

中药治疗癫痫的前沿进展：聚焦神经炎症、胶质细胞重塑与肠脑轴

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摘要

癫痫是全球最常见的慢性神经系统疾病之一, 其核心病理并非单纯的神经元异常放电, 而是由兴奋/抑制失衡、神经炎症、胶质细胞反应、血脑屏障破坏、氧化应激、细胞死亡、肠脑轴紊乱与脑网络重构共同驱动的动态过程。尽管现代抗癫痫发作药物可有效控制部分患者发作, 仍约三分之一患者发展为药物难治性癫痫, 且认知障碍、焦虑抑郁、海马神经元损伤和生活质量下降等共病问题尚缺乏理想干预策略。中药复方、单味药及其活性成分具有多成分、多靶点、多通路协同调节特征, 近年来在癫痫发作控制、抗癫痫发生、海马神经保护、胶质细胞调控和肠脑轴干预等方面显示出新的研究价值。本文以“神经炎症-胶质细胞重塑-肠脑轴”为主线, 系统梳理2022~2025年中药治疗癫痫的前沿进展, 重点总结天麻、钩藤、石菖蒲、黄芩、黄连、丹参、枸杞等相关复方及天麻素、钩藤碱、 α -细辛醚、黄芩苷/黄芩素、小檗碱、槲皮素、等活性成分的药理机制。现有证据提示, 中药干预可能通过恢复GABA/谷氨酸稳态、抑制IL-1 β /HMGB1/TLR4/NF- κ B和NLRP3炎症小体、调控星形胶质细胞A1-like/A2-like功能状态、降低铁死亡和焦亡、改善菌群-脂质代谢轴及保护血脑屏障等途径, 发挥抗癫痫与神经保护效应。然而, 临床证据质量、药材质量控制、复方物质基础、药代动力学、药物相互作用和长期安全性仍是制约转化的关键瓶颈。未来研究应以标准化动物模型、连续脑电监测、多组学整合、单细胞/空间组学、真实世界研究和高质量随机对照试验为核心, 推动中药从经验性辅助治疗走向机制明确、证据充分、可转化的癫痫疾病修饰策略。

关键词

癫痫, 中药, 神经炎症, 星形胶质细胞, 肠脑轴, 天麻素, 小檗碱, 药物难治性癫痫

Frontiers in the Use of Traditional Chinese Medicine for Epilepsy Treatment: Focusing on Neuroinflammation, Glial Cell Remodeling and the Gut-Brain Axis

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Abstract

Epilepsy is one of the most common chronic neurological disorders worldwide. Its core pathophysiology is not merely abnormal neuronal firing, but a dynamic process driven by excitation/inhibition imbalance, neuroinflammation, glial responses, blood-brain barrier disruption, oxidative stress, cell death, gut-brain axis dysregulation, and large-scale brain network reconfiguration. Although current antiseizure medications effectively control seizures in a subset of patients, approximately one-third develop drug-resistant epilepsy. Moreover, comorbidities such as cognitive impairment, anxiety, depression, hippocampal neuronal loss, and diminished quality of life remain inadequately addressed by existing therapeutic strategies. Chinese herbal formulas, single herbs, and their bioactive constituents exhibit synergistic regulation with multi-component, multi-target, and multi-pathway features. In recent years, they have shown renewed research value in seizure control, anti-epileptogenesis, hippocampal neuroprotection, glial modulation, and gut-brain axis intervention. This review focuses on the “neuroinflammation, glial remodeling, gut-brain axis” and systematically examines the frontier advances in traditional Chinese medicine for epilepsy from 2022 to 2025. We highlight the pharmacological mechanisms of representative formulas containing *Gastrodia elata*, *Uncaria rhynchophylla*, *Acorus tatarinowii*, *Scutellaria baicalensis*, *Coptis chinensis*, *Salvia miltiorrhiza*, and *Lycium barbarum*, as well as active ingredients including gastrodin, rhynchophylline, α -asarone, baicalin/baicalin, berberine and quercetin. Available evidence suggests that Chinese herbal interventions may exert antiseizure and neuroprotective effects through restoring GABA/glutamate homeostasis, suppressing IL-1 β /HMGB1/TLR4/NF- κ B and NLRP3 inflammasome pathways, modulating the A1-like/A2-like functional states of astrocytes, reducing ferroptosis and pyroptosis, improving the microbiota-lipid metabolism axis, and preserving blood-brain barrier integrity. However, key translational bottlenecks remain, including the quality of clinical evidence, quality control of medicinal materials, material basis of formulas, pharmacokinetics, drug-drug interactions, and long-term safety. Future research should prioritize standardized animal models, continuous electroencephalographic monitoring, multi-omics integration, single-cell and spatial omics, real-world studies, and high-quality randomized controlled trials, so as to advance traditional Chinese medicine from empirical adjunctive therapy toward mechanistically defined, evidence-based, and translatable disease-modifying strategies for epilepsy.

