植物代谢组学在药材质量评价中的研究进展与展望

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摘要: 药材质量直接影响中药有效性和安全性, 是保证中医药产业健康发展的前提, 全面精准控制和评价药材质量对中药产业发展具有重要意义。药材化学成分的复杂性和动态性使中药质量评价研究成为业内关注的重点和难点。植物代谢组学具有整体性、全面性和动态性研究特点, 基于代谢物的整体研究思路与中医药整体观理论相契合。其化学信息完整且可动态研究, 有助于中药质量追溯体系的建立, 为药材质量评价研究提供新思路和新方法。植物代谢组学在药材质量评价中的研究逐渐增多, 其核心是借助化学计量学方法筛选鉴定差异代谢物或特异性标志化合物, 为植物代谢组学在药材质量控制和评价的推广应用提供思路和参考。本研究重点关注影响药材质量的主要因素, 如产地、逆境、品种、部位、采收期、商品规格和炮制加工, 系统阐述植物代谢组学结合化学计量学方法在药材质量控制和评价中的应用和成效, 归纳总结其中存在的问题, 并提出未来研究方向与趋势。代谢组学在药材质量评价方面发挥着越来越重要的作用, 但植物代谢组学整体化学信息的绝对定性和定量还需进一步探索, 且单一组学方法无法从药效和基因层面进行深层次解析。未来应积极提升植物代谢组学方法标准化和数据库完备性, 将植物代谢组学助力于质量标志物探索。同时, 将代谢组学方法与其他组学方法整合, 完善药材质量控制和评价体系。

关键词: 植物代谢组学; 药材; 质量评价; 差异代谢物; 化学计量学; 质量标志物

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Research progress and prospects for the use of plant metabolomics in quality evaluation of traditional Chinese medicinal materials

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Abstract: The quality of traditional Chinese medicine has a direct impact on the effectiveness and safety of its use, and is the premise necessary to ensure the healthy development of the traditional Chinese medicine industry. Comprehensive and accurate control and evaluation of the quality of medicinal materials is of great significance to the traditional Chinese medicine industry, but the complexity and dynamics of the chemical composition of medicinal materials makes their quality evaluation a challenge. Plant metabolomics provides an integrated and comprehensive analysis that is consistent with the holistic approach of traditional Chinese medicine. Chemical information therein promotes the establishment of a traceable system and provides new ideas and methods for the quality evaluation of medicinal materials. Plant metabolomics in the quality evaluation of medicinal materials is gradually increasing, and the core is the screening and identification of differential metabolites or specific marker

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compounds by means of stoichiometry. This study focused on the main factors that affect the quality of medicinal materials, such as origin, environmental adversity, varieties, harvest time, commercial specification and TCM processing. We describe the research progress in plant metabolomics combined with chemometrics analysis for the quality control and evaluation of medicinal materials, summarize existing problems, identify trends, and propose future research directions. Metabolomics plays an increasingly important role in the quality evaluation of medicinal materials, but the absolute qualitative and quantitative information of metabolomics needs to be further developed, and a single 'omics' technique is not sufficient for an in-depth analysis of medicinal value. In the future, standardization of plant metabolomics methods and a more complete database should be actively promoted, and plant metabolomics should be integrated into quality marker exploration. Plant metabolomics will need to be integrated with other 'omics' methods to improve the quality and evaluation system of medicinal materials.

Key words: plant metabolomics; traditional Chinese medicinal material; quality evaluation; differential metabolite; chemometrics; quality marker

中医药事业的振兴发展, 对全面推进健康中国建设具有十分重大的意义[1]。中药材质量是中医药事业和中医药产业可持续高质量发展的生命线, 是中药发挥临床疗效的重要保障, 已成为中医药界关注的焦点[2]。精准控制中药材质量, 确保中药安全性和有效性至关重要[3]。然而, 由于其多基原 (多品种)、多基源 (多产地)[4]及中药多成分协同作用[5]等特性, 中药材质量一直难以规范控制, 严重影响产业发展和临床应用[6]。

中药质量评价技术和方法为业内关注的重点和难点[7]。目前, 主要技术方法包括指标成分含量测定[8]、指纹图谱[9]、DNA 条形码[10]和一测多评[11]等。此外, 中药质量标志物 (quality marker, Q-marker)[4]和质量综合评价指数[12]等概念被先后提出并用于药材质量综合评价与等级划分。这些探索为中药质量评价和控制奠定了坚实基础。从单一成分含量测定到一测多评, 再到质量标志物和质量综合评价指数的应用, 表明一种或几种成分的质量评价方法难以被共识所接受[13], 中药质量评价模式正呈现多元化发展态势。其中, 质量标志物开创了中药质量研究新模式, 是近 5 年来中药质量评价和控制研究领域的热点[3]。质量标志物的核心研究内容是基于特有性、可测性、有效性、传递性和中医药理论关联性而建立[14], 特有性使其在药材有效鉴别、合理评价和质量控制等方面呈现重要价值[15]。但中药是一个复杂体系, 具有整体发挥作用的特点, 将药材所含化学成分整体进行质量评价和控制才具科学性和合理性[16]。

代谢组学 (metabolomics) 是指在特定条件下, 对生物所含代谢物整体进行定性和定量分析[17]。代谢组学是后基因组时代的研究热点, 可揭示特定时间和特定条件下代谢物的种类和含量, 具有覆盖范围广、灵敏度和准确性高等特点[18]。与传统质量评价方法相比, 代谢组学具有诸多优势。与基于指标成分含量测定方法相比, 代谢组学具有整体性特点和更强专属性[19]。与进行相似度评价的指纹图谱技术相比, 代谢组学可提供更加精准的成分定性和定量[20]。一测多评法需要满足特定条件才推荐使用, 即待测成分含量需高于 1 mg·g^{-1} [11]。在药材种质鉴别方面, 目前流行的标准植物 DNA 条形码, 如叶绿体片段 *mat*K、*rbc*L、*trn*H-*psb* 和核糖体基因及其转录间隔区 ITS/ITS2, 对属间及属以上类群能较好鉴定, 但对某些属内近缘物种的区分并不理想[21,22], 尤其是对分类疑难类群束手无策, 如淫羊藿属 *Epimedium*[23]。同时, DNA 条形码对不同生长年限及同一基原栽培与野生种质的鉴别也存在困难[24]。

代谢组学思路与中药作用的整体观一致。根据研究目的和代谢物检测范围, 代谢组学研究分为非靶向代谢组学和靶向代谢组学。非靶向代谢组学旨在分析样品中所有可检测的代谢物, 可兼顾新化合物发现。而靶向代谢组学是研究具有已知化学结构和生物化学注释的代谢物, 化合物鉴定精确度比非靶向代谢组学方法高[25], 但已知代谢物数量有限。代谢组学适用于解决药物作用的物质基础和中药复杂体系问题。将其应用于药材种质资源、药效物质基础、作用机制、安全性和方剂配伍等研究, 对中药现代化具有重要意义[26]。

