

人参及人参皂苷在自身免疫性疾病中作用的研究进展

梁丹丹¹, 杨少雷¹, 景德怀², 周广玺², 朱凤琴²

¹济宁医学院临床医学院, 山东 济宁

²济宁医学院附属医院消化内科, 山东 济宁

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摘要

人参中所含的人参皂苷, 是主要的活性组分, 具有较高的药用价值, 尤其是在是由自身免疫紊乱引发的疾病中, 如桥本氏甲状腺炎、溃疡性结肠炎、类风湿性关节炎及系统性红斑狼疮等多方面多系统疾病。与传统免疫抑制剂和激素疗法相较, 人参皂苷具有化学构成多样、结构复杂、低毒性和轻微副作用的特点。其发挥作用的机理复杂多样, 能够多方面地调控免疫细胞活性、细胞因子平衡及信号传导通路, 维持免疫系统的微环境稳态, 为深入研究和临床应用奠定了有力的理论基础, 提供了新方法新思路。

关键词

人参皂苷, 自身免疫性疾病, 作用机制

Research Progress on the Role of Ginseng and Ginsenosides in Autoimmune Diseases

Dandan Liang¹, Shaolei Yang¹, Dehuai Jing², Guangxi Zhou², Fengqin Zhu²

¹Clinical Medical College of Jining Medical University, Jining Shandong

²Department of Gastroenterology, The Affiliated Hospital of Jining Medical University, Jining Shandong

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Abstract

Ginsenosides, the core active components found in ginseng, have demonstrated remarkable medicinal potential, particularly in treating autoimmune disorders such as Hashimoto's thyroiditis, ulcerative colitis, rheumatoid arthritis, and systemic lupus erythematosus. Compared to traditional

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immunosuppressants and hormone therapies, ginsenosides stand out due to their diverse chemical composition, complex structures, low toxicity, and minimal side effects. Their mechanisms of action are intricate, enabling multi-dimensional regulation of immune cell activity, cytokine balance, and signaling pathways, thereby maintaining the microenvironmental stability of the immune system. This provides a solid theoretical foundation and new approaches for further research and clinical applications.

Keywords

Ginsenosides, Autoimmune Diseases, Mechanism of Action

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1. 引言

自身免疫性疾病[1] [2] (Autoimmune disease, AID), 由遗传背景、环境因素、免疫调节失衡、自身抗原及交叉反应性抗原等多重诱因所触发的体内异常自身免疫活动, 表现为人体免疫系统在某些特定情境下, 无法清晰辨识外来异物与自体细胞之间的界限, 错误地将自体细胞当作攻击目标, 产生针对性的自身抗体, 进而引发异常的免疫应答。这一连串的免疫反应会导致机体细胞受损, 自身组织和细胞成分遭受破坏, 最终引发组织损伤及器官功能异常。AID 可被分为器官特异性型与系统性型两大类。这类疾病治疗困难, 费用昂贵, 目前临床上常用免疫抑制剂、激素等来缓解症状及控制病情进展且副作用大, 在临床上治疗具有局限性。人参皂苷, 作为传统中药人参的关键活性成分之一, 据多项研究显示, 它具备抗炎、抵抗氧化应激、调节免疫系统、激活糖皮质激素受体或展现类似糖皮质激素的活性等多重效能, 目前, 在糖尿病、心脑血管疾病、肥胖症等多种疾病的临床前模型中得到了应用。本文旨在深入解析了人参皂苷在治疗 AID 中的作用机理及其潜在的应用价值, 旨在为 AID 的临床药物治疗提供理论依据。

2. 人参与人参皂苷的结构及特点

人参乃众中草药中颇为常见的一种, 隶属于五加科之下的人参属, 自古以来便是我国备受尊崇的珍稀药材, 其功效卓越, 能补益人体元气、促进津液生成、稳固虚脱之症、增强智慧。在临床上, 人参被广泛应用于治疗诸如骨质疏松、糖尿病、肿瘤以及肝纤维化等多种疾病。而人参中尤为关键的活性成分——人参皂苷, 拥有相似的基础构造, 其核心为由三十个碳原子巧妙排列成四个环状结构的甾烷类固醇核。人参皂苷在强化机体免疫防线、遏制癌细胞增殖势头、阻断癌细胞转移路径、诱导癌细胞走向凋亡与分化, 以及展现出出色的抗炎、抗氧化效能等方面, 均展现出了非凡的潜力。虽然人参皂苷具有多种益处, 但也存在一定的副作用, 如 1) 血压升高: 人参皂苷能够刺激交感神经兴奋性增加, 导致肾素 - 血管紧张素 - 醛固酮系统激活, 进而引起血压上升; 2) 心律失常: 人参皂苷具有促进心肌细胞代谢的作用, 但同时也可能影响心脏传导系统功能, 从而引发心律失常。可能出现窦性心动过速、房颤等心律失常症状。3) 皮疹: 人参皂苷可以增强机体免疫应答, 若个体对其中某些成分产生过敏反应, 则会引起皮肤炎症和红斑丘疹。4) 消化道不适: 由于药物作用于胃肠道黏膜, 使胃肠蠕动减慢, 进而导致恶心呕吐、腹胀腹泻等不适症状发生。中枢神经系统紊乱: 人参皂苷通过激动中枢神经系统中的 5-HT 受体, 提高 5-羟色胺水平, 导致情绪高涨、失眠多梦等现象等副作用。然而, 关于人参皂苷在免疫疾病治疗领域的具体药理机