Keywords

Epilepsy, Traditional Chinese Medicine, Neuroinflammation, Astrocytes, Gut-Brain Axis, Gastrodin, Berberine, Drug-Resistant Epilepsy

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1. 引言

癫痫以反复自发性发作为主要临床表现，但其本质是脑内异常兴奋性网络长期形成、扩散与重塑的

结果。世界卫生组织资料显示,全球约有 5000 万癫痫患者,癫痫仍是最重要的慢性神经系统疾病之一[1];基于全球疾病负担研究的最新分析进一步提示,2021 年全球癫痫患病人数约为 5170 万,且继发性癫痫负担随人口老龄化、脑血管病、创伤和感染等因素而持续增加[2]。现代抗癫痫发作药物(anti-seizure medications, ASMs)可通过调节钠通道、钙通道、GABA 能传递或谷氨酸能兴奋性降低发作风险,但其主要目标仍偏向“抑制发作”,对癫痫发生过程、海马硬化、神经炎症和认知共病的修饰作用有限。与此同时,近年来更新的癫痫分类强调,准确识别癫痫类型、癫痫综合征及潜在病因,对于选择高收益检查、优化治疗方案及判断发作控制与共病预后具有重要意义[3]。Perucca 等[4]、Auvin 等[5]及 Sander 等[6]均指出,药物难治性癫痫不仅是临床治疗失败的结果,更反映了病灶结构、神经网络、炎症微环境、血脑屏障和药物转运系统等多层级异常的共同作用。

过去十年,癫痫机制研究的核心正在从“神经元中心论”转向“神经元-胶质细胞-免疫-代谢网络”整合模型。神经炎症被认为可降低发作阈值、促进异常同步放电并驱动发作后的慢性网络重构[7]-[12]; mTOR、IL-1 β 、HMGB1/TLR4、NF- κ B、NLRP3 炎症小体、补体级联、铁死亡和焦亡等信号通路构成癫痫发生发展的关键分子枢纽[13]-[32]。此外,星形胶质细胞不再被视为被动瘢痕化细胞,而是通过钾离子缓冲、谷氨酸摄取、乳酸代谢、突触可塑性调控、AQP4/Kir4.1 功能、炎症因子释放以及 A1-like/A2-like 功能状态转换参与癫痫网络形成[15]-[21]。肠道菌群及其代谢物也被纳入癫痫病理框架,菌群紊乱可通过短链脂肪酸、色氨酸代谢、胆汁酸、脂质代谢、免疫炎症和血脑屏障影响脑兴奋性[33]-[39]。这些新认识为中药多靶点干预提供了理论基础。

中医药治疗癫痫具有悠久历史,传统认识多从“风、火、痰、瘀、虚”论治,强调平肝息风、化痰开窍、活血通络、清热解毒和扶正安神。近年来,随着网络药理学、多组学、药代动力学和成像技术的发展,中药抗癫痫研究逐渐从经验性疗效观察转向机制验证和靶点发现。2022~2025 年发表的多篇综述和研究显示,天麻钩藤饮、柴胡疏肝散、康痫胶囊、涤痰汤类方、鲜玉胶囊、WQPR 疗法以及天麻素、钩藤碱、 α -细辛醚、黄芩素、小檗碱、丹参酮、芍药苷、和榭皮素等均显示出一定抗癫痫或神经保护潜力[40]-[70]。本文聚焦“中药通过神经炎症-胶质细胞重塑-脑轴治疗癫痫”这一前沿方向,对近年高质量文献进行整合评述,以期后续中药抗癫痫疾病修饰药物研发提供思路。