植物代谢组学是代谢组学重要分支, 主要基于化学计量学 (chemometrics) 对植物整体代谢物进行定性和定量分析[27]。化学计量学是通过数学或统计方法将化学系统或过程的测量值与系统状态相关联的科学[28]。化学计量学针对复杂体系所产生的数据分析问题, 逐渐发展出多元统计分析方法, 如: 回归分析、聚类分析、判别分析、主成分分析 (principal component analysis, PCA)、偏最小二乘判别分析 (partial least-squares discrimination analysis, PLS-DA) 和正交偏最小二乘判别分析 (orthogonal partial least-squares discrimination analysis, OPLS-DA) 等[29]。这些方法成为处理

和深度分析复杂而庞大数据集, 进而提取有效信息, 深入理解代谢组学中化学过程的有力工具[30]。同时, 通过比较样本间异同, 在海量代谢组学数据集中筛选重要差异代谢物[31]。植物代谢组学主要应用于植物代谢组谱分析和植物遗传分析[32]。代谢谱分析在药用植物上主要应用于不同产地、逆境、品种、部位、采收期和炮制加工等的代谢产物比较和代谢途径辅助研究等。关注样品间化学成分种类和含量差异, 进而进行种质鉴别和样品分类[33-36], 为药材质量评价和控制提供科学依据[20]。

加强中药质量控制, 对保障用药安全和促进中医药产业发展具有重要意义。本文通过文献整理, 围绕植物代谢组学在药材质量评价中的研究进行系统梳理, 重点关注影响药材质量的重要因素, 如产地、逆境、品种、部位、采收期、炮制加工和商品规格等, 阐述植物代谢组学揭示这些因素对药材质量影响的研究应用、成效和不足, 并提出未来研究方向与趋势。

1 植物代谢组学方法分析产地对药材质量影响

特定地域的自然环境造就独特生态系统, 药用植物作为生态系统的重要组分, 不同地域产出的中药材质量差异显著[37]。其中, 道地药材具有优形、优质和优效特征, 是产地对药材质量影响的典范[38]。东汉《神农本草经》描述道地药材: “药有……采收 (造) 时月, 生熟, 土地所出, 真伪陈新, 显各有法”[39]。2017 年 7 月 1 日,《中华人民共和国中医药法》明确道地药材的含义: “经过中医临床长期应用优选出来, 产在特定地域, 与其他地区所产同种中药材相比, 品质和疗效更好, 且质量稳定, 具有较高知名度的中药材”[40]。

植物代谢组学通过代谢物的全面分析, 对不同产地药材进行鉴别, 且通过多元统计分析, 可进一步锁定标志化合物以控制药材质量[41]。甘草 Glycyrrhizae Radix et Rhizoma 是临床广泛使用的药材, 甘草 *Glycyrrhiza uralensis* Fisch. 为中国药典收录的 3 个基原之一[42]。Bai 等[43]利用代谢组学对甘肃省 3 个甘草产地的生物活性成分进行研究, 结果表明, 不同产地代谢产物的种类差异较大, 如: 甘草香豆素、甘草素 Z、甘草素和二羟基甘草酚 H 主要存在于酒泉产地, 而新甘草苷、6′-乙酰甘草苷、甘草酮 B、异黄酮醇、甘草醛和甲基化乌拉豆素主要存在于兰州产地。Mais 等[44]利用基于液相色谱−质谱联用 (liquid chromatography-mass spectrometry, LC-MS) 技术的代谢组学方法对来自加纳和中国各 40 批鲜生姜进行产地鉴别, 鉴定出 16 种差异代谢物, 其中 6 种为两国生姜鉴别的标志化合物。Cao 等[45]利用非靶向代谢组学方法对 85 份黄连 Coptidis Rhizoma 样品进行产地鉴别, 四川省、湖北省和重庆市不同产地的鉴别准确率为 100%, 且首次发现 11 个具较强鉴别能力的标记化合物, 可用于产地快速鉴定。《道地药材图典》收录 408 种道地药材, 其中 96 种道地药材获得 227 个地理标志产品保护[38]。说明即使获得地理标志产品保护的道地药材也可能存在多个产地。但不同产地药材有效成分和疗效均可能存在差异, 建立药材产地快速鉴别的可靠技术备受关注。

植物代谢组学通过多元统计分析筛选不同产地药材的差异代谢物作为鉴别标记物, 可快速准确鉴别产地。相关研究已开展较多, 详细案例见表 1[42-51]。部分药材, 如天麻, 因缺乏足够研究基础导致部分化合物无法准确鉴定, 则基于标志离子建立模型进行产地鉴别[42]。根据标志化合物, 代谢组学方法或可助力中药材信息化追溯体系, 实现来源可查目标。

2 植物代谢组学方法分析逆境对药材质量影响

植物体作为一个开放体系, 从外界摄取物质、能量和信号的同时, 也受到各种生物环境和非生物环境的影响[52]。植物在自然界遇到环境条件的剧烈变化, 对正常生长不利, 称为逆境或胁迫 (stress)[53]。植物面临逆境时, 产生部分初级和次生代谢产物进行保护, 而中药材活性成分正是次生代谢物[54]。Huang 等[55]提出逆境是促进道地药材的形成重要机制之一, 即顺境出产量, 逆境促品质。代谢组学方法分析逆境药用植物的代谢物, 可探索特定逆境对药用植物化学成分的影响[56]。Rahnamaie-Tajadod 等[57]采用诱导逆境反应的信号分子茉莉酸甲酯对虎杖进行外源处理, 刺激其产生次生代谢物, 可提高芳香族化合物的产量。Zhang 等[58]利用菌根真菌 *Ceratobasidium* sp. AR2 诱导金线莲, 其金钱草素、水仙素、芦丁、异鼠李素、异鼠李素-3-*O*-*β*-*D*-葡萄糖苷、槲皮素、槲皮素-7-*O*-葡萄糖苷、山柰酚-3-*O*-葡萄糖苷和丹桂素含量显著增加, 证实适当的逆境利于活性成分积累。Cao 等[59]对比正常氮和缺氮处理条件下板蓝根的代谢组学图谱, 结果表明缺氮对板蓝根初级代谢和次生代谢均产生影响, 适度减氮利于其活性成分积累。Zhang 等[60]对 280～315 nm 波长紫外光 (ultraviolet-B radiation, UV-B) 辐射不同时长 (12、24、48 和 96 h) 的甘草叶片进行代谢组学分析, 发现具抗氧化作用的邻位二羟基 B 环黄酮类化合物含量随处理时间增加而增加, 但超过植物耐受范围的逆境将导致产量和质量下降, 甚至引起植株死亡。Zhan 等[61]采用基于 LC-MS 的代谢组学方法对正常红色丹参和橙色丹参进行分析, 结果表明, 丹参酮 IIA 等脱氢呋喃环丹参酮含量减少导致橙色丹参表型变化和质量下降。橙色丹参有 7 种化合物, 包括正常丹参中含量最丰富的活性成分丹参酮 IIA 和丹参酮 I, 含量显著降

