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文献综述

黄芪在风湿免疫疾病中的应用

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摘要：风湿免疫病（痹症）是一类主要由于正气不足或外邪侵袭所致的疾病，表现为关节和肌肉疼痛、肿胀及功能障碍，包括类风湿关节炎、系统性红斑狼疮等多种免疫相关疾病。中药黄芪作为主要的补气药物，具有显著的免疫调节作用，广泛应用于风湿免疫病的治疗。其活性成分如黄芪多糖、黄酮和皂苷等通过多靶点机制，促进免疫稳态，抑制炎症因子释放并增强免疫细胞功能。临床上，黄芪常与桂枝、防己、乌头、人参、当归、白术和防风等中药配伍，形成经典方剂，能够协同减缓风湿免疫病的症状并改善实验室指标。现代医家在使用黄芪时强调辨证施治，以“扶正固本”为核心理念，关注分期论治，在活动期需谨慎使用，以防止免疫过度激活。此外，黄芪的不同炮制品（如生黄芪、蜜黄芪）因成分差异而在功效上有所侧重，相关研究亟需深化。未来应结合前沿技术，深入探索黄芪的不同炮制品及与其他药物配伍的精准应用策略，以优化其在风湿免疫病中的疗效和安全性。

关键词：黄芪；免疫调节；配伍；风湿免疫疾病；痹症

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前言

风湿免疫病也称痹症、痹病等，是因人体正气不足，或由风、寒、湿、热、燥等外邪侵袭，或由痰湿、瘀滞、热毒等内侵而起，出现以肢体关节肌肉等疼痛、重著、麻木、肿胀、屈伸不利，甚至变形，或累及脏腑为特征的一类病证的总称。[1,2] 其以皮肉脉筋骨，甚或脏腑的经络气血不通、不荣为主要病机，临床上有慢性、渐进性、反复发作等特点。风湿病包括现代医学分类中的类风湿关节炎、系统性红斑狼疮、强直性脊柱炎、原发性干燥综合征、骨关节炎、痛风等疾病。每种风湿病的病理损伤部位不一，发病机理也不尽相同，共同点是均由机体的免疫调节缺陷引起。[3]

中药黄芪是豆科植物蒙古黄芪 *Astragalus membranaceus* (Fisch.) Bge.*var.mongholicus* (Bge.) Hsiao 或膜荚黄芪 *Astragalus membranaceus* (Fisch.) Bge. 的干燥根，味甘，性微温，归肝、脾、肺、肾经。有补气升阳，益卫固表，脱毒生肌，利水退肿，行滞通痹之功效，是补气要药，是治疗风湿免疫病的常用中药。[4] 本文总结了目前关于黄芪免疫调节作用的药理研究，梳理了其常见的临床配伍用法，分析了当代知名医家的实际应用经验，旨在帮助中医临床医师更好地理解和运用黄芪在风湿免疫病治疗中的实际应用（见图 1）。

1. 黄芪免疫调节作用的化学基础和作用机制

黄芪的免疫调节作用主要源于其丰富的活性成分，包括多糖、黄酮、皂苷、氨基酸及微量元素等（见图 1）。[5,6] 多糖类是黄芪的核心活性物质，以黄芪多糖（astragalus polysaccharide，APS）

为代表。[7,8] 研究表明，APS 能显著抑制 Th17 细胞的分化和功能，同时促进 Treg 细胞的增殖与活性，通过调节 Th17/Treg 平衡改善自身免疫性疾病、过敏性疾病等过度免疫反应。[9] APS 还能激活巨噬细胞、NK 细胞、树突状细胞等多种免疫细胞，促进 IL-4、IL-10 等抗炎因子的释放。[10] 黄酮类成分，如毛蕊异黄酮通过上调 miR-4766-5p 调控 Th17/Treg 平衡，而黄芩素和黄芩苷则能显著抑制 TNF-α、IL-1β、IL-6 等促炎因子的产生。[8,11] 皂苷类成分，比如研究广泛的黄芪皂苷除了具有类似 APS 的调节 Th17/Treg 平衡、增强免疫细胞的免疫应答能力的作用之外，[8,9] 还可通过 PI3K/AKT/eNOS 通路增强血管内皮功能，并通过抑制 ROS/NLRP3 炎症小体减轻内皮细胞凋亡。[9,10] 此外，黄芪中的氨基酸（如天冬酰胺、γ-氨基丁酸）和微量元素（如硒 Se、锌 Zn 等）也协同参与免疫调节。[7,10] 这些成分共同构成黄芪多靶点、多途径协同调控免疫稳态的化学基础。