2. 文献检索策略与纳入范围

本文围绕“traditional Chinese medicine”“herbal medicine”“epilepsy”“seizure”“neuroinflammation”“astrocyte”“microglia”“gut microbiota”“ferroptosis”“pyroptosis”“gastrodin”“rhynchophylline”“baicalein”“berberine”“Acorus”等关键词,优先检索 PubMed、PMC、Web of Science 可检索期刊页面、Nature/Springer、Frontiers、Lancet 系列及相关开放数据库。时间重点限定为 2022 年 1 月至 2025 年 12 月,同时保留少量奠基性经典文献用于概念界定。纳入文献类型包括系统综述、叙述性综述、机制研究、动物实验、多组学研究、网络药理学研究和临床系统评价。由于中药治疗癫痫的高质量随机对照试验仍有限,本文不进行定量 Meta 分析,而采用机制导向的叙述性综述框架,对证据质量、可重复性和转化瓶颈进行综合判断。

3. 中药治疗癫痫的现代病理基础:从单一发作控制到疾病修饰

传统 ASMs 通常围绕“神经元兴奋性”设计,例如增强 GABA 能抑制、抑制电压门控钠通道或钙通道、减少谷氨酸释放等。然而药物难治性癫痫的发生表明,单一通道或单一受体干预难以覆盖慢性癫痫的完整病理网络[4]-[6] [71]。癫痫发生后,反复发作可诱导海马 CA1、CA3 及齿状回神经元损伤,促进苔藓纤维出芽、突触重塑和异常环路形成;同时小胶质细胞、星形胶质细胞、内皮细胞和外周免疫细胞

释放促炎因子,使局部脑组织长期处于低度炎症状态[7]-[12]。这种炎症并非单纯继发结果,而可通过改变谷氨酸转运、GABA 受体功能、NMDA 受体磷酸化、血脑屏障通透性和离子稳态直接参与癫痫发生。

中药在癫痫治疗中的潜在优势并不在于替代所有现代 ASMs,而在于其可能通过“多成分-多靶点-多环节”方式补足现有治疗的不足。复方可同时包含平肝息风药、化痰开窍药、清热解毒药、活血化痰药和补益安神药,其现代药理学效应常对应于离子通道调节、抗炎、抗氧化、抗兴奋毒性、改善线粒体功能和调节肠道菌群等多层级作用[40]-[43]。这一特点与癫痫的网络性病理相契合。尤其在慢性颞叶癫痫和药物难治性癫痫中,神经炎症、胶质细胞活化、海马神经元丢失和认知共病共同构成持续进展链条,中药若能同时降低发作负荷并改善神经微环境,则更接近“疾病修饰”目标。

4. 复方研究进展:从经验方到多组学机制解析

天麻钩藤饮是中医“平肝息风”治法的代表方,常用于肝阳上亢、风动抽搐、头痛眩晕等证候。数据挖掘研究显示,原发性癫痫处方中天麻钩藤饮与二陈汤加减构成常见核心组合,提示“息风化痰”仍是中医治疗癫痫的重要处方逻辑[48]。从现代药理看,天麻、钩藤、黄芩、栀子等药物分别对应 GABA 能调控、谷氨酸受体抑制、抗炎抗氧化和神经保护等作用。Tao 等[42]总结指出,天麻钩藤饮联合 ASMs 在部分临床研究中可降低发作频率、改善症状和生活质量,但其证据主要来自样本量较小、设计质量有限的研究,仍需严格随机、双盲和长期随访验证。

康痫胶囊及相关复方体现了“化痰开窍、息风止痉、活血通络”的复合治法。网络药理学和分子对接研究提示,康痫方可能通过 PI3K-Akt、MAPK、TNF、IL-17、神经递质突触和细胞凋亡等通路干预癫痫病理[49]。与单体成分相比,复方研究的优势在于更接近临床真实用药,但挑战在于物质基础复杂、有效成分暴露水平不清、药物相互作用难以拆分。近年来鲜玉胶囊(Xianyu capsule)研究较具代表性,其 2025 年多组学研究显示,该方可通过调节肠道菌群和血清脂质代谢改善锂-匹罗卡品诱导癫痫相关神经炎症和甘油磷脂代谢异常[50]。这类工作提示,中药复方抗癫痫研究已由“观察发作减少”逐步转向“菌群-代谢-炎症-脑网络”整合机制。