制,目前学界尚未形成一致见解,至于人参皂苷能否安全有效地应用于临床实践,仍有待科研人员开展更为深入的探索与研究[3]-[7]。

3. 人参与人参皂苷在自身免疫性疾病的作用机理

3.1. 器官特异性自身免疫性疾病

器官特异性免疫疾病是指,特定组织或器官遭受的病理伤害与功能异常,仅限于抗体或致敏淋巴细胞所攻击的某一特定部位[8][9]。主要包括主要有桥本甲状腺炎、1型糖尿病、重症肌无力、溃疡性结肠炎、IgA肾病、自身免疫性肝炎、自免性脑髓炎等。目前研究表明人参与人参皂苷在上述多种疾病中发挥作用,包括桥本甲状腺炎、溃疡性结肠炎、自身免疫性肝炎、自免性脑髓炎等。

3.1.1. 桥本甲状腺炎

桥本氏甲状腺炎(Hashimoto's thyroiditis, HT),其特征主要体现为体内特异性甲状腺自体抗体的产生,伴随甲状腺组织淋巴细胞的浸润现象,这一过程最终导致甲状腺结构受损及功能减退。当前医疗手段尚未能提供较好的治疗方案,多数情况下,患者只能接受定期监测,直至出现甲状腺功能状况受损或甲状腺肿大程度达到需干预的标准时,才采取相应治疗措施[10][11]。有研究表明,人参皂苷对HT具有一定作用潜能。冯晓红等人的研究表明,人参皂苷能有效削减甲状腺自体抗体的水平,它通过遏制Th1细胞功能的过度活跃,经由免疫调节机制为甲状腺组织提供保护屏障[12]。马成军等人的研究显示,人参皂苷Rg3对HT小鼠的甲状腺功能具有显著提升效果,能够通过调节CD3⁺CD8⁺IL-4⁺及CD3⁺CD8⁺IFN- γ ⁺辅助T淋巴细胞,来减少IL-4与IFN- γ 的分泌量,进而减轻自身免疫性小鼠的免疫反应[13]。另一方面,黄琦等人的研究则揭示,人参皂苷有助于降低HT大鼠血清中的TGAbs和TPOAbs水平,同时能下调IL-2并上调IL-4,证明了人参皂苷在治疗HT方面的有效性,其作用机理可能是通过免疫调节,抑制Th1细胞功能的过度活跃,并促进Th1向Th2方向的转化[14]。Jie等人揭示,人参皂苷能有效调控T-bet与GATA结合蛋白3表达失衡的状态起到明显作用,其机制:通过抑制T-bet的表达,人参皂苷能够减少Th1型细胞因子IFN- γ 的分泌;与此同时,通过提升GATA-3的表达水平,它又促进了Th2型细胞因子IL-4的分泌[15],这一系列作用有助于缓解HT症状。

3.1.2. 溃疡性结肠炎

溃疡性结肠炎(Ulcerative colitis, UC)是一种慢性且易复发的非特异性炎症性病症,主要在直肠与乙状结肠区域,形成浅表性溃疡。该病反复发作,导致肠壁结缔组织异常增生。尽管医学界持续探索,但其确切的病因与发病机制至今尚未完全揭晓。普遍认为,溃疡性结肠炎的发作与遗传背景、环境因素、肠道上皮屏障功能受损、微生物群落失衡及免疫应答异常等多重因素紧密相连。当前,临床上常用的治疗手段包括皮质类固醇、氨基水杨酸类药物及免疫抑制剂等,但这些药物在疗效上存在局限性,且伴随较大的副作用。因此,研发一种既安全经济又高效的治疗溃疡性结肠炎的新药显得尤为迫切[16]。Bo等人发现人参皂苷Rd单体通过减少体内和体外M1巨噬细胞的促炎细胞因子产生来实现的,包括TNF- α 、IFN- γ 、IL-6等促炎因子及通过NF-KB和P38MAPK途径抑制小鼠促炎细胞因子的产生,促进结肠炎的恢复[17]。Xuan等人研究阐明了人参皂苷Rh2单体治疗UC与其降低STAT3/miR-214信号通路中促炎细胞因子及相关蛋白水平的能力密切相关[18]。Zhong等人发现人参皂苷Rg1单体可通过调节肠道微生物-脂质代谢-Th1/Th2/Th17细胞轴减轻UC[19],人参皂苷Rg1单体还可以通过调节肠道菌群丰富度、恢复肠道屏障及调节免疫等多种途径[20]-[28]。除此之外,人参皂苷20(S)-原人参二醇皂苷[29]、Rg3[30]、Rk3[31]、Rk2[32]等多种单体可通过各种途径缓解与治疗UC。