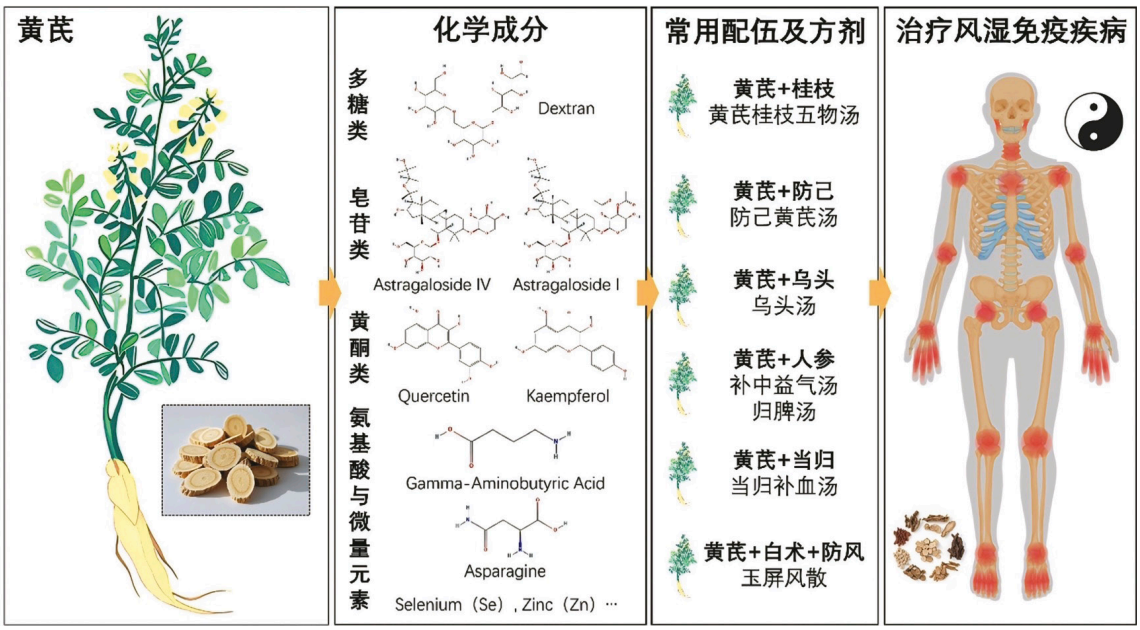


图 1 黄芪治疗风湿免疫疾病的化学基础和临床常用配伍及方剂

2. 风湿免疫病治疗中的常用黄芪配伍

2.1 黄芪配桂枝

黄芪甘温益气，可补在表之卫气。桂枝辛散而温经通痹，共用可通经络、利血脉、止痹痛，临床多用于正虚不足、感受外邪所致的气血运行不畅的血痹病，代表方剂为黄芪桂枝五物汤。黄芪桂枝五物汤出自《金匮要略》，由黄芪、桂枝、芍药、生姜、大枣组成，主治“外证身体不仁，如风痹状”，临床报道在治疗类风湿关节炎、干燥综合征、硬皮病、雷诺氏综合征有较好疗效。[12-16] 黄芪用量一般为 15-30 克，多生用或未说明特殊炮制方法，通过辨证可在原方基础上加减独活、羌活、细辛、山甲、全蝎、蜈蚣、地龙、僵蚕、鸡血藤、海风藤、络石藤、青风藤、川芎、补骨脂、骨碎补、威灵仙、汉防己、防风、乳香、没药等药物。[12] Zhang HS, Wang YY[17] 观察中药黄芪桂枝五物汤加味联合西药来氟米特治疗类风湿关节炎，结果显示疗联合用药可显著改善类风湿关节炎（rheumatoid arthritis, RA）患者免疫指标紊乱，降低血沉（erythrocyte sedimentation rate, ESR）和 C 反应蛋白（C-reactive protein, CRP）等活动性指标，较快地缓解患者关节肿胀晨僵疼痛症状，改善其生活质量，控制病情发展。Lin ZH, Xu GG[18] 发现加味黄芪桂枝五物汤有助于长期服用糖皮质激素的 RA 患者的激素撤减及临床症状缓解。