Table 1 Application examples of plant metabolomics in analyzing the influence of origin on the quality of traditional Chinese medicine. *Artemisia rupestris* L. was not included in The Chinese Pharmacopoeia, so the Latin name of the medicinal materials was not listed, and the Latin name of the plant was used instead

Medicinal material	Origin	Analytical technique	Key result	Reference
Gastrodiae Rhizoma	Hubei, Sichuan and Yunnan	LC-MS	Based on the relative intensities of discriminant ions, support vector machines (SVM) was employed to predict the geographical origins of *Gastrodia elata*. The obtained SVM model showed excellent prediction performance with an average prediction accuracy of 100%.	[42]
Glycyrrhizae Radix et Rhizoma	Jiuquan, Lanzhou and Wuwei in Gansu province	LC-MS	16 potential biomarkers of licorice taproots from different geographical origins were screened.	[43]
Zingiberis Rhizoma Recens	Ghana and China	LC-MS	16 differential metabolites were identified between the gingers from the two geographical locations, six of which were identified as the marker compounds responsible for the discrimination.	[44]
Coptidis Rhizoma	Hubei, Sichuan and Chongqing	LC-MS	11 effective marker compounds were screened for discriminating Coptidis Rhizoma samples from different geographic origins.	[45]
Ophiopogonis Radix	Zhejiang and Sichuan	LC-MS	There were many differences between the metabolic profile data of *Ophiopogon japonicas* from different producing areas, the samples from Sichuan showed higher level steroidal saponins and samples from Zhejiang had higher contents of homoisoflavonoids specifically.	[46]
Gentianae Macrophyllae Radix	Qinghai, Sichuan and Gansu	LC-MS	Eight characteristic compounds were identified to determine the geographical origin of 42 samples.	[47]
Croci Stigma	Bozhou, Anhui province and Jiaxing, Zhejiang province	LC-MS	The chemical compositions in saffron from these two areas were similar, Saffron produced from Bozhou contained higher quantities of safranal, crocetin and picrocrocin than that from Jiaxing.	[48]
Pogostemonis Herba	Wanning, Hainan province and Zhaoqing, Yangjiang and Zhanjiang in Guangdong province	GC-MS	Eight differential compounds (*β*-caryo-phyllene, norpatchoulenol, globulol, patchouli alcohol, pogostone) were identified, which could be used to classify their chemical types and habitats.	[49]
Artemisia rupestris L.	Aletai fuyun and Hami in Xinjiang	LC-MS	For artificial varieties, 29 structural category known metabolites were screened out; for wild varieties, 45 structural category known metabolites were screened out.	[50]
Ecliptae Herba	Hunan, Hubei and Guangxi	GC-MS	Eight different metabolites were identified, which could be used for habitats identification.	[51]

低。结合转录组数据分析发现, 橙色丹参中2个抗逆和4个蛋白降解相关基因表达显著上调, 推测是受逆境或疾病影响。Cai等[62]采用LC-MS结合多元统计分析金银花在不同浓度盐胁迫下代谢产物变化, 发现与抗氧化能力相关的次生代谢物, 如酚酸、黄酮和环烯醚萜等的生物合成均受到影响。低盐处理组和高盐处理组的生物活性成分相对含量分别显著高于和低于对照组, 说明土壤中适度低盐处理利于提升药材质量, 但过量盐分对植物生长发育和药材品质均有害。

利用代谢组学方法分析逆境下药用植物的代谢物, 可探索特定逆境对化学成分的影响。结合代谢组和转录组方法, 整合分析道地药材表型、基因型和生境的相互关系, 可深入研究道地药材适应逆境的生理及分子机制, 为培育适应性强而优质的种质奠定基础。

3 植物代谢组学方法分析品种对药材质量影响

药材品种鉴定是中药质量控制的源头环节, 品种正确是优质药材栽培、采收、加工和疗效的首要保证[63]。Xie[64]曾精辟指出: “品种一错, 全盘皆否”。中药的多基原由来已久,《新修本草》和《图经本草》均记载多基原现象, 如石斛 Dendrobii Caulis[65]、黄芪 Astragali Radix[66]等。2015版中国药典中共收载522种中药材, 其中131种 (25.1%) 为多基原药材[67], 药材品种的复杂性可略见一斑。随着中药材资源缺口增大和栽培产区扩大, 药农随市场导向盲目引种现象普遍[68]。加之药材市场流通缺乏有力监管, 中药品种实际使用情况更加复杂[69]。

代谢组学在药用植物品种鉴定中受到越来越多关注。基于核磁共振 (nuclear magnetic resonance spectroscopy, NMR)[70-72]、LC-MS和气相色谱–质谱联用 (gas chromatography-mass spectrography, GC-MS)[73-75]技术的代谢组学方法对药材化学信息全面分析, 用于药用植物品种鉴定被证实卓有成效。

贝母为镇咳祛痰之要药。Liu等[73]利用基于LC-MS的代谢组学和化学计量学相结合的方法, 对8种贝母共73批 [太白贝母 *Fritilaria taipaiensis* P. Y. Li、瓦布贝母 *F. unibracteata* Hsiao et K. C. Hsia var. *wabuensis* (S.

Y. Tang et S. C. Yue) Z. D. Liu, S. Wang et S. C. Chen、梭砂贝母 *F. delavayi* Franch.、暗紫贝母 *F. unibracteata* Hsiao et K. C. Hsia、甘肃贝母 *F. przewalskii* Maxim.、川贝母 *F. cirrhosa* D. Don、平贝母 *F. ussuriensis* Maxim. 和浙贝母 *F. thunbergii* Miq.] 进行分析, 鉴定出 21 个特异性标志化合物, 不仅能对贝母品种进行精准鉴别, 且可对 16 种含有贝母的中成药产品进行原料药品种鉴别。Tao 等[76]对 40 批豨莶草 (17 批腺梗豨莶 *Siegesbeckia pubescens* Makino、13 批豨莶 *S. orientalis* L. 和 10 批毛梗豨莶 *S. glabrescens* Makino) 进行代谢组学分析, 共筛选出 412 种化学成分。其中, 6 种成分可作为品种鉴别的潜在标志化合物。Farag 等[77]对 3 种马齿苋 (*Portulaca oleracea* L.、*P. rausii* Danin 和 *P. granulatostellulata* (Poelln.) Ricceri & Arrigoni) 11 个样本进行代谢组学分析, 共鉴定出 85 种代谢物, 进而筛选出 4 种马齿苋酰胺类生物碱, 即马齿苋酰胺 A、马齿苋酰胺 C、马齿苋酰胺 K 和马齿苋酰胺 N, 可用于品种鉴别。