3.1.3. 自身免疫性肝炎

自身免疫性肝炎(Autoimmune hepatitis, AIH)乃一种由慢性免疫机制驱动的炎症性肝病,患者间的临床表现多样性,轻者可能毫无症状或仅有轻中度反应,重者则可能突发急性肝衰竭。当前,针对此类肝炎的治疗策略主要在于激素与免疫抑制剂的联合应用,然而,这一方案伴随有不少副作用,在临床实践中受到了不小的限制。而人参皂苷在治疗 AIH 有相关报道, Kehui 等人研究发现人参皂苷通过 Hippo-YAP/TAZ 信号通路调控先天性免疫,激活先天免疫,从而促进 MDSCs 的增殖,促进其向 M-MDSCs 分化,进而促进 Arg-1、iNOS 和 NO 的分泌,激活适应性 T 细胞免疫,使 Treg 浓度升高, Th17 浓度降低,抑制促炎细胞因子的产生从而影响 AIH 免疫微环境[33]。Xiang 等人通过实验证明人参皂苷 Rg3 通过抑制活化 HSC 和释放促纤维化因子 TGF- β 1,减轻脂质过氧化和炎症浸润以及胶原纤维沉积,促使肝纤维化的消退[34]。Zhou 等发现 20(R)-G-Rg3 通过激活 PI3K/AKT 信号通路抑制肝细胞坏死和凋亡,对肝损伤起到保护作用[35]。也有研究表明,人参皂苷 Rg1 通过降低 Keap1 表达,增加 p-Nrf2 水平,抑制 NLRP3、NLRP1 和 AIM2 炎性小体,通过促进 Nrf2 与 Keap1 的解离,进而激活 Nrf2 通路,进一步抑制肝细胞炎症小体来减轻脂多糖诱导的慢性肝损伤[36]。

3.1.4. 自免性脑髓炎

自身免疫性脑脊髓炎(Autoimmune myelitis, AE)是指一组由自身免疫反应触发的脑炎病症。此类疾病在临床上的特征性表现为精神行为失常、癫痫发作以及近期记忆受损等,这些症状可能呈现为多灶性或弥漫性的脑功能损害。在治疗手段上,尽管临床主要依赖免疫治疗策略,但其疗效达不到预期效果。Bo 及其团队的研究揭示人参皂苷 Rd 对于体内及体外环境下的 AE 均展现出较好的治疗潜力,其可通过下调促炎性细胞因子 IL-6 与 IL-17 的水平,同时上调抑制性细胞因子 TGF- β 与 IL-10,有效调节了 Treg 与 Th17 细胞之间的失衡状态。人参皂苷 Rd 能够针对性地通过调节炎症反应及自身免疫机制,发挥对 AE 的治疗作用[37]。人参皂甙 Rd 具备降低血脑屏障通透性的能力,并能调节 IFN- γ 与 IL-4 以及 BDNF 与 NGF 的产生及表达水平,从而对 AE 小鼠的临床症状产生显著的改善效果[38]。人参皂苷 Rb1/Rg1 通过抑制 Th1、Th17 细胞和上调调节性 T 细胞缓解 AE [39]。Jin 等研究发现可以通过下调 TLR4 及其子信号 MyD88 和 NF-KB 信号通路,减轻 EAE 小鼠的主要症状运动障碍,从而减轻脊髓脱髓鞘的炎症细胞浸润和血脑屏障破坏[40]。Min 等研究证明人参皂苷 Rg3 可能通过调节 NOX2/4 的表达,通过改善血脑屏障通透性,从而发挥其抗炎和抗氧化作用,达到治疗慢性 AE 的作用[41]。

3.2. 系统性自身免疫性疾病

系统性自身免疫性疾病,是抗原-抗体复合物在血管壁等部位的广泛沉积,从而引发全身多个器官受损的状况,也常常被称为胶原病或结缔组织病。此病症的原因在于免疫系统的异常攻击,导致血管壁及其间质发生纤维素样坏死性炎症,并随后触发多器官内的胶原纤维异常增生[42]。

3.2.1. 系统性红斑狼疮

系统性红斑狼疮该病(Systemic lupus erythematosus, SLE),是一种慢性自身免疫性疾病,免疫系统攻击身体几乎任何部位的健康自身组织,表现为多器官系统受累,可累及泌尿、血液、消化、心血管及神经系统等[43]。Zhen 等人研究发现原嘌呤二醇主要在胃肠道拟杆菌和真杆菌的作用下,由二醇型人参皂苷代谢产生,可以通过调节 PTX3/MAPK/ERK1/2 通路缓解狼疮性肾炎[44]。凌长泉等人以及赵伟刚的临床研究均表明,人参皂苷与糖皮质激素联合治疗 SLE 可以更好地调节患者的免疫功能,有助于强的松的顺利戒断反应[45] [46]。杨帆与其研究团队发现人参皂苷 Rb1 可以缓解 SLE,其作用机理:抑制 SLE 患者外周血 T 淋巴细胞增殖活性,同时增加 CD4⁺CD25⁺T 细胞比例,维持 Th1/Th2 免疫平衡达到缓解 SLE

的作用[47]。

3.2.2. 类风湿关节炎

类风湿关节炎(Rheumatoid arthritis, RA)是一种常见的慢性炎症性疾病和全身性自身免疫性疾病,主要累及滑膜关节,其特点是关节滑膜免疫调节被破坏,出现全身炎症和自身抗体的存在[48]。有许多研究表明[43] [49]-[57],人参皂苷代谢产物 K 作用于 RA,主要通过以下三种机制发挥作用:1) 可通过干扰 TNF- α 和 2 型肿瘤坏死因子受体介导的滑膜细胞功能发挥关节保护作用;2) 可以抑制 T 细胞和 B 细胞的活化、增殖、分化,减少 T 细胞和 B 细胞的相互作用,恢复 T 细胞和 B 细胞亚群的稳态,禁止自身抗体的产生,调节 M1、M2 和 M1/M2 相关炎症因子的比例,发挥免疫调节作用;3) 可抑制 MMPs 的产生,调节 OPG 和 RANKL 的分泌,减少 TRAP 阳性破骨细胞样细胞的形成,发挥骨保护作用。当然,除了人参皂苷代谢产物 K 以外,Tong 等人研究表明人参皂苷 Rg1 可能通过抑制 iNOS 的产生,以及降低 IL-6、TNF- α 的表达,促进淋巴引流,改善 RA [58]。Yan 等人也发现人参皂苷 Rg3 通过调节 CD4⁺CD25⁺Foxp3⁺ Treg 细胞减轻 RA [59]。

