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中药单体抑制雪旺细胞铁死亡改善糖尿病周围神经病变研究进展

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［摘要］ 糖尿病周围神经病变(DPN)作为糖尿病最常见的慢性并发症之一，其核心病理机制与高糖(HG)环境诱导的雪旺细胞(SCs)铁死亡密切相关。铁死亡(Ferroptosis)作为一种铁依赖性脂质过氧化驱动的程序性细胞死亡方式，通过铁过载、脂质过氧化及抗氧化系统失调等途径导致SCs功能障碍，进而引发周围神经损伤。近年研究发现，中药单体可通过多靶点调控铁死亡关键通路干预DPN。在调节铁代谢稳态方面，黄芪甲苷Ⅳ、三七皂苷R_1等皂苷类成分通过下调铁转运蛋白减少细胞内游离Fe^{2+}积累；葛根素、槲皮素等黄酮类化合物激活铁转运蛋白(FPN1)促进铁外排；白藜芦醇、丹酚酸A等多酚类化合物则通过缺氧诱导因子-2α(HIF-2α)、铁稳态等途径维持铁代谢平衡，从而减少芬顿反应(Fenton)引发的活性氧(ROS)的增多。在抑制脂质过氧化层面，中药单体靶向激活抗氧化防御体系。芍药苷、槲皮素等通过上调溶质载体家族7成员11(SLC7A11)表达促进谷胱甘肽(GSH)合成，增强谷胱甘肽过氧化物酶4(GPX4)活性，有效清除脂质过氧化物；黄芪甲苷Ⅳ、厚朴酚等则促进核因子红系2相关因子2(Nrf2)核转位，诱导血红素加氧酶-1(HO-1)、超氧化物歧化酶(SOD)等抗氧化酶表达，显著降低丙二醛(MDA)等脂质过氧化产物水平。此外，中药单体还通过调控关键信号网络发挥协同作用。黄芪甲苷Ⅳ经沉默信息调节因子1(SIRT1)/肿瘤蛋白p53轴抑制p53介导的铁死亡敏感性；枸杞多糖、天麻素等修复线粒体功能，阻断铁死亡相关的线粒体ROS释放；柚皮素、白藜芦醇则通过抑制核转录因子-κB(NF-κB)信号通路降低肿瘤坏死因子α(TNF-α)、白细胞介素-6(IL-6)等炎症因子表达，间接缓解氧化应激损伤。皂苷类、黄酮类、多酚类及多糖类中药单体通过调节铁代谢、增强抗氧化能力及修复细胞损伤三大途径抑制SCs铁死亡，为DPN治疗提供了新策略。未来需进一步开展临床转化研究，深化中药单体的探索。

［关键词］ 铁死亡；糖尿病周围神经病变；雪旺细胞；中医单体；研究进展

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Inhibition of Ferroptosis in Schwann Cells by Bioactive Monomers in Traditional Chinese Medicine to Ameliorate Diabetic Peripheral Neuropathy: A Review