2.2 黄芪配防己

黄芪益气固表、利水退肿，防己利水消肿、除湿止痛，两药搭配可共呈益气固表、利水除湿功效，代表方剂防己黄芪汤，出自《金匮要略》，该方由防己、黄芪、白术、甘草、生姜、大枣组成。[19,20] 主治“风湿，风水，脉浮，身重，汗出恶风”及“发热汗出，脉浮身重等”。Ma GQ[21] 认为防己黄芪汤可用于

治疗临床中老年女性骨关节炎、类风湿关节炎伴随的肢体沉重，甚或下肢可凹陷性水肿同时见面白虚浮，体型偏胖，肌肉少松弛无力而脂肪多，言语低声，疲倦貌。Chen Y，等[22] 研究显示在雷公藤片为基础治疗的类风湿关节炎患者上加用防己黄芪汤可提高疗效，减轻副反应。He KR，He MG[23] 发现防己黄芪汤加减车前草、山慈菇、黄柏、秦皮、川牛膝治疗湿热蕴结型痛风关节炎有较好疗效。

2.3 黄芪配乌头

黄芪甘温补脾益气，乌头辛温大热，二者合用共奏益气助阳驱寒散湿之功效。代表方剂为乌头汤，出自《金匮要略》，由川乌、黄芪、麻黄、芍药、甘草五味组成，其云“病厉节不可屈伸，疼痛，乌头汤主之”。[24,25] Li SR，Xie X[26] 采用乌头汤联合甲氨蝶呤治疗 RA 有效率为 92%。Luo SJ[27] 使用乌头汤联合甲氨蝶呤治疗类风湿关节炎可改善关节炎活动期的病情，疗效优于单用西药治疗。Zhong QS，等[28] 使用乌头汤联合强的松治疗寒湿痹阻型风湿性多肌痛，可显著改善风湿性多肌痛的症状及 ESR、CRP 等实验室指标。Gao CL[29] 研究发现，加味乌头汤联合艾灸辅治 RA，可提高疗效，改善多项指标且不增加不良反应。Jiang M[30] 研究表明，乌头汤联合塞来昔布治疗膝关节骨性关节炎，能提高疗效且安全。Wu D，等[31] 通过大鼠实验发现，乌头汤联合甲氨蝶呤治疗 RA 效果佳，其作用机制可能与抑制 p38/MAPK 信号通路有关。

2.4 黄芪配人参

黄芪和人参均为补气要药，黄芪补肺气，实皮毛，益中气，升清阳，人参能补下焦元气，壮脾胃谷气，益上焦肺气，代表方剂有补中益气汤、归脾汤等。[32-34] Sun XQ，Song LX[35] 运用补中益气汤治疗类风湿关节炎、皮肌炎、骨关节炎、白塞病和干燥综合征等各类风湿免疫疾病，均取得很好疗效。曾升平运用补中益气汤加减治疗系统性红斑狼疮脱发疗效显著，认为补中益气汤可调理脾胃、补益气血。[36] Ai XQ，等[37] 观察补中益气汤、归脾汤联合甲氨蝶呤治疗气血亏虚型类风湿关节炎疗效显著。Yang Z，等[38] 研究发现，补中益气汤联合针灸治疗绝经后骨质疏松症，疗效优于单一补中益气汤，能显著改善患者免疫功能、骨密度及骨代谢指标。Wang JX，等[39] 研究表明，补中益气汤可调控自身免疫性甲状腺炎（autoimmune thyroiditis，AIT）小鼠 Notch1/ROR-γt/Foxp3 信号通路，平衡免疫反应，修复甲状腺组织病理改变，缓解炎性损伤。Wang D，等[40] 研究发现，归脾汤加减治疗气血两虚型类风湿关节炎伴抑郁症，较阿米替林片治疗，能更好改善抑郁及 RA 病情。Liu WY[41] 研究表明，归脾汤合二至丸治疗系统性红斑狼疮合并慢性病性贫血，较常规西药治疗，在实验室指标、中医证候、症状改善及疾病活动控制方面更具优势。

