

补气补血药促造血作用现代医学研究进展

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摘要

现代医学研究发现, 传统中药在促进造血方面取得了令人瞩目的进展, 多种中药可通过多种复杂的机制发挥其促造血作用。在传统医学中, 造血过程被认为与气血的生成相关。研究表明许多中药及其活性成分可通过保护及促进造血干细胞增殖及分化、调节造血微环境、调控造血生长因子、激活造血相关信号通路等方式发挥促造血作用, 许多中药有望成为血液系统疾病治疗的良好制剂。文章综述了中药促造血机制, 以及近年来研究发现具有促造血作用的补气药及补血药。中药活性成分的复杂性和多样性使得其机制的研究变得困难, 中药的标准化和质量控制问题亟需解决。随着对中药活性成分的深入研究, 越来越多的中药制剂被应用于临床造血功能障碍的治疗。总的来说, 传统中药及其活性成分在造血过程中的研究正在不断深入, 未来将展现出广阔的发展前景。

关键词

中药, 造血系统, 补气药, 补血药, 信号通路

Advances in Modern Medical Research on the Hematopoietic Effect of Qi and Blood Replenishing Drugs

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Abstract

Modern medical research has found that traditional Chinese medicine has made remarkable progress in promoting hematopoiesis, and a variety of traditional Chinese medicines can exert their hematopoietic effects through a variety of complex mechanisms. In traditional medicine, the hematopoietic process is thought to be associated with the production of Qi and blood. Studies have shown that many traditional Chinese medicines and their active ingredients can play a role in promoting hematopoiesis by protecting and promoting the proliferation and differentiation of hematopoietic stem cells, regulating the hematopoietic microenvironment, regulating hematopoietic growth factors, and activating hematopoietic-related signaling pathways, and many TCMs are expected to become good preparations for the treatment of hematopoietic diseases. This article reviews the hematopoietic mechanism of traditional Chinese medicine, as well as the Qi tonic drugs and blood tonic drugs that have been found to promote hematopoiesis in recent years. The complexity and diversity of active ingredients in traditional Chinese medicine make it difficult to study their mechanisms, and the standardization and quality control of traditional Chinese medicine needs to be solved urgently. With in-depth research on the active ingredients of traditional Chinese medicine, more and more traditional Chinese medicine preparations are used in the treatment of clinical hematopoietic dysfunction. In general, the research on traditional Chinese medicine and its active ingredients in the hematopoietic process is deepening, and it will show broad development prospects in the future.

Keywords

Traditional Chinese Medicine, Hematopoietic System, Qi-Invigorating Drugs, Blood-Tonifying Drugs, Signal Pathway

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1. 引言

现代医学认为造血是指骨髓或其他造血器官及组织生成血细胞的过程，这一复杂的生理过程受到多种细胞因子和信号通路的调控。主要的造血细胞类型包括红细胞、白细胞和血小板等。在传统医学中，造血过程则被认为与气血的生成相关。在中医学中，“气”和“血”是维持生命活动的基本物质。气是生命的动力，而血则是滋养身体的重要物质。气与血的关系密切，可以概括为“气为血之帅”、“血为气之母”，气能推动血液的运行，血则为气提供物质基础。中医认为，造血是气与血相互作用的结果，良好的气血循环对于造血过程至关重要。随着现代药理学研究的进展，传统中药及其活性成分对造血的影响逐渐受到大家的重视。研究者们逐步揭示了中药在促进造血过程中的潜在作用机制和应用价值。以下是一些对造血有显著影响的补气补血中药及其相关机制的详细介绍。

2. 中药促进造血机制

2.1. 保护及促进造血干细胞增殖及分化

造血干细胞作为具有自我更新和分化潜能的前体细胞，能够通过细胞分裂保持自身细胞数量，以及

分化形成多种类型的细胞,包括髓系及淋巴系谱系细胞[1][2]。其自我更新及分化能力能够维持造血系统的平衡和功能,确保血细胞的持续生成,从而维持造血器官的造血功能[3]。如前所述,某些补气补血中药能够保护造血干细胞并刺激其增殖及分化,促进造血过程的有序进行。