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[**Abstract**] Diabetic peripheral neuropathy (DPN), as one of the most common chronic complications of diabetes mellitus, has a core pathologic mechanism closely related to ferroptosis in Schwann cells (SCs) induced by high glucose (HG) environment. Ferroptosis, iron-dependent lipid-peroxidation-driven programmed cell death, leads to SCs dysfunction through iron overload, lipid peroxidation, and dysregulation of the antioxidant system, which thereby causes peripheral nerve injury. In recent years, it has been found that bioactive monomers in traditional Chinese medicine can intervene in DPN through multi-targeted modulation of key pathways of ferroptosis. In regulating iron metabolism homeostasis, saponin constituents such as astragaloside Ⅳ and notoginsenoside R_1 reduce intracellular free Fe^{2+} accumulation by down-regulating ferroportin 1 (FPN1). Flavonoids such as puerarin and quercetin activate FPN1 to promote iron exocytosis. Polyphenolic compounds, such as resveratrol and salvianolic acid A, maintain iron metabolism homeostasis through the hypoxia-inducible factor 2-alpha (HIF-2α), iron homeostasis, and other pathways, which reduce the increase in reactive oxygen species (ROS) triggered by the Fenton reaction. At the level of inhibition of lipid peroxidation, bioactive monomers target the activation of the antioxidant defense system. Paeoniflorin and quercetin promote glutathione (GSH) synthesis and enhance glutathione peroxidase 4 (GPX4) activity by up-regulating the expression of solute carrier family 7 member 11 (SLC7A11), effectively scavenging lipid peroxides. Astragaloside Ⅳ and magnolol promote the nuclear translocation of nuclear factor erythroid 2-related factor 2 (Nrf2), induce the expression of antioxidant enzymes, such as heme oxygenase-1 (HO-1) and superoxide dismutase (SOD), and significantly reduce the levels of lipid peroxidation products, such as malondialdehyde (MDA). In addition, bioactive monomers in traditional Chinese medicine exert synergistic effects by modulating key signaling networks. Astragaloside Ⅳ inhibits p53-mediated ferroptosis sensitivity via the silent information regulator 1 (SIRT1)/p53 axis. Lycium barbarum polysaccharides and gastrodin repair mitochondrial function and block the release of mitochondrial ROS associated with ferroptosis. Naringenin and resveratrol reduce the expression of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and other inflammatory factors by inhibiting the nuclear factor- kappa B (NF-κB) pathway, indirectly alleviating oxidative stress injury. Bioactive monomers in traditional Chinese medicine of saponins, flavonoids, polyphenols, and polysaccharides inhibit ferroptosis in SCs through three major pathways: regulation of iron metabolism, enhancement of antioxidant capacity, and repair of cellular damage, which provides a new strategy for DPN treatment. Further clinical translational studies are needed to deepen the exploration of bioactive monomers of traditional Chinese medicine in the future.

[**Keywords**] ferroptosis; diabetic peripheral neuropathy; Schwann cells; bioactive monomers in traditional Chinese medicine; research progress

糖尿病作为一种全球性的慢性代谢性疾病,其高发病率和广泛并发症已成为公共健康领域的重大挑战。国际糖尿病联盟(IDF)预测到2045年,每8个成年人中就有1个(约7.83亿)患有糖尿病。糖尿病周围神经病变(DPN)是糖尿病最常见的并发症之一,其主要表现为周围神经系统的损害,在糖尿病并发症中的患病率为30%~50%。DPN最常见的症状是对称性多发性周围神经病变,临床特征主要是手脚麻木烧灼及对疼痛、温度和触觉的敏感性降低的"手套-袜套"样分布感觉异常,或者自发性或诱发性的疼痛,可能还会伴有肌无力、萎缩等运动症状,以及出汗异常或者跟腱反射减弱或者消失等情况[1-2]。当前临床治疗以血糖控制和对症镇痛为主,但无法逆转神经损伤。因此,探索DPN的新型病理机制及靶向治疗策略具有重大临床意义。DPN的核心病理之一是雪旺细胞(SCs)功能障碍。持续性高血糖(HG)通过诱导SCs氧化应激、铁代谢紊乱及炎症反应,引发周围神经脱髓鞘和轴突退化[3-4]。近年研究发现,铁死亡(Ferroptosis)在DPN进程中起关键作用。HG环境能够抑制谷胱甘肽过氧化物酶4(GPX4)活性,促进谷胱甘肽(GSH)合成,激活脂质过氧化,触发SCs铁死亡,加剧神经损伤[5]。此外,HG还能通过影响System Xc^-/GSH/GPX4轴及核因子红系2相关因子2(Nrf2)信号通路,诱导SCs脂质过氧化和铁的累积,驱动铁死亡的发生[6-8],而铁死亡抑制剂Ferrostatin-1在可减轻DPN[9]。目前部分中药复方在临床显示DPN改善作用[10],但其活性成分及机制不明,中药单体通过调控铁死亡治疗DPN的研究也尚未系统整合。从中药单体通过改善SCs铁死亡干预DPN的角度出发,探究DPN中SCs铁死亡的核心机制,以及皂苷类、黄酮类、多酚类及多糖类等中药单体干预SCs发生铁死亡的相关靶点及途径,旨为DPN治疗提供新的思路。