3.3. 其他免疫性疾病

除了以上免疫性疾病以外,人参皂苷 Rb1 还可以通过降低单核细胞(MNCs)中 Th17 细胞的百分比,增加 MNCs 中 Treg 和 Th2 细胞的数量,对重症肌无力带来显著效果[60]。而人参皂苷 Rg1 通过调节 NLRP3 和 Keap1/Nrf2/HO-1 通路,抑制 NO 和 ROS 的生成,抑制 p53 和 p21 的表达,抑制 caspase-9、-3、-7 和 PARP 的裂解激活,从而阻止细胞因子诱导的胰腺细胞凋亡,达到改善胰腺和脾脏的炎症和自噬,有效阻止了细胞因子触发的胰腺细胞凋亡,进而改善了胰腺与脾脏的炎症状态及自噬活动,为小鼠抵御链脲佐菌素诱导的 1 型糖尿病筑起了一道坚实的防线[61]-[63]。人参皂苷 Rd 在自身免疫性神经损伤过程中,展现出其主要保护作用,它能减少外周血液及受损组织中经典型单核细胞与粒细胞的数目,同时提升非经典型单核细胞的比例,并促进溶解阶段的巨噬细胞向病灶区域浸润[64]。

4. 总结与展望

综上所述,人参是一种著名的传统草药,人参皂苷是人参主要提取物之一,现代药理研究表明,人参皂苷对不同免疫细胞亚群具有不同影响:人参皂苷能够激活巨噬细胞,增强其吞噬和杀伤病原体的能力并通过激活 NF- κ B 信号通路,增强巨噬细胞的吞噬功能和产生炎性因子的能力;人参皂苷可以激活树突状细胞,促进其成熟分化,并增强其抗原呈递能力,还能促进树突状细胞与 T 细胞的相互作用,增强 T 细胞的免疫应答;人参皂苷能够激活自然杀伤细胞(NK),增强其细胞毒性和对肿瘤细胞及受感染细胞的杀伤能力,促进其分泌细胞因子。人参皂苷可以刺激 CD4⁺ T 细胞的表达,增加其活性,促进分泌抗肿瘤细胞因子(如 IFN- γ 、IL-2 等),并上调 CD4⁺/CD8⁺ T 细胞比例,通过“双通路调控”,既直接抑制肿瘤信号转导,又间接激活抗肿瘤免疫,使 CD8⁺ T 细胞中 IFN- γ + Granzyme B⁺亚群扩增,细胞毒性提升;人参皂苷直接刺激 B 细胞产生 IgA、IgG 和 IgM,抑制 B 细胞增殖和分泌,其中 Rh1 的抑制效果最明显。人参皂苷 Rd 可上调 Foxp3 表达,促进调节 T 细胞(Treg)分化,诱导 IL-10、TGF- β 和 IL-35 的生成,还可促进 Treg 向 Th1 细胞分化,抑制 Th2 细胞活性,降低机体的过敏反应。除此之外,不同的人参皂苷单体起到相互促进的作用,即增强免疫细胞活性、调节细胞因子分泌等作用,如人参皂苷 Rg3 与化疗药物联合使用时,可显著提高外周血中 CD3⁺、CD4⁺、CD8⁺ T 淋巴细胞亚群水平及 CD4⁺/CD8⁺比值;人参皂苷 Rg1 可促进 IL-4 和 IL-10 的分泌,而 Rg3 则可增强 IFN- γ 、IL-2 等细胞因子的分泌。人参皂苷具有双向免疫调节作用,能提高非特异性免疫和特异性免疫功能,而多种自身免疫性疾病表明其应用临床具有