2.2. 调节造血微环境,保持造血微环境稳定

骨髓造血微环境作为造血干细胞增殖、分化以及成熟的场所,能够保护造血干细胞免受外部复杂因素的伤害,保证造血干细胞正常有序地生成。细胞成分(造血干细胞、骨髓间充质干细胞、基质细胞、成骨细胞、破骨细胞、内皮细胞、脂肪细胞、神经元和免疫细胞)和非细胞成分共同构成了骨髓微环境,非细胞成分由细胞外基质(如胶原蛋白、纤维连接蛋白等)和液体环境(生长因子、细胞因子等)组成[4]。常见对造血产生作用的生长因子如集落刺激因子 2 (Colony-Stimulating Factor 2, CSF2)、红细胞刺激因子(Erythropoietin, EPO)和巨核细胞生长发育因子(Megakaryocyte Growth Development Factor, MGDF)等,其对造血干细胞的增殖和分化起着关键作用,确保了不同类型血细胞的生成,维持了造血微环境的稳定[5]。常见的影响造血的细胞因子有白介素-6 (IL-6)、白介素-7 (IL-7)、恶液质素(TNF- α)和白介素-1 β (IL-1 β)等[5][6]。中药可通过对非造血细胞成分和细胞因子、生长因子等非细胞成分的影响来干预骨髓造血微环境。

2.3. 调控造血生长因子,激活造血相关信号通路

造血生长因子通过与特定受体的结合,激活下游信号通路,进而引发细胞的生物化学反应。主要的造血相关信号通路包括:干细胞因子/酪氨酸激酶受体(Stem Cell Factor/c-Kit, SCF/c-Kit)通路、磷脂酰肌醇 3-激酶/蛋白激酶 B (Phosphoinositide 3-Kinase/Protein Kinase B, PI3K/AKT)信号通路、Janus 激酶信号转导-转录激活因子(Janus Tyrosine Kinase-Signal Transducer and Activator of Transcription, JAK-STAT)信号通路、核因子 κ B (Nuclear Factor kappa-B, NF- κ B)信号通路、Wnt/ β -连环蛋白(Wnt/ β -catenin)信号通路、骨形态发育蛋白(Bone Morphogenetic Protein, BMP)信号通路、Notch 信号通路、p38 丝裂原活化蛋白激酶(p38 Mitogen-Activated Protein Kinase, p38 MAPK)信号通路等。研究发现,SCF/c-Kit 信号通路能够增强造血干细胞的自我更新和分化潜能,促进血细胞的生成[7][8]。PI3K/AKT 信号通路的激活可促进造血和血小板生成[8],可参与调节细胞的增殖、存活和代谢[9]-[11]。JAK-STAT 信号通路的激活可促进造血干细胞及其前体细胞的增殖[12][13]。NF- κ B 信号通路的激活可使造血干细胞快速应对变化,确保血细胞的生成及释放[14]。Wnt/ β -catenin 信号通路可促使造血干细胞向特定的血细胞谱系分化,从而维持造血的效率和造血细胞的质量[15]。BMP 信号通路可确保造血干细胞在适当的微环境中获得正确的信号,维持自我更新及分化能力[16]。Notch 信号可与其他信号通路(如 Wnt 信号通路)相互作用影响造血过程[17]。p38 MAPK 信号通路的激活可促进造血干细胞在应激条件下的增殖,进而维持造血功能[18]。

3. 具有促进造血作用的补气补血药

许多补气补血中药具有促进造血作用。

3.1. 补气药

1) 黄芪

有研究表明,黄芪的活性成分黄芪多糖能够通过激活 Wnt/ β -catenin 信号通路直接保护造血干细胞,减轻化疗引发的骨髓抑制,恢复造血干细胞的造血功能[19]。另有研究发现黄芪多糖可通过上调 FOS 基因的表达直接保护造血干细胞免受化疗引发的骨髓抑制[20]。黄芪多糖可通过促进 BMP9 的表达诱导骨髓间充质干细胞的增殖与分化[21]。黄芪多糖能够通过激活 PI3K/Akt 信号通路促进造血干细胞和祖细胞的增殖[22]。黄芪多糖可通过调节线粒体 Caspase-3 信号通路抑制巨核细胞的凋亡,从而促进骨髓抑制小