品种鉴定的另一内涵是区分正品和伪品。2020 年全国中药材及中药饮片抽检中发现, 主要质量问题为伪品冒充正品、掺伪掺杂和栽培中药材品质下降等[78]。其中, 伪品主要来源于性状相似品种或近缘种属药材[78]。陈皮 Citri Reticulatae Pericarpium 为芸香科植物橘 *Citrus reticulata* Blanco 及其栽培变种的干燥成熟果皮, 柑橘新品种的推出将原有品种分布格局打破, 导致不同栽培品种来源陈皮鉴别尤为困难。Li 等[79]采用代谢组学方法对川陈皮及其常见混伪品不知火橘皮进行黄酮类成分分析, 共鉴定出 228 种黄酮类化合物, 筛选出 52 种差异代谢物。其中, 川陈皮中鉴定出 15 种特有成分, 混伪品鉴定出 16 种特有成分。Shen 等[80]采用植物代谢组学方法对酸枣仁 Ziziphi Spinosae Semen、伪品理枣仁及不同比例掺伪的粉末进行分析发现, 缬氨酸、乳酸、丙氨酸、γ-氨基丁酸和半胱氨酸随掺伪比例的增加出现信号强度逐渐减弱的趋势, 当掺伪比例超过 40% 时, 酸枣仁粉和掺伪品化学信息在 PLS-DA 模型中完全分开。Wallace 等[81]通过非靶向代谢组学方法对白毛茛 *Hydrastis canadensis* L. 和其伪品黄连 *Coptis chinensis* Franch. 进行代谢物多元统计分析, 可鉴别 5%～95% 掺假率的白毛茛。植物代谢组学方法与多元统计分析结合, 可明显区分药材正品、混伪品和伪品, 且为药材和中药饮片的正本清源提供理论依据。

综上所述, 植物代谢组学已被广泛用于植物药品种鉴别。相关研究实例见表 2[73-77,82-97]。代谢组学对药用植物品种具有较强区分力, 通过筛选特异性标志化合物, 对不同药材品种、药材混伪品及中成药所用原料药的品种均可鉴别。对无法清晰区分品种的药用植物, 也可通过多元统计分析, 根据代谢物整体特征将品种区分。但部分研究基础薄弱的药用植物, 可能因常用数据库收集的结构信息不全, 暂无法对特异性标志

Table 2 Application examples of plant metabolomics in analyzing the influence of taxon on the quality of traditional Chinese medicine. *Taxus*, *Swertia*, *Fritillaria*, *Callicarpa*, *Citrus* and flower bud of *P. ginseng*, *P. quinquefolius* and *P. quinquefolius* were not included in The Chinese Pharmacopoeia, so the Latin names of the medicinal materials were not listed, and the Latin names of its plant were used instead

Medicinal material	Taxon	Analytical technique	Key result	Reference
Fritillaria	*Fritillaria taipaiensis* P. Y. Li *F. unibracteata* Hsiao et K. C. Hsia var. *wabuensis* (S. Y. Tanget S. C. Yue) Z. D. Liu, S. Wang et S. C. Chen *F. delavayi* Franch. *F. unibracteata* P. K. Hsiao & K. C. Hsia *F. przewalskii* Maxim. *F. cirrhosa* D. Don *F. ussuriensis* Maxim. *F. thunbergii* Miq.	LC-MS	21 specific chemical markers were identified from eight fritillaria species. These specific chemical markers can not only accurately identify *Fritillaria* species, but also identify the *Fritillaria* species in 16 kinds of commercially relevant products.	[73]
Arecae Semen	*Areca catechu* L. *A. triandra* Roxb. ex Buch.-Ham.	LC-MS	A total of 791 metabolites were identified, 154 different metabolites were screened out, but *A. catechu* and *A. triandra* primary and secondary metabolites species were similar.	[74]
Paridis Rhizoma	*Paris polyphylla* var. *chinensis* (Franch.) H. Hara *P. polyphylla* var. *yunnanensis* (Franch.) Hand.-Mazz. *P. fargesii* var. *fargesii*	GC-MS	33 different metabolites were screened out, which could be used to discriminate *Paris* species. The utilization efficiency of sucrose and protein abundance were higher in the sugar metabolic pathway of *P. polyphylla* var. *chinensis*. The pyruvate content and efficiency of acetyl-CoA-utilization in saponin biosynthesis were also higher in *P. polyphylla* var. *chinensis*.	[75]

Continued

Medicinal material	Taxon	Analytical technique	Key result	Reference
Siegesbeckiae Herba	*Siegesbeckia pubescens* Makino *S. orientalis* L. *S. glabrescens* Makino	LC-MS	Six specific chemical markers were identified, which could be used to discriminate Siegesbeckiae Herba.	[76]
Portulacae Herba	*Portulaca oleracea* L. *P. rausii* Danin *P. granulatostellulata* (Poelln.) Ricceri & Arrigoni	LC-MS	85 metabolites were identified, and four previously undescribed cyclodopa alkaloids were screened out, which could be used for varieties identification and classification.	[77]
Crataegi Fructus	*Crataegus pinnatifida* Bge. *C. pinnatifida* Bge. var. *major* N. E. Br.	LC-MS	47 differential compounds were identified, which were then used to build a partial least squares discriminant analysis model that successfully discriminate two species.	[82]
Curcumae Radix	*Curcuma wenyujin* Y. H. Chen et C. Ling *C. Longa* L. *C. kwangsiensis* S. G. Lee et C. F. Liang *C. phaeocaulis* Vai.	LC-MS	Multivariate statistical analysis confirms that the chemical constituents of the four turmeric species were significantly different. Four chemical markers were identified: curcumin, curcumenone, curcumenol and zederone, which could be used to identify 33 different batches of Curcumae Radix from four *Curcuma* species.	[83]
Citri Reticulatae Pericarpium	*Citrus reticulata* Chachi *C. reticulata* Blanco	LC-MS	92 compounds were identified, of which 19 differential metabolites could be identified as potential markers for distinguishing between Citri Reticulatae Blanco Pericarpium and Citri Reticulatae Chachi Pericarpium.	[84]
Aconiti Radix Aconiti Kusnezoffii Radix Aconiti Lateralis Radix Praeparata	*Aconitum carmichaelii* Debx. *A. kusnezoffii* Reichb.	LC-MS	The metabolites of *A. carmichaelii* Debx (CHW) and *A. carmichaelii* Debx (SFZ) were the same, but the contents of 22 metabolites were different. 13 metabolites were identified between the CHW and *A. kusnezoffii* Reichb (CW), songorine, carmichaeline and isotalatizidine only did exist in the SFZ and CHW.	[85]
Moutan Cortex	*Paeonia ostii* T. Hong & J. X. Zhang *P. qiui* Y. L. Pei & D. Y. Hong *P. rockii* (S. G. Haw & Lauener) T. Hong & J. J. Li ex D. Y. Hong *P. jishanensis* T. Hong & W. Z. Zhao *P. decomposita* Hand. -Mazz. *P. ludlowii* (Stern & G. Taylor) D. Y. Hong *P. delavayi* var. *alba* Bean *P. delavayi* var. *lutea* (Delavay ex Franch.) Finet & Gagnep *P. delavayi* var. *angustiloba* Rehder & E. H. Wilson	LC-MS	A total of 384 compounds were identified in nine species, which were divided into two subgroups by multivariate statistical analysis: *Vaginatae* and *Delavayanae*. Procyanidin B-1, 3-*O*-gallate and paeonihybridin were potential chemical markers in different wild tree peonies.	[86]
Taxus	*Taxus fuana* Nan Li & R. R. Mill T. *yunnanensis* W. C. Cheng & L. K. Fu	LC-MS	4 986 metabolites were identified, of which 1 972 were differential metabolites. The taxol content of *T. yunnanensis* is 3.1 times as much as *T. fauna*.	[87]
Pulsatillae Radix	*Pulsatilla chinensis* (Bunge) Regel *P. dahurica* (Fisch. ex DC.) Spreng. *P. turczaninovii* Krylov & Serg. *P. cernua* (Thunb.) Bercht. & J. Presl	LC-MS	157 triterpenoid saponins were identified, of which 34 constituents were reported in *Pulsatilla* Adans for the first time, 81 were identified as differential components, and 12 chemical ingredients were characterized as potential chemical markers to differentiate the four officinal *Pulsatilla* Adans herbs.	[88]
Gentianae Radix et Rhizoma	*Gentiana scabra* Bunge. *G. rigescens* Franch. ex Hemsl.	LC-MS	87 compounds were identified, of which 29 were common to both species. 11 differential metabolites were screened out, and seven characteristic components identified as (+)-syringaresinol, lutonarin, trifloroside, 4-*O*-*β*-*D*-glu-trifloroside, 4"-*O*-*β*-*D*-glucopyranosy1-6'-*O*-(4-*O*-*β*-*D*-glucaffeoyl)-linearroside, macrophylloside A and scabraside were selected as the chemical markers for the recognition of two *Gentiana* species.	[89]