巨大的潜力，为治疗免疫性疾病领域提供新的选择，它将对现代医学的发展起到促进作用，也是对中医药的很好继承和重要发展。

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参考文献

- [1] Wang, L., Wang, F. and Gershwin, M.E. (2015) Human Autoimmune Diseases: A Comprehensive Update. *Journal of Internal Medicine*, **278**, 369-395. <https://doi.org/10.1111/joim.12395>
- [2] Miller, F.W. (2023) The Increasing Prevalence of Autoimmunity and Autoimmune Diseases: An Urgent Call to Action for Improved Understanding, Diagnosis, Treatment, and Prevention. *Current Opinion in Immunology*, **80**, Article ID: 102266. <https://doi.org/10.1016/j.coi.2022.102266>
- [3] Chopra, P., Chhillar, H., Kim, Y., Jo, I.H., Kim, S.T. and Gupta, R. (2021) Phytochemistry of Ginsenosides: Recent Advancements and Emerging Roles. *Critical Reviews in Food Science and Nutrition*, **63**, 613-640. <https://doi.org/10.1080/10408398.2021.1952159>
- [4] Zheng, M., Xu, F., Li, Y., Xi, X., Cui, X., Han, C., et al. (2017) Study on Transformation of Ginsenosides in Different Methods. *BioMed Research International*, **2017**, Article ID: 8601027. <https://doi.org/10.1155/2017/8601027>
- [5] Li, J., Li, F. and Jin, D. (2023) Ginsenosides Are Promising Medicine for Tumor and Inflammation: A Review. *The American Journal of Chinese Medicine*, **51**, 883-908. <https://doi.org/10.1142/s0192415x23500416>
- [6] Li, J., Zhao, J., Wang, X., Lin, Z., Lin, H. and Lin, Z. (2024) Ginsenoside—A Promising Natural Active Ingredient with Steroidal Hormone Activity. *Food & Function*, **15**, 1825-1839. <https://doi.org/10.1039/d3fo05484e>
- [7] Chen, J. (2020) Advances in Ginsenosides. *Biomolecules*, **10**, Article 681. <https://doi.org/10.3390/biom10050681>
- [8] Quinn, M.J. (2009) Organ-Specific “Autoimmune” Disease. *Journal of Clinical Gastroenterology*, **43**, 386-387. <https://doi.org/10.1097/mcg.0b013e318173e10e>
- [9] Lesage, S. and Goodnow, C.C. (2001) Organ-Specific Autoimmune Disease: A Deficiency of Tolerogenic Stimulation. *The Journal of Experimental Medicine*, **194**, F31-F36. <https://doi.org/10.1084/jem.194.5.f31>
- [10] Höftberger, R. and Lassmann, H. (2018) Immune-Mediated Disorders. *Handbook of Clinical Neurology*, **145**, 285-299. <https://doi.org/10.1016/b978-0-12-802395-2.00020-1>
- [11] Ralli, M., Angeletti, D., Fiore, M., D’Aguanno, V., Lambiase, A., Artico, M., et al. (2020) Hashimoto’s Thyroiditis: An Update on Pathogenic Mechanisms, Diagnostic Protocols, Therapeutic Strategies, and Potential Malignant Transformation. *Autoimmunity Reviews*, **19**, Article ID: 102649. <https://doi.org/10.1016/j.autrev.2020.102649>
- [12] 冯晓红, 黄琦, 张寅晓, 陈颀, 王东, 袁晓. 人参皂苷对实验性自身免疫性甲状腺炎大鼠 TNF- α 及 IL-6 影响的研究[J]. 新中医, 2015, 47(1): 217-219.
- [13] 马成军, 陈明, 张穹, 张金凤. 人参皂苷 RG3 对自身免疫性甲状腺炎小鼠甲状腺功能和辅助型 T 细胞亚群的影响及相关机制[J]. 临床和实验医学杂志, 2021, 20(14): 1464-1467.
- [14] 黄琦, 冯晓红, 张寅晓, 赵闫丽, 苗青, 林筱洁. 人参皂苷对实验性自身免疫性甲状腺炎大鼠 Th1/Th2 相关细胞因子的影响[J]. 中医杂志, 2013, 54(24): 2132-2134.
- [15] Chen, J., Feng, X. and Huang, Q. (2015) Modulation of T-Bet and GATA-3 Expression in Experimental Autoimmune Thyroiditis Rats through Ginsenoside Treatment. *Endocrine Research*, **41**, 28-33. <https://doi.org/10.3109/07435800.2015.1066800>
- [16] Yuan, L., Li, W., Hu, S., Wang, Y., Wang, S., Tian, H., et al. (2024) Protective Effects of Ginsenosides on Ulcerative Colitis: A Meta-Analysis and Systematic Review to Reveal the Mechanisms of Action. *Inflammopharmacology*, **32**, 3079-3098. <https://doi.org/10.1007/s10787-024-01516-w>
- [17] Qu, B., Cao, T., Wang, M., Wang, S., Li, W. and Li, H. (2021) Ginsenosides RD Monomer Inhibits Proinflammatory Cytokines Production and Alleviates DSS-Colitis by NF- κ B and P38MAPK Pathways in Mice. *Immunopharmacology and Immunotoxicology*, **44**, 110-118. <https://doi.org/10.1080/08923973.2021.2012482>
- [18] Zhao, X., Yuan, W., Yang, L., Yan, F. and Cui, D. (2024) Ginsenoside Rh2 Suppresses Ferroptosis in Ulcerative Colitis

