移风险与法规管控. *中国塑料*, 2022, 36(2): 139-146. doi: 10.19491/j.issn.1001-9278.2022.02.020.
- [7] REN P, ZHAO J, JU Y, *et al*. Migration risk and regulatory control of primary aromatic amines in food contact materials. *China Plastics*, 2022, 36(2): 139-146. doi: 10.19491/j.issn.1001-9278.2022.02.020.
- [8] BIDOKHTI S M, MAHDAVI H. Improving polyurethane adhesives by partially replacing hydroxypropyl-maleate modified soda lignin with polyethylene glycol: a sustainable approach to biomass-based adhesive technology. *J Polym Environ*, 2025, 33(9): 4237-4246. doi: 10.1007/s10924-025-03635-z.
- [9] 常亮, 饶艳春, 陈珍珍. 药用复合膜在不同温度水中甲苯二胺的浸出量比较. *药品评价*, 2020, 17(17): 27-29.
- [10] CHANG L, RAO Y C, CHEN Z Z. Comparison of toluene diamine leaching amount of medicinal composite membrane in water at different temperatures. *Drug Research*, 2020, 17(17): 27-29.
- [11] PIERGIOVANNI M, TERMOPOLI V, MAFFEZZONI C, *et al*. Condensed phase membrane introduction mass spectrometry: a new frontier for the real-time monitoring of hazardous chemical migration from food contact materials. *Green Anal Chem*, 2025, 12: 100199. doi: 10.1016/J.GREEAC.2024.100199.
- [12] 谢威民, 戎伟丰. 工作场所空气中芳香族胺类化合物检测方法研究进展. *中国职业医学*, 2023, 50(1): 110-116. doi: 10.20001/j.issn.2095-2619.20230219.
- [13] XIE W M, RONG W F. Research progress on detection methods for aromatic amine compounds in workplace air. *Chin Occup Med*, 2023, 50(1): 110-116. doi: 10.20001/j.issn.2095-2619.20230219.
- [14] 中华人民共和国国家卫生健康委员会. 食品安全国家标准 食品接触用塑料材料及制品: GB 4806.7-2023. 北京: 中国标准出版社, 2023.
- [15] National Health Commission of the People's Republic of China. National Food Safety Standard - Food Contact Plastic Materials and Articles: GB 4806.7-2023. Beijing: Standard Press of China, 2023.
- [16] 张璞, 吴红洋, 曹汐, 等. 药用复合膜中苯二胺含量测定及限度标准研究. *中国药业*, 2020, 29(23): 43-45. doi: 10.3969/j.issn.1006-4931.2020.23.011.
- [17] ZHANG P, WU H Y, CAO X, *et al*. Content determination and limit standard of phenylenediamine in laminated films for pharmaceutical packaging. *China Pharmaceuticals*, 2020, 29(23): 43-45. doi: 10.3969/j.issn.1006-4931.2020.23.011.
- [18] CHORMEY S D, ZAMAN T B, MALTEPE E, *et al*. Simultaneous determination of harmful aromatic amine products of Azo dyes by gas chromatography-mass spectrometry. *J Anal Chem*, 2020, 75(10): 1330-1334. doi: 10.1134/S1061934820100044.
- [19] 肖湾, 马红青, 郝晓红. 气相色谱-质谱法测定胺类固化剂中23种有害芳香胺. *化学分析计量*, 2023, 32(8): 30-34. doi: 10.3969/j.issn.1008-6145.2023.08.007.
- [20] XIAO W, MA H Q, HAO X H. Determination of 23 harmful aromatic amines in amine curing agents by gas chromatography-mass spectrometry. *Chemical Analysis and Meterage*, 2023, 32(8): 30-34. doi: 10.3969/j.issn.1008-6145.2023.08.007.
- [21] 陈晓红, 赵永纲, 金米聪. 固相萃取-高效液相色谱/荧光法测定全血中苯胺. *卫生研究*, 2015, 44(2): 299-302.
- [22] CHEN X H, ZHAO Y G, JIN M C. Determination of aniline in whole blood by using solid-phase extraction and high performance liquid