Continued

Medicinal material	Taxon	Analytical technique	Key result	Reference
Uncariae Ramulus Cum Uncis	*Uncaria rhynchophylla* (Miq.) Miq. ex Havil. *U. hirsuta* Havil. *U. sinensis* (Oliv.) Havil. *U. macrophylla* Wall. *U. sessilifructus* Roxb.	LC-MS	Principal component analysis and chemical fingerprinting spectra showed that five official species were differentiated from each other except for *U. hirsuta* and *U. sinensis*, and the SVM model could be established to recognize five species 100% accurately	[90]
Swertia	*Swertia mussotii* Franch. *S. chirayita* (Roxb.) H. Karst.	^{1}H NMR	The metabolites of *S. mussotii* and *S. chirayita* were significantly different. The contents of gentiopicrin, isoorientin, glucose, loganic acid, and choline in *S. mussotii* were higher, whereas *S. chirayita* exhibite higher levels of swertiamarin, oleanolic acid, valine, and fatty acids.	[91]
Callicarpa	*Callicarpa kwangtungensis* Chun *C. macrophylla* Vahl *C. nudiflora* Hook. & Arn.	LC-MS	34 compounds were identified, including 30 chemical markers, which were identified for the discrimination of three officinal *Callicarpa* herbs.	[92]
Citrus	*Citrus* × *aurantium* L. *C. reticulata* Blanco	LC-MS	Multivariate statistical analysis showed that primary metabolites enable the discrimination of species, whereas secondary metabolites were associated with species and the ripening process.	[93]
Curcumae Rhizoma	*Curcuma phaeocaulis* Valeton *C. kwangsiensis* S. G. Lee & C. F. Liang *C. wenyujin* Y. H. Chen & C. Ling	GC-MS	Principal component analysis effectively distinguished the samples from different species, and multivariate statistical analysis selected curzerenone, germacrone, curdione and epicurzerenone as chemical markers for discrimination and quality control among different groups of samples.	[94]
Ginseng Radix et Rhizoma Panacis Quinquefolii Radix	*Panax ginseng* C. A. Mey. *P. quinquefolium* L.	LC-MS	Multivariate statistical analysis effectively distinguisheed the samples from two species, ginsenosides Rf, Rb2 and Rc together with their isomers and derivatives were more likely to be present in Ginseng Radix et Rhizoma, whereas ginsenoside Rb1, pseudoginsenoside F11 and ginsenoside Rd together with their isomers and derivatives tended to be present in Panacis Quinquefolii Radix.	[95]
Flower bud of *P. ginseng*, *P. quinquefolius* and *P. quinquefolius*	*Panax ginseng* C. A. Mey. *P. quinquefolius* L. *P. notoginseng* (Burkill) F. H. Chen	LC-MS	A total of 32 components were identified as the potential markers, of which Rb3, Ra1, isomer of m-Rc/m-Rb2/m-Rb3, isomer of Ra1/Ra2, Rb1, and isomer of Ra3 were the most important for differentiating among flower bud of *P. ginseng*, *P. quinquefolius* and *P. quinquefolius*.	[96]
Ginseng Radix et Rhizoma Panacis Quinquefolii Radix Notoginseng Radix et Rhizoma	*Panax ginseng* C. A. Mey. *P. quinquefolius* L. *P. notoginseng* (Burkill) F. H. Chen	GC-MS	Multivariate statistical analysis effectively distinguished the samples from three species, and three unique chemical markers were screened for species identification.	[97]

化合物进行定性分析。

4 植物代谢组学方法分析部位对药材质量影响

药用植物所含有效成分群因部位不同而有所差异, 为保证疗效, 多数药用植物仅有一个最佳药用部位[63], 如大青叶 Isatidis Folium 用叶、西红花 Croci Stigma 用柱头、黄芪 Astragali Radix 用根、五味子 Schisandrae Chinensis Fructus 用果实等。当然, 也存在多部位品种, 但不同部位往往被作为不同饮片, 其功能主治也存在差异, 如麻黄根 Ephedrae Radix et Rhizoma 功能为固表止汗, 用于自汗和盗汗; 而麻黄 Ephedrae Herba 草质茎功能为发汗散寒、宣肺平喘和利水消肿, 用于风寒感冒、胸闷喘咳和风水浮肿[42]。

Qi 等[98]基于核磁共振氢谱 (^{1}H nuclear magnetic resonance spectroscopy, ^{1}H NMR) 的植物代谢组学方法对款冬茎和叶的化学成分进行分析, 共鉴定出 40 个化合物, 多元统计分析表明款冬茎和叶中均存在含量较

高的酚酸类成分和倍半萜类成分。款冬叶中, 缬氨酸、亮氨酸和款冬酮等含量高于茎, *α*-葡萄糖、*β*-葡萄糖含量则低于款冬茎。Pan 等[99]利用基于 ^{1}H NMR 技术的植物代谢组学方法研究藏药独一味地上部分与地下部分的化学成分差异, 两个部位的差异主要体现在初生代谢产物, 地下部分葡萄糖、蔗糖、果糖含量高于地上部分, 而脂肪酸低于地上部分。Wu 等[100]采用靶向代谢组学方法分析刺五加 *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. 和无梗五加 *E. sessiliflorus* (Rupr. & Maxim.) S. Y. Hu 的根、茎和叶, 鉴定出 19 种酚类物质, 均在根中含量最高。其中, 原儿茶酸、五味子苷 B、五味子苷 E、异秦皮苷、金丝桃苷、山柰酚和齐墩果酸在 2 种五加中均主要存在根和茎中。Wu 等[101]通过非靶向代谢组学方法对蒙古黄芪 *Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao 根、茎和叶进行分析, 共鉴定 2 190 种化合物, 茎和叶中化学成分含量普遍较高, 但生物活性成分主要富集于根中。该研究为黄芪 Astragali Radix 根部入药提供了科学依据。