- by Targeting Specific Protein 1 by Upregulating MicroRNA-125a-5p. *European Journal of Medical Research*, **29**, Article No. 450. <https://doi.org/10.1186/s40001-024-02025-w>
- [19] Zhong, Y., Xiao, Q., Huang, J., Yu, S., Chen, L., Wan, Q., *et al.* (2023) Ginsenoside Rg1 Alleviates Ulcerative Colitis in Obese Mice by Regulating the Gut Microbiota-Lipid Metabolism-Th1/Th2/Th17 Cells Axis. *Journal of Agricultural and Food Chemistry*, **71**, 20073-20091. <https://doi.org/10.1021/acs.jafc.3c04811>
- [20] Chen, Y., Zhang, Q., Sun, L., Liu, H., Feng, J., Li, J., *et al.* (2023) Ginsenoside Rg1 Attenuates Dextran Sodium Sulfate-induced Ulcerative Colitis in Mice. *Physiological Research*, **72**, 783-792. <https://doi.org/10.33549/physiolres.935182>
- [21] Cheng, H., Liu, J., Zhang, D., Wang, J., Tan, Y., Feng, W., *et al.* (2022) Ginsenoside Rg1 Alleviates Acute Ulcerative Colitis by Modulating Gut Microbiota and Microbial Tryptophan Metabolism. *Frontiers in Immunology*, **13**, Article 817600. <https://doi.org/10.3389/fimmu.2022.817600>
- [22] He, X., Gao, Z., Liang, W. and Sun, Y. (2022) Ameliorative Effect of Ginsenoside Rg1 on Dextran Sulfate Sodium-Induced Colitis: Involvement of Intestinal Barrier Remodeling in Mice. *Annals of Translational Medicine*, **10**, Article 1328. <https://doi.org/10.21037/atm-22-5467>
- [23] Long, J., Liu, X., Kang, Z., Wang, M., Zhao, H., Huang, J., *et al.* (2022) Ginsenoside Rg1 Ameliorated Experimental Colitis by Regulating the Balance of M1/M2 Macrophage Polarization and the Homeostasis of Intestinal Flora. *European Journal of Pharmacology*, **917**, Article ID: 174742. <https://doi.org/10.1016/j.ejphar.2022.174742>
- [24] Shen, Y., Cui, X., Jiang, S., Qian, D. and Duan, J. (2019) Comparative Pharmacokinetics of Nine Major Bioactive Components in Normal and Ulcerative Colitis Rats after Oral Administration of Lizhong Decoction Extracts by UPLC-TQ-MS/MS. *Biomedical Chromatography*, **33**, e4521. <https://doi.org/10.1002/bmc.4521>
- [25] Wan, Y., Dong, Z., Li, H., Yang, L., Li, W., Zhu, K., *et al.* (2022) Comparative Pharmacokinetics of the Main Active Components in Normal and Ulcerative Colitis Rats after Oral Administration of Zingiberis Rhizoma-Ginseng Radix Et Rhizoma Herb Pair and Its Single Herb Extracts by LC-MS/MS. *Journal of Separation Science*, **45**, 2228-2238. <https://doi.org/10.1002/jssc.202101019>
- [26] Xu, X., Wang, W., Chen, Y., Zhang, Q., Li, B., Zhong, Y., *et al.* (2021) Simultaneous Determination of Ten Bioactive Components from Shenling Baizhu San in Rat Plasma by UHPLC-MS/MS: Application to a Comparative Pharmacokinetic Study in Normal and Two Models of Ulcerative Colitis Rats. *Evidence-Based Complementary and Alternative Medicine*, **2021**, Article ID: 3518241. <https://doi.org/10.1155/2021/3518241>
- [27] Zhang, R., Zhang, Q., Chen, Y., Zhao, Q., Zhang, B., Wang, L., *et al.* (2022) Combined Treatment with Rg1 and Adipose-Derived Stem Cells Alleviates DSS-Induced Colitis in a Mouse Model. *Stem Cell Research & Therapy*, **13**, Article No. 272. <https://doi.org/10.1186/s13287-022-02940-x>
- [28] Zhang, Y., Li, W., Wang, Y., Fan, Y., Wang, Q., Liu, C., *et al.* (2024) Investigation of the Material Basis and Mechanism of Lizhong Decoction in Ameliorating Ulcerative Colitis Based on Spectrum-Effect Relationship and Network Pharmacology. *Journal of Ethnopharmacology*, **323**, Article ID: 117666. <https://doi.org/10.1016/j.jep.2023.117666>
- [29] Chen, J., Lu, P., Liu, J., Yang, L., Li, Y., Chen, Y., *et al.* (2023) 20(S)-Protopanaxadiol Saponins Isolated from *Panax notoginseng* Target the Binding of HMGB1 to TLR4 against Inflammation in Experimental Ulcerative Colitis. *Phytotherapy Research*, **37**, 4690-4705. <https://doi.org/10.1002/ptr.7938>
- [30] Ullah, H.M.A., Saba, E., Lee, Y.Y., Hong, S., Hyun, S., Kwak, Y., *et al.* (2022) Restorative Effects of Rg3-Enriched Korean Red Ginseng and *Persicaria tinctoria* Extract on Oxazolone-Induced Ulcerative Colitis in Mice. *Journal of Ginseng Research*, **46**, 628-635. <https://doi.org/10.1016/j.jgr.2021.07.001>
- [31] Tian, M., Ma, P., Zhang, Y., Mi, Y. and Fan, D. (2020) Ginsenoside RK3 Alleviated DSS-Induced Ulcerative Colitis by Protecting Colon Barrier and Inhibiting NLRP3 Inflammasome Pathway. *International Immunopharmacology*, **85**, Article ID: 106645. <https://doi.org/10.1016/j.intimp.2020.106645>
- [32] Huang, X., Xiao, J., Wen, M. and Liang, J. (2022) Ginsenoside Rk2 Protects against Ulcerative Colitis via Inactivating ERK/MEK Pathway by Sirt1. *Journal of Environmental Pathology, Toxicology and Oncology*, **41**, 89-98. <https://doi.org/10.1615/jenvironpatholtoxicoloncol.2021039648>
- [33] Goel, A. and Kwo, P. (2024) Treatment of Autoimmune Hepatitis. *Clinics in Liver Disease*, **28**, 51-61. <https://doi.org/10.1016/j.cld.2023.07.001>
- [34] Liu, X., Mi, X., Wang, Z., Zhang, M., Hou, J., Jiang, S., *et al.* (2020) Ginsenoside Rg3 Promotes Regression from Hepatic Fibrosis through Reducing Inflammation-Mediated Autophagy Signaling Pathway. *Cell Death & Disease*, **11**, Article No. 454. <https://doi.org/10.1038/s41419-020-2597-7>
- [35] Zhou, Y., Hou, J., Liu, W., Ren, S., Wang, Y., Zhang, R., *et al.* (2018) 20(r)-Ginsenoside Rg3, a Rare Saponin from Red Ginseng, Ameliorates Acetaminophen-Induced Hepatotoxicity by Suppressing PI3K/AKT Pathway-Mediated Inflammation and Apoptosis. *International Immunopharmacology*, **59**, 21-30. <https://doi.org/10.1016/j.intimp.2018.03.030>
- [36] Zhou, H., Liu, Y., Su, Y., Ji, P., Kong, L., Sun, R., *et al.* (2024) Ginsenoside Rg1 Attenuates Lipopolysaccharide-Induced Chronic Liver Damage by Activating NRF2 Signaling and Inhibiting Inflammasomes in Hepatic Cells. *Journal of*