临床证据方面,Zhao 等[44]对 20 项随机对照试验、1830 例难治性癫痫患者进行系统评价,发现中药联合 AEDs 较 AEDs 单用可降低月发作频率和脑电异常率,并改善生活质量,同时不良事件发生率较低;但纳入研究普遍存在随机化、盲法、分配隐藏和发表偏倚等问题。Cai 等[45]对 WQPR 治疗癫痫的系统评价也提示其可能提高总有效率、减少发作频率和持续时间,但同样强调证据质量不足。针药联合也被纳入近年临床研究框架,Xue 等[46]和 Su 等[47]关注针刺联合中药治疗原发性癫痫认知障碍和儿童癫痫的有效性与安全性。这些研究共同说明,中医药在临床辅助治疗中具有潜力,但距国际高质量证据标准仍有明显差距。

5. 单味药与活性成分:多靶点抗癫痫药物发现的重要资源

天麻及其主要成分天麻素是中药抗癫痫研究中证据较为集中的对象。Dai 等[51]报道天麻素可减轻锂-匹罗卡品诱导幼年大鼠 SE 后的神经炎症和损伤;Zhou 等[52]进一步提示天麻素可改善实验性癫痫动物学习记忆并降低海马神经元凋亡、氧化应激和炎症水平。早期 Yang 等[53]在锂-匹罗卡品颞叶癫痫模型中发现天麻素可增强 GABA 能传递并减轻兴奋毒性。2025 年关于天麻神经药理作用的综述亦强调,天麻及天麻素具有调节 GABA/谷氨酸平衡、抗氧化、抗炎、抗凋亡和改善神经可塑性的潜在价值[54]。因此,天麻素可被视为“神经递质稳态+炎症调控+认知保护”三重作用的代表性中药单体。然而,从药物开发角度评价天麻素,不能仅依据动物模型中的药效结果,还应考虑其体内暴露、脑组织分布和代谢特征。现有药代动力学研究显示,天麻素可被快速吸收并广泛分布,在给药后较短时间内即可在脑组

织中检测到，但其脑/血分布比例相对有限，提示原型药物的血脑屏障通透性并不十分理想，其脑内作用可能同时受到快速代谢及代谢产物羟基苯甲醇(HBA)暴露的影响[55]。因此，“天麻素能够进入脑组织”属于动物药代动力学实验证实，而“其主要通过直接作用于某一脑内靶点发挥抗癫痫作用”则仍需结合靶点占有、脑内暴露－效应关系等进一步验证。

Table 1. Comparison of pharmacological actions among TCM ingredients
表 1. 不同中药成分的药理作用比较

药物/成分	主要作用靶点或通路	证据模型	研究价值	文献
天麻/天麻素	GABA 能增强、抗炎、抗氧化、抗凋亡	Li-Pilo、PTZ、SE 模型	减轻发作和海马损伤，改善认知	[51]-[55]
钩藤/钩藤碱	NMDA 受体、Nav1.6、IL-1 β /BDNF/TLR	KA、pilocarpine 模型	降低兴奋性与炎症，具有息风止痉潜力	[40] [58]
石菖蒲/ α -细辛醚	GABA 转氨酶、GABA _A 、NMDA、代谢调节	PTZ、KA、慢性模型	延长潜伏期、降低发作严重程度，但需关注安全窗	[56] [57]
黄芩/黄芩素	NLRP3/GSDMD、NF- κ B、抗焦亡	Li-Pilo SE 模型	抗 SE、减轻神经元损伤	[59] [60]
黄连/小檗碱	肠道菌群、脂质代谢、抗炎抗氧化	KA 急性癫痫、TLE 理论研究	连接肠脑轴与抗癫痫的新兴候选物	[61]-[63]
鲜玉胶囊	菌群－血清脂质－神经炎症	Li-Pilo 急性癫痫多组学	复方多组学验证的代表性研究	[50]
槲皮素/黄酮类	NLRP3/NF- κ B、抗氧化、抗神经元死亡	KA、缺氧相关发作	抗炎、抗氧化、改善认知共病	[64]-[69]