中药大健康产业的快速发展使药用植物资源需求量剧增, 但中药资源产业结构与工业化需求不匹配, 导致药用植物野生资源急剧减少[68]。传统非药用部位作为新药材资源原料进行开发利用, 对资源的最大化综合利用具有极重要意义[102], 有助于推进资源节约型和环境友好型中药资源循环经济体系建设, 为中药资源产业的可持续发展提供科技支撑和驱动力, 并利于中药产业的节能减排、碳达峰与碳中和目标的实现[102]。植物代谢组学方法可鉴别药用植物不同部位, 并通过多元统计分析筛选差异化合物, 为药用植物入药部位的确定和非药用部位的开发利用提供科学支撑, 具有重要经济效益和社会效益。

5 植物代谢组学方法分析采收期对药材质量影响

药用植物次生代谢产物的种类和含量决定药材质量。随着植物发育阶段变化, 次生代谢产物的种类和含量通常相应变化, 药材质量呈现动态变化。药用植物的采收时间和过程直接影响中药材质量, 我国唐代著名医学家孙思邈在《千金翼方》中记载: “夫药采取, 不知时节, 不以阴干暴干, 虽有药名, 终无药实, 故不依时采取, 与朽木不殊。”[103]。民间谚语“三月茵陈四月蒿, 五月六月当柴烧”就是采收期重要性的最生动总结。

Yang 等[104]通过代谢组学方法探索黄芩叶不同采收期化学成分的变化规律, 发现一年生和两年生黄芩存在 28 个差异代谢物。不同月份采收黄芩叶的化学成分含量也差异明显, 主要成分如: 红花素-7-*O*-葡萄糖醛酸苷、野黄芩苷和异红花素-7-*O*-葡萄糖醛酸苷等在 5 月和 6 月含量较高。*L*-谷氨酰胺、柠檬酸、黄芩苷、二氢黄芩苷和白杨素等在 7 月和 8 月含量较高。Jing 等[105]通过代谢组学方法对 10 批不同物候期栽培远志 (4 月龄至 16 月龄) 进行分析, 共鉴定出 31 种次级代谢物。不同月龄栽培远志可分为 3 个阶段: I (休眠期)、II (花果期) 和III (休眠期)。I阶段次级代谢物含量均较低, II阶段次级代谢物含量先升高后降低, 但均高于第I阶段, III阶段蔗糖酯类成分含量逐渐升高, 低聚糖酯类和皂苷类成分逐渐降低。Geng 等[106]采用基于 LC-MS 技术的代谢组学方法, 对 1～7 年生川贝母的 42 个样本 (每个年份 6 个生长期样本) 进行次生代谢物分析。得到 4 种生物碱类差异代谢物可作为标志化合物用于不同年份生长期的分类和鉴别。从评价指标来看, 若依据中国药典西贝母碱含量为标准, 采收期应尽可能早, 但过早采收将影响药材产量、其他成分及营养成分的含量。Qin 等[107]采用基于 LC-MS 技术的代谢组学方法, 研究淫羊藿叶片在栽培条件下 4 个典型生长阶段的代谢产物组成变化。在 32 个物种中共鉴定 403 种代谢产物。其中, 302 种代谢物受生长阶段影响, 大部分黄酮类化合物、单宁类、木脂素类和香豆素类化合物含量在盛花期至采收期随叶片生长和成熟而上调。该研究阐明了淫羊藿叶片成分, 尤其是黄酮类化合物, 在盛花期后的整体发育规律。

植物初生代谢物和次生代谢物均随植物生理代谢过程变化[108]。每种植物可产生 4 000～20 000 个代谢物[109]。代谢组学为药用植物提供整体代谢物分析, 可提升对生长过程中代谢动态变化和发育调节的全面理解, 相关研究实例见表 3[84,104-107,110-112]。药材采收期的确定需掌握总体代谢物动态变化, 依据多组分评价质量, 同时应兼顾药用部位生物量变化, 即结合药材质量和产量, 考察药用植物不同生长期有效成分积累总量变化, 提升资源利用率和可持续发展。

6 植物代谢组学方法分析炮制对药材质量影响

中药炮制是中国第一批非物质文化遗产, 为中医药特色和优势[113]。中药炮制在降低不良反应发生率、减轻不良反应症状、提高疗效、增加临床适应性和方便贮藏运输等方面发挥重要作用[114-116]。中药炮制可发生大量化学变化, 如水解、氧化、分解和异构化等, 导致炮制前后成分发生变化, 从而达到增效减毒的作用。因此, 利用现代技术分析中药炮制前后所有化学成分变化规律, 可探索和阐明中药炮制的科学机制。

Liu 等[117]采用基于 LC-MS 技术的代谢组学方法对黄芪生品和炮制品的化学成分进行研究, 多元统计分析表明黄芪生品和炮制品中化学物质发生明显变化,

Table 3 Application examples of plant metabolomics in analyzing the influence of harvest period on the quality of traditional Chinese medicine. *Peganum harmala* L. and the leaves of *Scutellaria baicalensis* Georgi were not included in The Chinese Pharmacopoeia, so the Latin name of the medicinal materials were not listed, and the Latin names of its plant were used instead

Medicinal material	Analytical technique	Key result	Reference
Citri Reticulatae Pericarpium	LC-MS	31 metabolites were identified to distinguish Citri Reticulatae Chachi Pericarpium in different storage years, and metabolite levels increased in 3−10 years and decreased after 15−30 years.	[84]
Leaves of *Scutellaria baicalensis* Georgi	LC-MS	28 differential metabolites were identified, and the relative contents of carthamin-7-*O*-glucuronide, isocarthamin-7-*O*-glucuronide, scutellarin, were higher in May and June, while the relative contents of *L*-glutamine, citric acid, baicalin, dihybaicalin and chrysin were higher in July and August.	[104]
Polygalae Radix	LC-MS	A total of 31 species of secondary metabolites were identified from 10 batches of cultivated *Polygala tenuifolia* with different phenological periods. The content of secondary metabolites change dynamically with the phenological periods, and sucrose esters and xanthone decreased first and then increased. Oligosaccharides esters and saponins decreased firstly, then increased and then decreased, and the fruit and fruit period reached the peak.	[105]
Fritillariae Cirrhosae Bulbus	LC-MS	Four alkaloid differential metabolites were screened from 42 samples covering growth of cultivated Fritillariae Cirrhosae Bulbus ranging in age from one to seven years old. The harvest time could be as early as possible based solely on the *Fritillaria* alkaloid content. However, considering the yield, biological activity and nutrient accumulation of different components, it was recommended to harvest after four years of cultivation.	[106]
Epimedii Folium	LC-MS	The 302 metabolites in *Epimedium pubescens* leaves were showed the growth/development-dependent alterations, and most flavonoids, tannins, lignans and coumarins were upregulated with leaf growth and maturation from full flowering stage to harvest stage.	[107]
Aurantii Fructus	LC-MS	44 compounds were identified and Aurantii Fructus was recommended to be harvested from June 11 to July 7, when the content of bioactive components and antioxidant activity were higher.	[110]
Peganum harmala L.	^{1}H NMR	There were significant differences in the chemical composition of *P. harmala* L. during the four growth stages of May, August, October and December. The contents of vasicine, choline and sucrose were high in May, betaine, lysine, 4-hydroxyisoleucine and proline were high in August, and phosphorylcholine, glucose, acetic acid and vasicinone were the highest in December.	[111]
Lonicerae Japonicae Flos	LC-MS	A total of 157 metabolites were identified, flavonoids, phenolic acid and iridoid glycosides decreased significantly with the process of flowering stages. For the primary metabolites, the contents of most amino acids, nucleosides and oxidized fatty acids decreased significantly, while the contents of most lysophosphatidylcholine, lysophosphatidylethanolamine and fatty acids increased significantly.	[112]