鼠造血功能的恢复[23]。研究发现,黄芪多糖可通过促进巨噬细胞、自然杀伤细胞、树突状细胞、T 淋巴细胞、B 淋巴细胞和小胶质细胞的活性,诱导多种细胞因子和趋化因子的表达,增强机体免疫功能,改善骨髓微环境,从而促进造血细胞的发育和成熟[24]。另有研究指出,黄芪的活性成分黄芪甲苷(Astragaloside IV, AS-IV)能够通过激活 AKT/GSK-3 β / β -连环蛋白信号通路,促进骨髓血管生成,从而改善骨髓血流供应,增加营养物质和氧气的输送,为造血细胞的增殖和分化创造良好的条件[25]。黄芪可通过促进骨髓基质细胞表面粘附因子的表达,增加骨髓造血细胞与骨髓基质细胞之间的粘附,进一步促进造血[7]。黄芪可通过抑制肿瘤坏死因子(TNF)、白介素-6(IL-6)等炎症因子的活性,减轻对造血细胞的抑制作用,从而促进造血功能的恢复[26]。黄芪多糖还可通过提高红细胞生成素(EPO)、血小板生成素(TPO)等造血生长因子的水平,促进红细胞和血小板生成[23]。

2) 党参

有研究表明,党参的活性成分党参多糖可通过激活 β -catenin 信号通路,促进骨髓造血干细胞的增殖分化[27]。该多糖还被发现可通过激活 p53-p21 信号通路,减轻辐射引起的造血干细胞衰老[28]。其可通过刺激促红细胞生成素(EPO)分泌,提高造血功能[29]。党参可通过降低肿瘤坏死因子 α (TNF- α)、白细胞介素-6(IL-6)、白细胞介素-1 β (IL-1 β)等细胞因子的表达,调节免疫系统,间接影响骨髓造血功能[30][31]。党参分离物异单叶大黄素可通过抑制 PI3K/Akt 信号通路的激活,保护细胞免受氧化应激损伤,维持造血干细胞的造血功能[32]。研究发现,党参可通过抑制 CDK1/PDK1/ β -catenin 信号轴因子的表达,调节细胞周期,促进造血干细胞增殖,进而提高血细胞生成速率[33]。党参还可通过调节下丘脑-垂体-肾上腺轴(HPA 轴)的活动,促进造血相关激素的分泌,间接影响血细胞的生成[31]。

3) 西洋参

研究发现,西洋参的活性成分之一人参皂苷 Rg1 可通过调节 MAPK 信号通路,促进造血干细胞的增殖和分化,改善造血功能[34]。西洋参的总皂苷成分可能通过抑制 GSK-3 β 的活性,促进造血干细胞的增殖分化[35]。西洋参的总皂苷成分能够通过调节红细胞生成素(EPO)的分泌,促进红细胞的生成,改善造血功能[36]。西洋参的活性成分之一人参二醇皂苷(PDS-C)可通过上调 GATA-1、GATA-2 蛋白表达水平,增强其磷酸化活性状态,促进骨髓造血功能的恢复[32]。西洋参的活性成分人参皂苷可通过刺激抗氧化酶(如超氧化物歧化酶和谷胱甘肽过氧化物酶等)的表达,降低氧化应激反应,间接促进造血[37][38]。研究发现,西洋参皂苷 Rb1 和 Re 可以延缓免疫系统的衰退,有效促进老年患者造血功能的恢复[39]。另外,西洋参能够促进细胞因子(如刺激 Th1 和 Th2 免疫反应的细胞因子)的产生,使得西洋参在增强免疫功能的同时,能促进造血过程的有效进行[40]。