注：表中“研究价值”强调机制线索与转化潜力，不等同于已获临床充分证实。

钩藤和钩藤碱主要与 NMDA 受体、钠通道和神经炎症相关。既往研究显示，钩藤提取物及钩藤碱可减轻 KA 或匹罗卡品诱导的癫痫行为，并下调 IL-1 β 、BDNF、TLR 相关炎症和兴奋性信号[40] [58]。Sun 等[40]综述指出，钩藤碱可能抑制 Nav1.6 依赖的持续钠电流和 NMDA 受体电流，这与癫痫神经元异常兴奋性密切相关。石菖蒲及其 α -细辛醚/ α -asaronol 也具有较强的抗癫痫研究基础。Zhao 等[56]显示 α -asaronol 可延长 PTZ 诱导发作潜伏期并降低发作严重程度；Chen 等[57]在 2025 年报道石菖蒲可改善 PTZ 癫痫大鼠发作潜伏期和病理改变，且与 GABA 转氨酶抑制及代谢调节相关。这些结果提示，芳香开窍类药物可能通过神经递质代谢、血脑屏障穿透和神经网络抑制发挥作用，但 α/β -细辛醚的潜在毒性和安全窗仍需严格评价。

黄芩相关黄酮类成分是连接抗炎、抗焦亡和抗癫痫的关键药物来源。Wu 等[59]在 2025 年报道黄芩素可延长锂－匹罗卡品诱导 SE 及发作潜伏期，改善癫痫发展；Kang 等[60]进一步显示，黄芩素可通过抑制 NLRP3/GSDMD 焦亡通路减轻 SE 小鼠神经元损伤。黄连和小檗碱则体现了“肠脑轴－脂质代谢－神经炎症”方向的突破。Dai 等[61]发现，小檗碱可通过重塑肠道菌群相关脂质代谢减轻 KA 诱导急性癫痫发作；Jivad 等[62]和 Als fouk 等[63]也从抗氧化、抗炎、抗凋亡和神经保护角度总结了小檗碱作为难治性癫痫和颞叶癫痫候选干预物的合理性。由于小檗碱本身具有较强肠道菌群调节能力，其在癫痫中的价值可能并不局限于中枢直接作用，而在于外周代谢－免疫信号对脑兴奋性的间接调控(见表 1)。

其他中药活性成分也显示出值得关注的抗癫痫潜力。槲皮素在 KA、缺氧诱导和炎症相关发作模型中可降低神经元死亡、氧化应激和炎症反应[64] [65]；网络药理学研究提示黄连中槲皮素、加拿达定等成分可能通过多靶点调控癫痫相关通路[66]。雷公藤内酯醇虽具有较强抗炎活性，Lu 等[67]提示低剂量可能通过改善海马 GABA 能环路抑制癫痫发作，但其毒性较大，临床转化应格外谨慎。大黄素可通过调节

NRP2/NF- κ B 轴降低氧化应激和神经炎症[68]。近年黄酮类和天然生物碱综述进一步强调,植物来源化合物可通过 GABA 受体、NMDA 受体、钠通道、炎症因子、氧化应激和线粒体功能多环节参与抗癫痫过程[69][70](见表 1)。

6. 神经炎症与胶质细胞重塑：中药抗癫痫的核心前沿靶点

神经炎症是近年来癫痫研究中最活跃的方向之一。Dingledine 等[7]指出,癫痫相关神经炎症涉及小胶质细胞、星形胶质细胞、内皮细胞、周细胞和外周免疫细胞等多种细胞群,它们释放 IL-1 β 、TNF- α 、IL-6、HMGB1、趋化因子和补体分子,改变突触传递和血脑屏障功能。Sanz 等[8]和 Li 等[9]进一步强调,炎症既可由发作诱导,也可反过来降低发作阈值、促进癫痫发生。需要指出的是,炎症相关机制的证据强度在不同研究中存在明显差异。例如,IL-1 β /TLR4/NF- κ B、NLRP3/GSDMD 等通路在动物 SE 模型中具有较多组织学、蛋白表达及药理学干预证据,但这并不意味着所有上游或下游分子均已被证明是中药直接结合的靶点。对于网络药理学研究所预测的炎症靶点,应与动物实验中的通路变化、特异性抑制剂或基因操作结果区分开来。只有当“候选成分暴露-靶点结合-通路变化-细胞表型-发发表型”形成完整因果链时,才能将其称为较高可信度的机制。