1 高糖环境导致的SCs铁死亡发生与DPN

1.1 SCs损伤与DPN SCs损伤与DPN的病理过程有关。SCs是源自神经嵴细胞的胶质细胞,大致可分为髓鞘和非髓鞘两大类型,这两种类型的SCs共同包裹周围神经的轴突,为这些轴突提供保护屏障并提供营养支持,促进神经冲动传导[11-12]。DPN是一种特殊类型的周围神经损伤,主要病理特征是髓鞘缺陷、神经传导速度受损、感觉和本体感觉异常,与轴突萎缩和再生能力降低有关[13]。而SCs作为周围神经系统中最丰富的神经胶质细胞,是维系周围神经健康和功能的核心组成部分。SCs具有高度的可塑性,在周围神经损伤后能够迅速响应损伤信号,进入修复程序,通过去分化和再编程转化为修复表型,促进轴突再生,同时分泌神经营养因子以支持受损神经元的存活,并且清除损伤部位的髓鞘碎片,

为再生创造有利环境，此外，SCs还通过形成结构引导再生的轴突回到原始靶点，并在轴突再生后重新髓鞘化，恢复神经功能[14-16]。持续性高血糖是糖尿病的临床特征之一，也是导致DPN的主要致病因素。研究证实，HG导致SCs的功能、代谢受损，导致神经损伤中间产物积累，神经元支持因子减少，发生髓鞘变薄甚至脱髓鞘，加剧轴突退化和内皮功能障碍，以及SCs分泌的相关血管生成因子减少，导致微血管功能障碍，加剧周围神经病变[17-18]。此外，糖尿病相关的病理产物晚期糖基化终产物（AGEs）和过量的活性氧（ROS）导致氧化应激和内质网应激，可直接或间接或通过相互作用导致DPN中SCs的死亡[19-21]。

1.2　铁死亡的发生机制　铁死亡是一种由铁依赖性脂质过氧化驱动的特殊的新型程序性细胞死亡形式，其不同于传统的凋亡、坏死和自噬等细胞死亡方式，而是依赖于铁离子和磷脂多不饱和脂肪酸的过氧化损伤[22]。铁死亡的发生发展主要依赖以下途径。见图1。

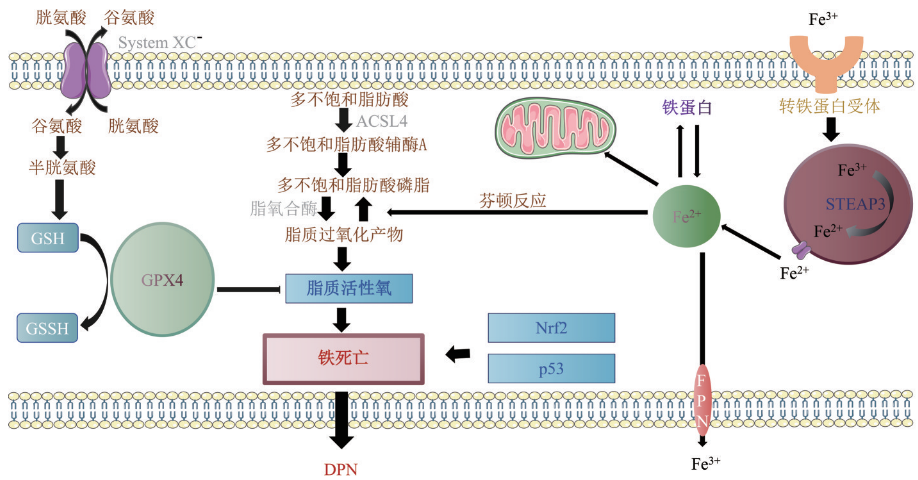

图1　糖尿病周围神经病变与铁死亡

Fig. 1　Diabetic peripheral neuropathy and ferroptosis

1.2.1　铁过载　铁作为生物体内必需的微量金属元素，在铁死亡的发生机制中发挥着核心作用。三价铁离子（Fe^{3+}）在细胞内转化为具有高度活性的二价铁离子（Fe^{2+}）被释放到细胞质不稳定铁池中后被细胞中的铁蛋白（Ferrtin）捕获，用于后续的生物过程或作为储存形式。当Fe^{2+}水平超过铁蛋白的缓冲能力时，多余的Fe^{2+}会通过Fenton反应生成大量ROS，引发脂质过氧化反应[23]，促进细胞膜多不饱和脂肪酸生成脂质过氧化物（PLooH），PLooH可通过多种机制转化为脂质活性氧（Lipid ROS），引起细胞膜结构破坏，膜通透性增加，导致细胞发生铁死亡[24]。