4) 人参

人参可通过激活过氧化物酰化体增殖物激活受体(PPAR)信号通路,促进骨髓造血干细胞增殖[41]。人参可通过激活 Wnt/ β -连环蛋白信号通路,促进造血干细胞增殖,同时抑制其凋亡,从而增强造血功能[42][43]。人参的成分还可通过正向调节 AMPK 和 PI3K/Akt 等多种胰岛素信号通路,在调节细胞代谢和增殖的同时,促进造血干细胞增殖分化[41][44]。人参的活性成分人参皂苷 Rb1 可通过靶向作用于尼莫样激酶(NLK),促进红细胞的生成[45]。人参皂苷 Rg1 可通过提高脾脏造血来支持细胞的活性,改善脾脏微环境,以提高骨髓的造血功能[46]。人参皂苷 Rg1 可通过抑制促炎细胞因子的分泌,降低骨髓微环境的炎症反应,恢复造血干细胞造血功能[47]。人参中的某些活性成分(如人参皂苷 Rg1)可通过促进干扰素- γ (IFN- γ)等细胞因子的分泌,增强 NK 细胞的功能,促进造血细胞的生成[48]。人参的活性成分人参皂苷 Rg1 被发现可通过促进细胞因子的分泌,增强树突状细胞的免疫应答反应,促进造血干细胞的血细胞生成作用[49]。人参皂苷 Rg1 可通过激活 NRF2 信号通路,增强细胞对氧化应激的耐受性,保护造血干细胞造血功能[50]。人参皂苷可通过激活特定的凋亡信号通路,诱导肿瘤细胞凋亡,为骨髓造血功能的恢复

提供更好的微环境,间接促进造血[51]。

5) 白术

研究发现,白术可通过调节 JAK/STAT、Wnt/ β -catenin、Notch、TGF- β 等多种信号通路,促进造血干细胞增殖和分化[52]-[54]。白术可通过促进巨噬细胞分泌白细胞介素(IL)、肿瘤坏死因子(TNF)等多种细胞因子,刺激造血干细胞增殖和分化[55]。白术可通过激活抗凋亡信号通路,减少氧化应激引起的细胞凋亡,维持造血干细胞的造血功能,支持造血的持续进行[56]。

6) 大枣

研究发现,枣的水提取物可通过激活缺氧诱导因子(HIF)信号通路来刺激红细胞生成素(EPO)的表达,进而促进红细胞的生成[57] [58]。枣提取物还被发现可通过促进血红蛋白铁的再利用,维持铁的稳定供应,从而支持红细胞的生成[58]。枣提取物可通过抑制一氧化氮(NO)的生成,减少 NO 的释放,降低机体炎症反应,从而为造血细胞的生成提供更好的环境[57]。

7) 沙棘

研究发现,沙棘可通过激活过氧化物酶体增殖物活化受体(Peroxisome Proliferator-Activated Receptor, PPAR)信号通路增强脂肪酸代谢,改善肝脏功能,间接促进造血功能[59]。有研究表明,沙棘果提取物可有效提升血液中红细胞和白细胞的数量,发挥促造血作用[60]。沙棘可通过增强免疫细胞(如 T 细胞和 B 细胞)的活性来增强机体的免疫反应,间接促进良好造血微环境的形成[61]。沙棘的某些成分可调节免疫系统的平衡,防止过度的免疫反应,维持骨髓正常造血[62]。

3.2. 补血药

1) 当归

有研究表明,当归的主要活性成分之一当归多糖可通过激活 PI3K/AKT 信号通路促进造血干细胞的增殖和分化,从而提高血细胞生成效率[63]。调节性 T 细胞(Treg)和辅助性 T 细胞 17 (Th17)是免疫系统的两种重要 T 细胞亚群。Treg 细胞主要负责抑制免疫反应,防止自身免疫病的发生。而 Th17 细胞则参与促进炎症反应,尤其在抵御细菌和真菌感染中发挥重要作用。二者之间的平衡可维持免疫系统的稳态。而适当的免疫反应则有助于防止造血干细胞的提前衰老。有研究显示,当归多糖能够通过调节 Treg 和 Th17 细胞的比例,维持造血干细胞的功能[64]。此外,当归多糖还被发现能够减轻氧化应激引起的造血细胞的衰老,从而维持正常的造血功能[65]。当归能够通过影响多种细胞因子的表达影响造血过程。有研究表明,当归可能通过增加 EPO 的水平来促进红细胞的生成[66]。当归的某些成分还可能通过促进血小板生成素(TPO)的产生,促进血小板的生成,影响造血过程[67]。