星形胶质细胞是连接中药抗炎作用与脑网络稳定性的关键细胞。Vezzani 等[15]、Hayatdavoudi 等[16]和 Çarçak 等[17]均强调,星形胶质细胞可通过谷氨酸摄取、钾离子缓冲、代谢供能和炎症信号调控直接影响癫痫网络。2025 年相关研究进一步把星形胶质细胞代谢和神经炎症联系到药物难治性癫痫[20]。然而,目前大量中药研究仍主要通过 GFAP、Iba1 等单个标志物判断胶质细胞活化,这只能说明细胞状态发生改变,而不能证明其功能已经恢复。对于星形胶质细胞,未来应进一步检测 EAAT2、Kir4.1、AQP4 极性及谷氨酸/钾离子稳态;对于小胶质细胞,则应结合炎症因子、吞噬功能和单细胞转录特征进行综合评价。只有从“表达变化”推进到“细胞功能恢复”,才能真正证明中药对胶质细胞重塑具有疾病修饰意义。

7. 肠脑轴、代谢重编程与中药复方的系统调控

肠脑轴已成为癫痫治疗的新兴方向。Zhu 等[33]和 Li 等[34]总结了肠道菌群通过免疫、代谢、神经内分泌和迷走神经通路影响癫痫的证据;Yang 等[35]的 Meta 分析提示难治性癫痫患者菌群结构相较健康人存在显著差异;Mousavi 等[36]进一步指出,癫痫患者中促炎相关菌属可能升高。中药复方通常含有多糖、黄酮、生物碱、皂苷和有机酸等成分,其吸收、代谢和药效均与肠道菌群密切相关,因此肠脑轴可能是中药治疗癫痫不可忽略的关键通路。

鲜玉胶囊和小檗碱研究为这一方向提供了直接证据。Yu 等[50]通过多组学显示鲜玉胶囊可调节肠道菌群和血清脂质代谢,从而改善锂-匹罗卡品癫痫模型中的神经炎症和甘油磷脂代谢异常;Dai 等[61]证明小檗碱通过肠道菌群相关脂质代谢重塑减轻 KA 急性癫痫发作。与之相呼应,ketogenic diet 研究也显示,肠道菌群对抗发作效应具有重要调节作用,Özcan 等[39]在 Nature Communications 报道不同临床生酮饮食配方可通过纤维含量和菌群变化影响抗发作效果。由此推测,中药复方未来可与饮食干预、益生元或代谢物补充形成组合策略,围绕菌群-脂质-炎症-脑兴奋性轴进行精准调控。

8. 临床前癫痫模型与人类疾病的转化挑战

不同癫痫动物模型模拟的是疾病过程中的不同环节,而不是完整复制人类癫痫。因此,中药抗癫痫研究不能将任何单一动物模型中的阳性结果直接等同于临床疗效。当前常用模型包括 PTZ 化学惊厥模型、最大电休克模型、KA 模型、锂-匹罗卡品模型、化学点燃模型以及遗传性癫痫模型,其诱导机制、病理

特征、慢性化程度和对 ASMs 的反应均存在明显差异。其中, PTZ 模型尤其适合早期药效筛选, 但其主要反映急性惊厥易感性, 因此如果某一中药仅在 PTZ 模型中延长发作潜伏期或降低评分, 应将证据等级定义为“抗惊厥初步证据”, 而不能直接称为“抗癫痫”或“疾病修饰”。相反, KA 和 Li-Pilo 模型能够形成 SE 后慢性自发性发作、海马神经元丢失和神经炎症, 因此更适合验证中药是否影响癫痫发生过程, 但其模型本身也具有明显的严重急性损伤特征。

因此, 未来研究应建立由“急性筛选-慢性模型-机制验证-药代动力学-安全性-临床验证”组成的分层转化路径。首先利用 PTZ 或 MES 进行候选成分初筛; 随后在 KA 或 Li-Pilo 慢性模型中评价自发性发作、海马病理和神经炎症; 进一步结合脑组织药物浓度和 PK/PD 分析确定有效暴露范围; 最后通过长期毒理学及与常用 ASMs 联合用药研究评价临床可行性。只有在多个独立模型中得到一致结果, 且药物暴露与药效之间具有明确关系时, 才能提高动物结果向人类癫痫转化的可信度。