且存在15个标志化合物。Su等[118]采用基于LC-MS技术的代谢组学方法, 结合多元统计分析综合比较五味子生品和醋炮制品的差异, 确定五味子素D、五味子甲素、五味子乙素和5-羟甲基糠醛是五味子生品和醋炮制品最具特征的化学标志物。为探索硫磺熏蒸和加热脱硫对党参的非糖类小分子代谢物和糖类物质影响, Xu等[119]采用基于LC-MS技术的代谢组学方法对党参、硫磺熏蒸党参和加热脱硫党参进行研究。结果表明, 硫磺熏蒸显著降低非糖类小分子代谢物含量, 而提高糖类物质含量。加热脱硫党参的二氧化硫和非糖小分子代谢物含量比硫磺熏蒸党参则更低。

中药炮制实质是促使化学成分变化, 但单一或少数标志成分的检测难以反映饮片整体质量变化。植物代谢组学多采用LC-MS技术结合多元统计分析, 搜寻标志化合物, 为中药炮制前后质量差异研究提供物质基础。此外, 植物代谢组学方法不仅有利于阐明炮制工艺安全性和科学性, 结合药理学和毒理学研究还可探索药材质量安全性评价的潜在质量标志物。相关研究实例见表4[117-125]。

7 植物代谢组学方法分析药材商品规格对药材质量影响

中药成分的复杂性决定其化学差异必然存在[13]。中国药典仅进行低限控制, 而优质优价才能促进市场公平和中药产业健康发展。传统意义上商品等级划分常依据外观质量及性状特征, 即辨状论质, 但其科学内涵尚未得到充分阐释[126]。

天竺黄Bambusae Concretio Silicea为禾本科植物青皮竹 *Bambusa textilis* McClure或华思劳竹 *Schizostachyum chinense* Rendle等秆内的分泌液干燥后的块状物, 自然资源短缺, 且化学成分研究滞后。Qin等[127]通过植物代谢组学方法分析天竺黄天然品和合成品间化学成分差异。发现天竺黄天然品和合成品差异明显, 且仅在正品中发现芦丁、苜蓿素和大黄素甲醚, 仅在合成品中发现石竹烯、阿魏酸和二羟基肉桂酸, 甜菜碱在正品和合成品间含量也存在显著差异。Li等[128]采用植物代谢组学方法对款冬花Farfarae Flos紫花和黄花两种规格进行多元统计分析, 发现两者代谢产物存在显著差异, 紫花中3,5-二咖啡酰奎尼酸、芦

Table 4 Application examples of plant metabolomics in analyzing the influence of processing on the quality of traditional Chinese medicine. *Wikstroemia indica* (L.) C. A. Mey. was not included in The Chinese Pharmacopoeia, so the Latin name of the medicinal materials was not listed, and the Latin name of its plant was used instead

Medicinal material	Analytical technique	Key result	Reference
Astragali Radix	LC-MS	Based on the multivariate statistical analysis of metabolites, the raw and processed products of *Astragalus membranaceus* were identified and 15 unique chemical markers were screened.	[117]
Schisandrae Chinensis Fructus	LC-MS	Combined with multivariate statistical analysis, the schisantherin D, schisandrin A and schisandrin B and 5-hydroxymethylfurfural were rapidly determined to be the most characteristic chemical markers of the crude and vinegar processed Schisandrae Chinensis Fructus.	[118]
Codonopsis Radix	LC-MS	The sulfur fumigation decreased 31 compounds and increased 14 compounds, and the heating desulfurization treatment accelerated the sulfur fumigation-caused content variations of some non-saccharide small-molecule metabolites but alleviated those of the free monosaccharides. After the heating desulfurization, the sulfur dioxide content may be reduced, however, the non-saccharide small-molecule metabolome and the glycome could not be recovered to the states before the sulfur fumigation.	[119]
Baizhu Shaoyao San (Atractylodis Macrocephalae Rhizoma, Paeoniae Radix Alba, and Citri Reticulatae Pericarpium)	LC-MS	62 marker compounds with significant differences between crude and processed Baizhu Shaoyao San were found by multivariate statistical analysis. In the processed samples, 23 compounds were significantly decreased and 39 compounds are significantly increased.	[120]
Glycyrrhizae Radix et Rhizoma	LC-MS	The chemical ingredients differed considerably depending on the extent of processing. A total of 57 chemical components were identified in *Glycyrrhiza uralensis*, and glycyrrhizic acid, licoricesaponin G2 and licoricesaponin E2 can be regarded as the chemical markers to differentiate the samples with different degrees of processing.	[121]
Glycyrrhizae Radix et Rhizoma	LC-MS	A total of 10 quality differential markers were searched from raw products, roasted products and honey-roasted products of Glycyrrhizae Radix et Rhizoma. The contents of 6"-*O*-acetylliquiritin apioside, 6"-*O*-acetylliquiritin apioside isomer, 6"-*O*-acetylliquiritin, formononetin and 11-deoxo-18*β*-glycyrrhetic acid were the highest in the raw products, the contents of 6"-*O*-acetylisoliquiritin apioside, 6"-*O*-acetylisoliquiritin, isoliquiritin and glycyrrhetic acid 3-*O*-glucuronide were the highest in the roasted products, the content of liquiritin was the lowest in the honey-roasted products.	[122]
Vaccariae Semen	LC-MS	Combined with multivariate statistical analysis, 46 kinds of primary metabolites were confirmed to have significant changes after processing Vaccariae Semen. Among them, the contents of 16 primary metabolites decreased significantly, and the contents of 30 primary metabolites increased significantly. Phenylalanine metabolic pathway was the most correlated metabolic pathway with different metabolites.	[123]
Strychni Semen	LC-MS	A total of 30 chemical components were identified in crude and fryed Strychni Semen, 12 differential metabolites were screened out by multivariate statistical analysis, strychnine, maltose, dattelic acid and oleic acid were the most significant compounds. After processing, the contents of brucine and strychnine decreased obviously, which met the quality standard of Chinese Pharmacopoeia.	[124]
Wikstroemia indica (L.) C. A. Mey.	LC-MS	The 20 compounds were identified from the raw product and processed product of Radix *Wikstroemia indica*, three diterpenoids (YH-10, YH-12 and YH-15) were proved to possess the high toxicity and decreased by 48%, 44% and 65%, which could be regarded as the potential Q-markers for quality/safety assessment of "sweat soaking method" processed Radix *Wikstroemia indica*.	[125]