- chromatography with fluorescence detector. *Journal of Hygiene Research*, 2015, 44(2): 299-302.
- [15] 王丽, 李峰, 文舒, 等. 超高效液相色谱快速分离 26 种致癌芳香胺. *纺织报告*, 2024, 43(9): 1-4.
WANG L, LI F, WEN S, *et al.* Ultra-performance liquid chromatography rapid isolation of 26 carcinogenic aromatic amines. *Fangzhi Baogao*, 2024, 43(9): 1-4.
- [16] ÂNGELA FAVARO PEREZ M, PADULA M, MOITINHO D, *et al.* Primary aromatic amines in kitchenware: determination by liquid chromatography-tandem mass spectrometry. *J Chromatogr A*, 2019, 1602: 217-227. doi: [10.1016/j.chroma.2019.05.019](https://doi.org/10.1016/j.chroma.2019.05.019).
- [17] ARRIZABALAGA-LARRAÑAGA A, De Juan P, BRESSAN C, *et al.* Ultra-high-performance liquid chromatography-atmospheric pressure ionization-tandem mass spectrometry method for the migration studies of primary aromatic amines from food contact materials. *Anal Bioanal Chem*, 2022, 414(9): 3137-3151. doi: [10.1007/s00216-022-03946-3](https://doi.org/10.1007/s00216-022-03946-3).
- [18] 邹佳佳, 杨乾展, 代磊, 等. 超高效液相色谱串联三重四级杆质谱法测定药用铝箔中 34 种芳香伯胺. *环境化学*, 2023, 42(5): 1763-1766.
ZOU J J, YANG Q Z, DAI L, *et al.* Determination of 34 primary aromatic amines in medicinal aluminum foil by ultra performance liquid chromatography tandem triple quadrupole mass spectrometry. *Environmental Chemistry*, 2023, 42(5): 1763-1766.
- [19] International Organization for Standardization. ISO/TS 16775: 2021, Packaging for terminally sterilized medical devices—Guidance on the application of ISO 11607-1 and ISO 11607-2. 2021.
- [20] HAQ U S, ALSHEHERY S. Entropy minimization in Casson fluid flow through a semi-porous curved channel with viscous heating and Arrhenius kinetics. *J Therm Anal Calorim*, 2025, 150: 22459-22471. doi: [10.1007/s10973-025-14672-0](https://doi.org/10.1007/s10973-025-14672-0).
- [21] International Organization for Standardization. ISO 10993-18: 2020, Biological evaluation of medical devices—Part 18: Chemical characterization of medical device materials within a risk management process. 2020.
- [22] ZHAO W, RISHENG L. Method validation for the determination of aniline and 3, 3'-dichlorobenzidine by gas chromatography-mass spectrometry. *EES*, 2021, 769(2): 22-26. doi: [10.1088/1755-1315/769/2/022026](https://doi.org/10.1088/1755-1315/769/2/022026).
- [23] DONG H, XIAN Y, LI H, *et al.* Analysis of heterocyclic aromatic amine profiles in Chinese traditional bacon and sausage based on ultrahigh-performance liquid chromatography-quadrupole-Orbitrap high-resolution mass spectrometry (UHPLC-Q-Orbitrap-HRMS). *Food Chem*, 2020, 310: 125937. doi: [10.1016/j.foodchem.2019.125937](https://doi.org/10.1016/j.foodchem.2019.125937).
- [24] 唐崇杰. 液液萃取-气相色谱-质谱法同时测定水质中 14 种芳香胺. *广州化学*, 2024, 49(4): 75-78. doi: [10.16560/j.cnki.gzhx.20240409](https://doi.org/10.16560/j.cnki.gzhx.20240409).
TANG C J. Simultaneous determination of 14 aromatic amines in water by liquid-liquid extraction with GC-MS. *Guangzhou Chemistry*, 2024, 49(4): 75-78. doi: [10.16560/j.cnki.gzhx.20240409](https://doi.org/10.16560/j.cnki.gzhx.20240409).
- [25] JANG H J, JEONG H S. Exposure risk assessment of di(2-ethylhexyl)phthalate (DEHP) using human population pharmacokinetic modeling of DEHP and its major in vivo metabolites. *Arch Toxicol*, 2025, 99(9): 3673-3687. doi: [10.1007/s00204-025-04083-3](https://doi.org/10.1007/s00204-025-04083-3).