- Ethnopharmacology*, **324**, Article ID: 117794. <https://doi.org/10.1016/j.jep.2024.117794>
- [37] Jin, B., Zhang, C., Geng, Y. and Liu, M. (2020) Therapeutic Effect of Ginsenoside Rd on Experimental Autoimmune Encephalomyelitis Model Mice: Regulation of Inflammation and TREG/Th17 Cell Balance. *Mediators of Inflammation*, **2020**, Article ID: 8827527. <https://doi.org/10.1155/2020/8827527>
 - [38] Zhu, D., Liu, M., Yang, Y., Ma, L., Jiang, Y., Zhou, L., *et al.* (2014) Ginsenoside Rd Ameliorates Experimental Autoimmune Encephalomyelitis in C57BL/6 Mice. *Journal of Neuroscience Research*, **92**, 1217-1226. <https://doi.org/10.1002/jnr.23397>
 - [39] Lee, M.J., Jang, M., Choi, J., Chang, B.S., Kim, D.Y., Kim, S., *et al.* (2015) Korean Red Ginseng and Ginsenoside-Rb1/-Rg1 Alleviate Experimental Autoimmune Encephalomyelitis by Suppressing Th1 and Th17 Cells and Upregulating Regulatory T Cells. *Molecular Neurobiology*, **53**, 1977-2002. <https://doi.org/10.1007/s12035-015-9131-4>
 - [40] Oh, J., Kwon, T.W., Choi, J.H., Kim, Y., Moon, S., Nah, S., *et al.* (2024) Ginsenoside-Re Inhibits Experimental Autoimmune Encephalomyelitis as a Mouse Model of Multiple Sclerosis by Downregulating TLR4/MyD88/NF- κ B Signaling Pathways. *Phytomedicine*, **122**, Article ID: 155065. <https://doi.org/10.1016/j.phymed.2023.155065>
 - [41] Lee, M.J., Choi, J.H., Oh, J., Lee, Y.H., In, J., Chang, B., *et al.* (2021) Rg3-Enriched Korean Red Ginseng Extract Inhibits Blood-Brain Barrier Disruption in an Animal Model of Multiple Sclerosis by Modulating Expression of NADPH Oxidase 2 and 4. *Journal of Ginseng Research*, **45**, 433-441. <https://doi.org/10.1016/j.jgr.2020.09.001>
 - [42] Wahren-Herlenius, M. and Dörner, T. (2013) Immunopathogenic Mechanisms of Systemic Autoimmune Disease. *The Lancet*, **382**, 819-831. [https://doi.org/10.1016/s0140-6736\(13\)60954-x](https://doi.org/10.1016/s0140-6736(13)60954-x)
 - [43] Yi, Y. (2019) Ameliorative Effects of Ginseng and Ginsenosides on Rheumatic Diseases. *Journal of Ginseng Research*, **43**, 335-341. <https://doi.org/10.1016/j.jgr.2018.04.004>
 - [44] Li, Z., Gan, H., Ji, K., Yang, M., Pan, T., Meng, X., *et al.* (2024) Protopanaxadiol Improves Lupus Nephritis by Regulating the PTX3/MAPK/ERK1/2 Pathway. *Journal of Natural Medicines*, **78**, 474-487. <https://doi.org/10.1007/s11418-023-01777-9>
 - [45] 赵伟刚. 人参皂苷(GS)联合泼尼松治疗系统性红斑狼疮随机平行对照研究[J]. 实用中医内科杂志, 2013, 27(2S): 93-95.
 - [46] 尤艳丽, 封颖璐, 蔡青, 管剑龙, 张兰玲, 徐美娟, 徐霞, 凌昌全. 人参皂苷联合强的松治疗系统性红斑狼疮的前瞻性随机双盲对照试验[J]. 中西医结合学报, 2010, 8(8): 762-766.
 - [47] 杨帆, 沈俊逸, 蔡辉. 人参皂苷 Rb1 对系统性红斑狼疮患者外周血 T 淋巴细胞体外活化的影响[J]. 实用药物与临床, 2021, 24(5): 418-422.
 - [48] Liu, X., Wang, Z., Qian, H., Tao, W., Zhang, Y., Hu, C., *et al.* (2022) Natural Medicines of Targeted Rheumatoid Arthritis and Its Action Mechanism. *Frontiers in Immunology*, **13**, Article 945129. <https://doi.org/10.3389/fimmu.2022.945129>
 - [49] Chen, J., Wu, H., Wang, Q., Chang, Y., Liu, K., Song, S., *et al.* (2014) Ginsenoside Metabolite Compound K Alleviates Adjuvant-Induced Arthritis by Suppressing T Cell Activation. *Inflammation*, **37**, 1608-1615. <https://doi.org/10.1007/s10753-014-9887-0>
 - [50] Choi, S. and Kim, T. (2023) Compound K—An Immunomodulator of Macrophages in Inflammation. *Life Sciences*, **323**, Article ID: 121700. <https://doi.org/10.1016/j.lfs.2023.121700>
 - [51] Choi, Y.S., Kang, E.H., Lee, E.Y., Gong, H.S., Kang, H.S., Shin, K., *et al.* (2013) Joint-Protective Effects of Compound K, a Major Ginsenoside Metabolite, in Rheumatoid Arthritis: *In Vitro* Evidence. *Rheumatology International*, **33**, 1981-1990. <https://doi.org/10.1007/s00296-013-2664-9>
 - [52] Li, Z., Han, S., Cui, G., Xue, B., Li, J., Man, Y., *et al.* (2023) Oral Liposomes Encapsulating Ginsenoside Compound K for Rheumatoid Arthritis Therapy. *International Journal of Pharmaceutics*, **643**, 123247. <https://doi.org/10.1016/j.ijpharm.2023.123247>
 - [53] Li, Z., Li, Y., Liu, C., Gu, Y. and Han, G. (2024) Research Progress of the Mechanisms and Applications of Ginsenosides in Promoting Bone Formation. *Phytomedicine*, **129**, Article ID: 155604. <https://doi.org/10.1016/j.phymed.2024.155604>
 - [54] Tang, M., Xie, X., Yang, Y. and Li, F. (2021) Ginsenoside Compound K-A Potential Drug for Rheumatoid Arthritis. *Pharmacological Research*, **166**, Article ID: 105498. <https://doi.org/10.1016/j.phrs.2021.105498>
 - [55] Wang, Y., Bao, X., Xian, H., Wei, F., Song, Y., Zhao, S., *et al.* (2023) Glucocorticoid Receptors Involved in Ginsenoside Compound K Ameliorate Adjuvant Arthritis by Inhibiting the Glycolysis of Fibroblast-Like Synoviocytes via the NF- κ B/HIF-1 α Pathway. *Pharmaceutical Biology*, **61**, 1162-1174. <https://doi.org/10.1080/13880209.2023.2241512>
 - [56] Yang, M., Mao, L., Yang, X., Xu, X., Tang, C., Wei, W., *et al.* (2023) Ginsenoside Compound K Exerts Anti-Inflammatory Effects through Transcriptional Activation and Transcriptional Inhibition of Glucocorticoid Receptor in Rheumatoid Arthritis Fibroblast-Like Synoviocytes. *International Immunopharmacology*, **125**, Article ID: 111080. <https://doi.org/10.1016/j.intimp.2023.111080>