2.5 黄芪配当归

黄芪补气，当归补血，两药合用，一气一血，一阴一阳，共奏补气生血之力。代表方剂为当归补血汤，由黄芪和当归两味药物组成，组成比例为 5 比 1。[42-44] Liang MR[45] 研究发现，当归补血汤合桂枝汤联合甲氨蝶呤治疗类风湿性关节炎，疗效优于单用甲氨蝶呤，能有效缓解关节疼痛和肿痛，且总有效率高达 96.7%。Mao XH[46] 研究发现，此联合疗法在总有效率、改善晨僵时间等方面均优于单用甲氨蝶呤，对类风湿性关节炎有较好疗效。Zhang ZT，等[47] 研究发现，当归补血汤可调控相关靶点与通路，抑制炎症反应，对糖尿病性骨质疏松有改善作用。Huang CQ，等[48] 研究发现，当归补血汤能恢复卵巢早衰（premature ovarian failure，POF）并发骨质疏松（osteoporosis，OP）大鼠雌二醇水平改善 OP，或与上调维生素 D（vitamin D）水平等有关。Huang H，等[49] 研究表明，当归补血汤可通过调控 PI3K/AKT 信号通路发挥免疫调节作用。Li L，等[50] 研究发现，当归补血汤合桂枝汤联合甲氨蝶呤治疗类风湿性关节炎，在多方面均优于对照组。

2.6 黄芪配白术、防风

黄芪有固表止汗之效，配合白术益气、祛湿，令水湿下行前阴，不从毛窍外泄，配合防风祛邪，更好的固表，代表处方玉屏风散。[51-53] MA JB，等[54] 在西医常规治疗的基础上加用黄芪桂枝五物汤合玉屏风散治疗 RA，可显著缩短晨僵时间、减轻疼痛、消除关节水肿，降低 IL-1、IL-2、IL-6、TNF-α 等炎症因子。Huang W[55] 通过对使用益赛普治疗类风湿关节炎患者预防性使用玉屏风散颗粒预防急

性上呼吸感染，发现玉屏风散可降低急性上呼吸道感染的频率。Zhao JH，等[56] 研究发现 AKT1、VEGFA、IL6、TNF、TP53 等可能是玉屏风散治疗系统性红斑狼疮的核心靶点。Ding Y[57] 研究发现，玉屏风散合黄芪桂枝五物汤治疗气血亏虚型类风湿关节炎疗效佳，可降疼痛积分、证候积分，总有效率 100%。

3. 现代医家对黄芪的认识及运用

辨证论治作为中医学的核心诊疗方法，在风湿病治疗领域展现出独特优势。风湿病多属“痹证”范畴，其发病与正气亏虚、外邪侵袭密切相关。现代研究表明，中医辨证治疗能有效调节免疫功能，减轻炎症反应，且副作用较小，为患者提供了重要治疗选择。

陈湘君教授提出“扶正固本”的治疗原则，认为正气亏虚是风湿病发生发展的关键。[58-62] 在干燥综合征治疗中，创制以黄芪为君药的干燥综合征 2 号方，体现“健脾益气、滋养肺胃”的治疗思路。对于强直性脊柱炎，强调温补脾肾与祛除寒湿并举，常用黄芪配伍川乌、麻黄等药物。在痛风治疗中注重标本兼顾，缓解期重用黄芪、白术健脾化湿。治疗狼疮性肾炎时，善用大剂量黄芪（30-60 克）消除蛋白尿，并辅助激素减量。

朱良春教授将痹证治疗分为三期：初期用药峻猛，中期宽猛相济，后期缓调取胜。注重气血双补，常以黄芪、当归配伍使用。[63] 宋欣伟教授视黄芪为“治痹主帅”，总结出系列药对配伍经验：配生石膏治湿热、配附子温阳、配蜈蚣全蝎通络等，形成系统的用药规范。[64] 特别强调舌淡、舌嫩为使用黄芪的重要指征。冯兴华教授提出“扶正祛邪，调理脾胃”的治疗理念；[65] 焦树德教授在化湿方中配伍黄芪、当归，既祛邪又防伤正。[66]

Li YY, Liu L[67] 的研究显示，黄芪桂枝五物汤是治痹高频方剂，体现了“补气活血、温经通络”的核心治法。然而，沈丕安教授指出，免疫性风湿病活动期需慎用黄芪，因其可能增强体液免疫而加重病情。[68] 黄胜杰教授认为含黄芪的方剂可能与传统免疫抑制治疗产生矛盾。[69] 当代中医名家治疗风湿病的经验表明，在药物选择上既要充分发挥黄芪等药物的治疗作用，又要注意规避其潜在风险。