丁和苏氨酸等含量明显高于黄花。Tarachiwin等[129]将根据感官评价分为A、B、和C三个等级的东当归进行植物代谢组学分析, PLS-DA结果表明感官质量等级与药理品质呈正相关, 其中感官品质最好的A级东当归中活性成分阿魏酸含量最高。Zhang等[130]采用植物代谢组学方法对不同生长年限的黄芩代谢物进行分析, 结合文献和多元统计分析, 筛选黄芩素、黄芩苷、汉黄芩素和汉黄芩苷作为黄芩药材质量评价指标成分。进而通过含量测定和验证, 推荐黄芩素、黄芩苷、汉黄芩素和汉黄芩苷分别高于0.1%、12.0%、0.03%和2.3%作为黄芩药材优质标准, 以上研究为优质药材标准的界定提供了有益探讨。

植物代谢组学方法通过不同规格或等级药材化学成分种类和含量的差异分析, 有助于构建以质量为核心的药材等级划分模式, 且利于阐明药材“辨状论质”的科学内涵。同时, 结合多元统计分析、含量测定及验

证, 并整合相关研究成果, 可为优质药材建立标准。此外, 化学质量特征结合药效学研究, 可筛选药材临床疗效指标性成分, 为质量标志物提供科学依据。

8 总结与展望

药材质量受多种因素影响, 加强药材品种、产地、入药部位、采收期、炮制加工、商品规格等级和种植生态的监督管理, 对提升中药产品质量, 保障生命健康极为重要。植物代谢组学以药材整体化学成分为切入点, 结合多元统计分析, 通过寻找专属性指标可实现药材产地和品种鉴别, 也可为采收期与入药部位的确定和中药炮制提供科学支撑。结合药理学和毒理学研究, 可探索药材质量安全性评价的潜在质量标志物。

植物代谢组学在药材质量评价上已具有广泛应用并产生积极影响, 但该方法目前仍处于发展阶段, 在技术提升、数据挖掘和药材质量优劣评价等方面存在一些不足, 如: ① 代谢组学方法只能从化学成分种类层面筛选差异代谢物或标志化合物来鉴别药材; ② 充分提取代谢物的条件与时间需进一步探索; ③ 缺乏对应化学标准品对差异代谢物或标志化合物进行定性分析; ④ 代谢物数据库不够完备且尚未实现共享; ⑤ 代谢途径和代谢网络分析较为复杂, 且药用植物代谢途径和代谢网络分析数量不多, 范围不广。

只有掌握代谢物在药材生长、采收和加工过程中的变化规律, 才能有效开展质量控制研究。结合药材质量控制方面的研究进展和研究趋势, 未来研究可从以下3方面进行深入。

8.1 加强对药材质量优劣的快速和全面评价 Liu等[4]提出, 药材质量应以存在于中药材或中药产品中固有或加工制备过程中形成的、与中药功能属性密切相关的化学物质进行控制和评价, 而药材质量的优劣由药效学指标直接反映。因此, 要实现药材质量优劣快速且全面评价, 药效学研究与植物代谢组学方法应齐头并进。在代谢组学和药效学基础上发展起来的代谢指纹图谱结合化学模式识别可寻找潜在质量标志物和生物标志物[125,131]。此外, 将植物代谢组学整合网络药理学进行研究, 也可用于发现中药潜在质量标志物[132]。代谢指纹图谱、植物代谢组和网络药理学整合策略, 可将整体化学成分研究与药效研究相关联, 对质量标志物进行探索。质量标志物结合化学成分量变规律研究, 进而实现对药材质量优劣进行快速和全面评价。

质量标志物由植物标志物衍生而来, 其研究从次生代谢物的化学本质出发[4]。植物代谢组学方法结合化学计量学方法正是从整体层面对不同逆境、品种、产地、入药部位、采收期、炮制加工和商品规格等级药用植物进行分析和鉴别, 然后筛选出对化学成分整体差异贡献最大的成分作为标志化合物, 这将最大限度表征质量标志物特有性的内涵。同时植物代谢组学对整体代谢物的瞬时表征有利于质量标志物建立着眼于全过程物质基础的动态变化的研究方法, 有利于质量标志物建立中药全程质量控制和质量溯源体系。因此, 融入植物代谢组学方法所建立的质量标志物, 会更好地助力药材质量控制和评价体系。

8.2 提升植物代谢组学方法标准化和数据库完备性 植物代谢组学具有整体性、全面性和动态性的显著优势[133], 但作为一门新兴学科, 尚在发展阶段。只能进行相对定量或定向的小范围定量, 且样本制备尚缺乏统一标准的现状使得不同研究团队结果难以重复, 也缺乏可比性和可整合性[134]。突破这一瓶颈, 需解决仪器和技术壁垒, 对样本中整体代谢物进行绝对定量, 然后基于大量数据确定浓度范围, 使代谢组学数据独立于所使用的分析平台和方法。此外, 由于植物代谢物种类繁多, 化合物结构鉴定即代谢物的绝对定性成为植物代谢组学发展的又一技术瓶颈。因此, 构建完备的植物代谢物数据库并进行全球知识共享成为迫切需求。另一方面, 代谢组学的海量数据渴望更先进分析手段以快速准确获取稳定数据。化学计量学将多变量分析方法引入化学研究, 其多元统计分析和人工神经网络算法的不断完善或将推动代谢组学数据分析的发展。

8.3 交叉和整合是未来发展趋势 随着中医药发展, 药材需求不断扩大, 野生资源已无法满足需求[135]。阐明活性成分合成途径, 制定有效成分含量提升策略, 实现药材高质量发展, 育种栽培将成为最重要领域之一[136]。全面阐明植物发育和胁迫响应生物学的生化和遗传机制及活性成分合成途径在很大程度上依赖系统组学方法的全面研究。植物代谢组学整合数量性状位点 (quantitative trait locus, QTL) 定位和全基因组关联研究 (genome wide association study, GWAS), 用于经济作物以提高作物产量和质量及品质改良和驯化已取得较大进展[137,138]。未来应将植物代谢组学与其他组学快速整合, 全面研究药用植物代谢的分子和生化机制和活性成分合成途径, 挖掘功能基因, 扩大对药用植物生长发育和活性成分合成代谢的理解, 促进药用植物良种选育、品质调控、种质改良、生态种植和生物合成等发展, 开辟药用植物高质量高产量和规范化生产新局面, 从源头解决药材质量问题。

随着中医药现代化进程的不断加快, 植物代谢组学方法必将在药材质量评价中发挥越来越重要的作用。

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