-
- [57] Zhang, M., Ren, H., Li, K., Xie, S., Zhang, R., Zhang, L., *et al.* (2021) Therapeutic Effect of Various Ginsenosides on Rheumatoid Arthritis. *BMC Complementary Medicine and Therapies*, **21**, Article No. 149. <https://doi.org/10.1186/s12906-021-03302-5>
- [58] Zhang, L., Zhu, M., Li, M., Du, Y., Duan, S., Huang, Y., *et al.* (2017) Ginsenoside Rg1 Attenuates Adjuvant-Induced Arthritis in Rats via Modulation of PPAR- γ /NF- κ B Signal Pathway. *Oncotarget*, **8**, 55384-55393. <https://doi.org/10.18632/oncotarget.19526>
- [59] Zhang, Y., Wang, S., Song, S., Yang, X. and Jin, G. (2020) Ginsenoside Rg3 Alleviates Complete Freund's Adjuvant-Induced Rheumatoid Arthritis in Mice by Regulating CD4⁺CD25⁺Foxp3⁺Treg Cells. *Journal of Agricultural and Food Chemistry*, **68**, 4893-4902. <https://doi.org/10.1021/acs.jafc.0c01473>
- [60] Chen, W., Meng, Q., Sui, J., Wang, Y., Li, X., Liu, S., *et al.* (2016) Ginsenoside Rb1: The New Treatment Measure of Myasthenia Gravis. *International Immunopharmacology*, **41**, 136-143. <https://doi.org/10.1016/j.intimp.2016.08.028>
- [61] Zong, Y., Yu, W., Hong, H., Zhu, Z., Xiao, W., Wang, K., *et al.* (2023) Ginsenoside Rg1 Improves Inflammation and Autophagy of the Pancreas and Spleen in Streptozotocin-Induced Type 1 Diabetic Mice. *International Journal of Endocrinology*, **2023**, Article ID: 3595992. <https://doi.org/10.1155/2023/3595992>
- [62] Kim, H.Y. and Kim, K. (2007) Protective Effect of Ginseng on Cytokine-Induced Apoptosis in Pancreatic β -Cells. *Journal of Agricultural and Food Chemistry*, **55**, 2816-2823. <https://doi.org/10.1021/jf062577r>
- [63] Gao, Y., Li, J., Chu, S., Zhang, Z., Chen, N., Li, L., *et al.* (2020) Ginsenoside Rg1 Protects Mice against Streptozotocin-Induced Type 1 Diabetic by Modulating the NLRP3 and Keap1/Nrf2/Ho-1 Pathways. *European Journal of Pharmacology*, **866**, Article ID: 172801. <https://doi.org/10.1016/j.ejphar.2019.172801>
- [64] Ren, K., Li, S., Ding, J., Zhao, S., Liang, S., Cao, X., *et al.* (2021) Ginsenoside Rd Attenuates Mouse Experimental Autoimmune Neuritis by Modulating Monocyte Subsets Conversion. *Biomedicine & Pharmacotherapy*, **138**, Article ID: 111489. <https://doi.org/10.1016/j.biopha.2021.111489>