结论

风湿免疫疾病是一类复杂的疾病，其发病机制与机体免疫调节缺陷密切相关。中药黄芪作为重要的补气药物，因其丰富的活性成分（如多糖、黄酮、皂苷等）在风湿免疫疾病的治疗中展现出良好的免疫调节作用。本文系统总结了黄芪在风湿免疫病中的常见临床配伍及应用，并梳理了当代著名风湿病医家对黄芪的应用经验。尽管黄芪在治疗风湿免疫疾病中展现出积极效果，但目前的研究仍存在明显局限性。首先，大多数临床研究的样本量较小，限制了结果的普遍性和可信度，导致对黄芪疗效的全面评估不足。其次，现有研究多集中于黄芪的单一作用，缺乏对其与其他中药或西药联合使用的系统性研究和评估，影响了临床实践中对黄芪的指导性价值。此外，目前研究未能充分探讨黄芪对不同类型风湿免疫病的适应性及其潜在副作用，尤其是在免疫性疾病活动期的应用风险。

黄芪的不同炮制品具有各自独特的药效特征。[70,71] 生黄芪长于固表止汗、脱疮生肌、利水退肿；炒黄芪性偏燥，补脾益气而不壅滞，多用于食少便溏、脾虚腹胀；蜜黄芪质偏润，长于补气生血，多用于肺虚气短、气虚血弱、气虚便秘；酒黄芪温升作用较强，适用于气虚肺寒及气虚下陷；盐制黄芪可引药入肾，增强补肾气、利水退肿的功效。不同炮制方法导致成分组成产生显著变化，这可能是黄芪不同炮制品功效差异的主要原因。[72] 研究表明，蜜黄芪和盐麸黄芪的总皂苷含量较高，炒黄芪皂苷含量降低；水溶性糖及还原性糖在生黄芪中含量最多，多糖在酒炙黄芪及蜜黄芪中含量较多；炙黄芪中镁（Mg）、锰（Mn）、铁（Fe）、锌（Zn）等微量元素含量较生黄芪显著升高。[70-72] 未来的研究应重点关注不同炮制方法的黄芪药性及临床作用，应用前沿生物医学研究方法掌握不同黄芪炮制品及与其他药物配伍的临床应用规律，以更精准地指导中医临床实践。[73] 同时，应扩大样本量，采用随机对照试验设计，深入证明黄芪在风湿免疫疾病中的疗效与安全性，并系统探讨黄芪及其不同炮制品与其他药物的联合应用及相互作用机制，为临床提供科学的

用药依据。这些努力将有望使黄芪在风湿免疫疾病的治疗中发挥更大潜力，为患者提供更有效的治疗选择。

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บทความปริทัศน์

การประยุกต์ใช้หวงฉีในโรคข้อและรูมาติสซั่ม

อู๋ จินเหลียน, เหมา เจี้ยนชุน
แผนกโรคข้อและรูมาติสซั่ม โรงพยาบาลหลงหัวสังกัดมหาวิทยาลัยการแพทย์แผนจีนเซี่ยงไฮ้