2) 熟地黄

HIF-1 α 是一种缺氧诱导因子, NF- κ B 则与炎症反应密切相关。这两个信号通路的过度激活可导致骨髓微环境的恶化,抑制造血功能。熟地黄的活性成分之一地黄多糖可抑制这些信号通路,改善骨髓造血微环境,促进造血细胞的增殖分化[68] [69]。研究表明,地黄多糖可通过促进促红细胞生成素(EPO)、粒细胞集落刺激因子(G-CSF)等这些细胞因子的表达,显著提高造血干细胞的增殖速率,并促进其向红细胞、白细胞及血小板等成熟血细胞分化[70] [71]。熟地黄还具有显著的抗氧化特性,可通过减轻氧化应激反应对造血系统的损害,发挥保护造血干细胞的潜能[72]。

3) 白芍

有研究发现,白芍药根可通过激活核苷酸结合寡聚化结构域样受体蛋白 3 (NOD-Like Receptor Protein 3, NLRP3)信号通路,调节炎症反应,间接促进造血干细胞活性[73]。某些研究表明,白芍药根的成分能够促进巨噬细胞分泌如白细胞介素(IL)和促红细胞生成素(EPO)等一些与造血相关的细胞因子,增强造血

功能,促进骨髓中的造血干细胞和前体细胞的分化及增殖[74]。研究发现,白芍药根中的多糖成分能够通过激活 PI3K/AKT 信号通路,促进造血干细胞的增殖和存活[75]。有研究发现,芍药的两种主要活性成分芍药苷(Paeoniflorin, PF)和芍药内酯苷(Albiflorin, AF)可通过提高骨髓中集落刺激因子(G-CSF)和粒细胞-巨噬细胞集落刺激因子(GM-CSF)水平,促进骨髓抑制小鼠骨髓造血功能的恢复[76]。

4) 阿胶

氧化应激是影响造血的一个关键因素,过量的自由基会损伤造血干细胞,抑制其增殖和分化。一些研究发现,阿胶中的抗氧化成分能够清除自由基,减少氧化应激对造血细胞的损伤,保护造血干细胞的功能[77]-[79]。研究发现,阿胶具有免疫增强的特性,能够促进白细胞的生成,增强机体对外界刺激的反应能力,从而为造血提供了良好的内环境[77]。

5) 何首乌

研究发现,何首乌提取物可通过刺激骨髓微环境的改变,增强造血干细胞增殖和分化的能力,提高红细胞、白细胞和血小板的生成率[80]。肝脏不仅负责合成多种血液成分,还参与调节造血因子的分泌。研究发现,何首乌中的某些成分可能通过改善肝细胞的功能,提高肝脏对造血的支持作用[81]。巨核细胞是血小板生成的前体细胞,其数量和成熟度直接影响血小板的生成。何首乌的提取物被发现可通过增加巨核细胞的数量及成熟度,促进血小板的生成[82]。

4. 其他促进造血中药

此外,现代医学研究还发现,白扁豆、饴糖、龙眼肉、鹿茸、淫羊藿、巴戟天、肉苁蓉、锁阳、补骨脂、菟丝子、核桃仁、冬虫夏草、紫河车、枸杞子、女贞子、鳖甲等中药亦具有促进造血作用。

5. 挑战与前景

尽管中药在造血领域显示出良好的应用潜力,但其现代化进程仍面临诸多挑战。首先,活性成分的复杂性和多样性使得其机制的研究变得困难。其次,中药的标准化和质量控制问题亟需解决,以确保其临床应用的安全性和有效性。此外,如何将传统中医理论与现代药理学相结合,以推动中药的国际化发展,也是一个重要课题[83]。

6. 总结

中医药在促进造血方面具有悠久的历史和丰富的实践经验。通过多种机制,这些中药能够刺激造血干细胞的增殖和分化,增强红细胞和白细胞的生成。随着对中药活性成分的深入研究,越来越多的中药制剂被应用于临床造血功能障碍的治疗。总的来说,传统中药及其活性成分在造血过程中的研究正在不断深入,展现出广阔的前景。通过现代药理学的工具和方法,我们能够更好地理解中药如何影响造血功能,从而为相关疾病的治疗提供新的思路 and 策略。未来,随着研究的深入和技术的进步,中药在造血领域的应用将更加广泛,成为现代医学的重要补充。

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