9. 证据短板与转化瓶颈

尽管近年来中药治疗癫痫研究增长迅速, 但要达到 SCI 高水平综述所要求的证据强度, 仍需正视几个关键问题。第一, 临床研究质量不足。现有系统评价提示中药联合 ASMs 可能降低发作频率并减少不良反应, 但许多试验缺乏严格随机、双盲、分配隐藏、样本量估算和长期随访, GRADE 证据质量偏低[44]-[47]。第二, 复方物质基础不清。中药复方成分复杂, 批次差异、炮制方法、提取工艺、药材产地和质量控制均可能影响疗效。第三, 药代动力学和脑暴露证据不足。许多活性成分在体外或动物模型中有效, 但其能否达到癫痫病灶区有效浓度尚未充分阐明。第四, 中药-ASMs 相互作用风险需要系统评估, 尤其是对 CYP450、P-gp、UGT 和血浆蛋白结合的影响。

在此基础上, 还应增加第五个关键问题, 即“机制证据等级不一致”。目前部分研究将网络药理学、分子对接预测与动物实验中的蛋白表达变化放在同一证据层级讨论, 容易造成机制过度解释。未来综述和实验研究应明确区分: 1) 计算预测; 2) 体外细胞实验; 3) 急性动物模型; 4) 慢性动物模型; 5) 靶点干预/基因操作验证; 6) 人体 PK 和临床试验。只有经过靶点干预、逆转实验和跨模型重复验证的机制, 才具有较高的因果证据强度。

10. 未来方向: 从经验方到机制明确的疾病修饰策略

中药抗癫痫研究的突破点不应停留在“是否减少发作”这一单一问题, 而应回答其能否阻断癫痫发生、减轻海马硬化、改善认知共病、降低药物难治性风险并提高长期生活质量。未来可从四个方向推进: 其一, 建立“候选成分-靶点-细胞类型-脑区-发作表型”的机制链条, 重点关注星形胶质细胞、微胶质细胞、内皮细胞和神经元之间的跨细胞互作; 其二, 以多组学技术解析复方物质基础和体内暴露成分, 结合网络药理学、分子对接和 DARTS/CETSA 等靶点验证技术识别真实作用靶点; 其三, 利用单细胞转录组和空间组学揭示中药对癫痫病灶微环境的时空调控; 其四, 开展符合 CONSORT 标准的多中心随机对照试验和真实世界研究, 明确不同癫痫类型、不同证候和不同合并用药状态下的获益人群。特别需要强调的是, 多组学和网络药理学不应成为机制研究的终点, 而应作为靶点发现工具。未来应采用“预测-实验验证-因果干预-体内重复”的路径: 首先通过网络药理学和转录组发现候选通路, 再通过细胞或动物实验验证通路变化, 随后利用特异性抑制剂、激动剂、基因敲除或过表达进行因果验证, 最后在不同癫痫模型中重复关键结果。这样的证据链比单纯增加网络药理学靶点数量更具有说服力。

在具体机制上, “神经炎症-胶质细胞重塑-肠脑轴”可作为未来中药治疗癫痫的优先研究主线。中药复方和活性成分可通过抑制 IL-1 β /HMGB1/TLR4/NF- κ B、NLRP3/GSDMD、mTOR 炎症耦联、铁死

亡和脂质过氧化,降低发作后神经元损伤;通过恢复 EAAT2、AQP4 和 Kir4.1 功能,改善星形胶质细胞对谷氨酸、钾离子和能量代谢的调控;通过重塑肠道菌群和脂质代谢,减少外周炎症对脑兴奋性的驱动。若这些环节能够被严格实验证实,中药将有望从辅助控制发作的经验疗法,转向具有疾病修饰潜力的综合干预策略。

11. 结论

2022~2025 年的研究表明,中药治疗癫痫正在经历从传统经验用药向现代神经药理和系统生物学转型的关键阶段。复方研究提示中药联合 ASMs 可能改善发作频率、脑电异常和生活质量;单体研究则揭示天麻素、钩藤碱、黄芩素、小檗碱、 α -细辛醚、槲皮素、和大黄素等可通过神经递质调节、抗炎、抗氧化、抗铁死亡、抗焦亡、胶质细胞重塑和肠脑轴调控发挥抗癫痫作用。总体来看,中药的最大价值不在于简单替代现代药物,而在于围绕慢性癫痫的多层级病理网络提供协同、温和、可长期干预的疾病修饰思路。未来只有在高质量临床证据、清晰物质基础、严格质量控制和机制闭环验证的共同支撑下,中药治疗癫痫才能真正进入国际高水平循证医学和转化神经科学体系。

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