บทคัดย่อ: โรคข้อและรูมาติสซั่ม (ปี้เจิ้ง) เป็นกลุ่มโรคที่มีสาเหตุหลักจากเจิ้งชี่พร่อง หรือการรุกรานของปัจจัยก่อโรคภายนอก ส่งผลให้เกิดอาการปวด บวม และการเคลื่อนไหวของข้อและกล้ามเนื้อผิดปกติ ซึ่งหมายรวมถึง โรคข้ออักเสบรูมาตอยด์ โรคแพ้ภูมิตัวเอง และโรคที่เกี่ยวข้องกับความผิดปกติของระบบภูมิคุ้มกัน หวงฉี (黄芪) เป็นตัวยาสมุนไพรจีนที่สำคัญ อยู่ในกลุ่มยาบำรุงชี่ มีบทบาทสำคัญในการปรับสมดุลการทำงานของระบบภูมิคุ้มกันและใช้กันอย่างแพร่หลายในการรักษาโรคข้อและรูมาติสซั่ม สารออกฤทธิ์สำคัญของหวงฉี (黄芪) เช่น astragalus polysaccharide, flavonoids และ saponins เป็นต้น ออกฤทธิ์ผ่านกลไกหลายเป้าหมาย ได้แก่ การส่งเสริมการรักษาสมดุลของระบบภูมิคุ้มกัน ยับยั้งสารก่อการอักเสบ และเพิ่มประสิทธิผลของเซลล์ภูมิคุ้มกัน ในทางคลินิก หวงฉี (黄芪) มักใช้ร่วมกับสมุนไพรจีนอื่นๆ เช่น กุ้ยจือ (桂枝) ฝางจี่ (防己) อูโถว (乌头) เหรินเซิน (人参) ตังกุย (当归) ไป๋จู๋ (白术) และฝางเฟิง (防风) เป็นต้น เพื่อประกอบเป็นตำรับยาที่สามารถบรรเทาอาการแสดงต่างๆ ของโรคข้อและรูมาติสซั่ม และช่วยปรับปรุงผลการตรวจทางห้องปฏิบัติการดีขึ้นได้อย่างมีประสิทธิผล แนวทางการใช้ตัวยาหวงฉี (黄芪) ของแพทย์จีนสมัยใหม่มุ่งเน้นหลักการตรวจวินิจฉัยจำแนกกลุ่มอาการเพื่อการรักษาตามศาสตร์การแพทย์แผนจีน โดยยึดหลักการเสริมเจิ้งชี่และพื้นฐานร่างกาย และให้ความสำคัญ ให้ความสำคัญกับการรักษาให้เหมาะสมตามระยะของโรค และเน้นย้ำการใช้หวงฉี (黄芪) อย่างระมัดระวังในช่วงโรคกำเริบ เพื่อหลีกเลี่ยงการกระตุ้นภูมิคุ้มกันมากเกินไป นอกจากนี้ หวงฉี (黄芪) ที่ผ่านการแปรรูปในรูปแบบที่ต่างกัน (เช่น หวงฉีสด และหวงฉีผัดน้ำผึ้ง) เนื่องจากมีองค์ประกอบทางเคมีและสรรพคุณแตกต่างกัน จึงเป็นประเด็นที่ควรได้รับการศึกษาเชิงลึกเพิ่มเติม ในอนาคตควรมีการประยุกต์ใช้เทคโนโลยีสมัยใหม่ในการศึกษาการใช้หวงฉี (黄芪) ที่ผ่านการแปรรูปในรูปแบบต่างๆ รวมถึงการนำไปใช้ร่วมกับสมุนไพรอื่นอย่างแม่นยำ เพื่อเพิ่มประสิทธิผลและความปลอดภัยในการใช้หวงฉีในการรักษาโรคข้อและรูมาติสซั่ม

คำสำคัญ: หวงฉี; ปรับสมดุลระบบภูมิคุ้มกัน; การใช้ร่วมกัน; โรคข้อและรูมาติสซั่ม; ปี้เจิ้ง

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Review Article

Application of *Astragalus membranaceus* in autoimmune rheumatic diseases

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Abstract: Autoimmune rheumatic diseases (Bi syndrome) are a category of disorders primarily caused by deficiency of Qi or invasion of external pathogens, characterized by joint and muscle pain, swelling, and dysfunction, including various immune-related conditions such as rheumatoid arthritis and systemic lupus erythematosus. The Chinese medicinal herb Astragalus (*Astragalus membranaceus*), as a primary qi-tonifying herb, exhibits significant immunomodulatory effects and is widely used in the treatment of autoimmune rheumatic diseases. Its active components, including astragalus polysaccharides, flavonoids, and saponins, act through multiple target mechanisms to promote immune homeostasis, inhibit the release of inflammatory factors, and enhance immune cell function. Clinically, *Astragalus membranaceus* is frequently combined with other Chinese herbs such as *Cinnamomum cassia, Stephania tetrandra, Aconitum kusnezoffii*, *Panax ginseng*, *Angelica sinensis*, *Atractylodes macrocephala*, and *Saposhnikovia divaricata* to synergistically alleviate symptoms and improve laboratory indicators of autoimmune rheumatic diseases. Modern medical practitioners emphasize syndrome differentiation when using *Astragalus membranaceus*. Some advocate the core concept of "supporting healthy Qi and consolidating the foundation" highlighting the importance of phased treatment, and avoid its use during active disease phases to prevent excessive immune activation. Furthermore, different processed forms of *Astragalus membranaceus* (e.g., raw Astragalus and honey-fried Astragalus) exhibit distinct therapeutic effects due to compositional variations, warranting further research. In the future, it is essential to integrate cutting-edge technologies to explore precise application strategies for various processed forms of *Astragalus membranaceus* and its compatibility with other herbs, with the goal of optimizing its efficacy and safety in the treatment of autoimmune rheumatic diseases.

Keywords: *Astragalus membranaceus*; immunomodulation; compatibility; autoimmune rheumatic diseases; Bi syndrome

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