- [26] CESTARO I B, NAGATA N, SILVA D G J B. Evaluation of polypropylene microporous membranes as extraction devices for determination of carcinogenic aromatic amines in smoker urine by GC-MS/MS. *J Chromatogr A*, 2024, 1729: 465030. doi: [10.1016/J.CHROMA.2024.465030](https://doi.org/10.1016/J.CHROMA.2024.465030).
- [27] International Organization for Standardization. ISO 10993-12: 2021, Biological evaluation of medical devices—Part 12: Sample preparation and reference materials. 2021.
- [28] 中华人民共和国国家药品监督管理局. 中华人民共和国药典四部 (2025 年版). 北京: 中国医药科技出版社, 2025.
- [29] 任建伟, 罗新月, 赵璇, 等. 固相萃取-高效液相色谱串联质谱测定人体尿液中芳香化合物代谢物的方法研究. *四川大学学报(医学版)*, 2020, 51(5): 695-701. doi: [10.12182/20200960205](https://doi.org/10.12182/20200960205).
REN J W, LUO X Y, ZHAO X, *et al.* Determination of aromatic compounds metabolites in human urine by solid phase extraction-liquid chromatography-tandem mass spectrometry. *J Sichuan Univ (Med Sci)*, 2020, 51(5): 695-701. doi: [10.12182/20200960205](https://doi.org/10.12182/20200960205).
- [30] SHI W Z, QIAN W, ZHI G W, *et al.* Photocatalytic reduction-based liquid microjunction surface sampling-mass spectrometry for rapid *in situ* analysis of aromatic amines originating from azo dyes in packaging papers. *Anal Bioanal Chem*, 2021, 413(26): 6649-6660. doi: [10.1007/s00216-021-03631-x](https://doi.org/10.1007/s00216-021-03631-x).
- [31] CHEN G L, YAN L Z, SHI Q Y, *et al.* First insights into 6PPD-quinone formation from 6PPD photodegradation in water environment. *J Hazard Mater*, 2023, 459: 132127. doi: [10.1016/J.JHAZMAT.2023.132127](https://doi.org/10.1016/J.JHAZMAT.2023.132127).
- [32] YAO M L, LEI Y, HAO M, *et al.* Enhanced hydrolytic resistance of fluorinated silicon-containing polyether urethanes. *Biomacromolecules*, 2020, 21(4): 1460-1470. doi: [10.1021/acs.biomac.9b01768](https://doi.org/10.1021/acs.biomac.9b01768).
- [33] International Organization for Standardization. ISO 10993-1: 2018, Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process. 2018.
- [34] European Chemicals Agency (ECHA). Application for authorisation: establishing a reference dose response relationship for carcinogenicity of technical MDA. (2015-03-26)[2025-09-11]. <https://echa.europa.eu/>.
- [35] International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). Q3D: Guideline for Elemental Impurities. (2022-04-26) [2025-10-15]. <https://www.ich.org/page/quality-guidelines>.
- [36] 田晨旭, 罗锋, 李洁华, 等. 一种聚氨酯微孔薄膜医用补片表层材料的制备及其性能研究. *四川大学学报(医学版)*, 2024, 55(4): 853-860. doi: [10.12182/20240760202](https://doi.org/10.12182/20240760202).
TIAN C X, LUO F, LI J H, *et al.* Preparation and performance of a novel polyurethane microporous film on polypropylene medical mesh surface. *J Sichuan Univ (Med Sci)*, 2024, 55(4): 853-860. doi: [10.12182/20240760202](https://doi.org/10.12182/20240760202).

(2025-07-08 收稿, 2025-12-23 修回)

编辑 何学令



开放获取 本文使用遵循知识共享署名—非商业性使用 4.0 国际许可协议 (CC BY-NC 4.0), 详细信息请访问

<https://creativecommons.org/licenses/by-nc/4.0/>。

OPEN ACCESS This article is licensed for use under Creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0). For more information, visit <https://creativecommons.org/licenses/by-nc/4.0/>.

© 2026 《四川大学学报(医学版)》编辑部

Editorial Office of *Journal of Sichuan University (Medical Sciences)*