1.2.2　脂质过氧化　System Xc^-/GSH/GPX4途径是调控铁死亡的重要抗氧化防御系统[25-26]。其中，System Xc^-作为半胱氨酸-谷氨酸逆向转运体，负责将胞外的半胱氨酸转运入胞内，是GSH合成的前提。GSH作为细胞内主要的还原性抗氧化剂，在GPX4的催化下，被氧化为谷胱甘肽二聚体（GSSG），同时将PLooH还原为无害的脂质醇，防止其对细胞膜造成损伤[27]。GPX4是抑制铁死亡的核心酶，维持其活性对于细胞抗氧化稳态至关重要[28]。当GPX4失活或表达受抑制时，PLooH无法被有效清除，逐渐积累，导致膜脂损伤、膜通透性升高，最终触发铁死亡。

此外，Nrf2与肿瘤抑制蛋白p53也是调控细胞铁死亡的关键路径。Nrf2作为抗氧化反应的主要调节因子，通过调控铁代谢相关蛋白、GSH合成途径的关键酶和系统及调控GPX4的表达，参与减轻脂质过氧化和防止细胞铁死亡[29]。p53参与调控细胞周期、DNA修复和凋亡等多种细胞过程，通过影响铁代谢、脂质代谢及GSH合成等通路，能够影响细胞内氧化应激水平和铁死亡的敏感性[30]。

1.3　HG导致SCs发生铁死亡　铁死亡参与HG诱导的SCs的死亡过程。HG影响细胞脂质过氧化途径，通过氧化应激和铁催化反应促进PLooH的生成和累积[31]，其中丙二醛（MDA）与蛋白质的氨基基团反应，导致蛋白质交联和变性，导致神经元中关键的酶和受体因而失去功能，影响信号传导和代谢活动，还能够与DNA中的碱基反应，导致DNA突变和基因表达调控异常，高反应性的脂质过氧化产物引发的氧化应激可以导致DNA链断裂，诱导细胞凋亡通路的激活[32-33]。WU等[34]研究证实，HG抑制SCs增殖活性，以及SCs中GPX4和铁代谢相关蛋白溶质载体家族7成员11（SLC7A11）表达水平下降，而铁死亡抑制剂能够显著逆转这一趋势，并且HG还能通过抑制Nrf2信号通路诱导SCs发生铁死亡，并且在后续临床实验中，DPN患者血清中GPX4和GSH水平显著下降，MDA水平显著升高，进一步证实铁死亡的发生。HG导致机体代谢紊乱，细胞内游离的Fe^{2+}增加，Fe^{2+}通过Fenton反应生成大量的ROS，ROS增加直接引起DNA损伤，影响神经元的正常功能和存活。CHANG等[35]研究证实，通过引发大鼠SCs中ROS增加，导致SCs的细胞内铁离子水平及MDA水平显著升高，GPX4、GSH的表达水平下降，并且通过流式细胞术、蛋白免疫印迹法检测凋亡相关蛋白，证实SCs铁死亡的发生。

因此，HG诱发SCs铁死亡与DPN的核心病理涉及SCs的损伤密切相关。SCs作为周围神经系统的重要支持者，其

功能障碍直接影响神经的修复与再生。HG状态下，SCs易受铁死亡影响，铁死亡涉及的铁离子介导的脂质过氧化，导致细胞膜损伤及细胞死亡。GPX4等抗氧化系统的失活进一步加剧铁死亡，而Nrf2信号通路的抑制则减少了细胞对氧化应激的防御能力。鉴于中医药在调节细胞代谢[36]、抗氧化[37]及抗炎[38]等方面的独特优势，其有望通过抑制SCs的铁死亡来改善DPN。

2 中药单体抑制SCs铁死亡改善DPN

在中医理论体系中，DPN被归类于"消渴"病及其相关的"痹证"范畴。消渴病久病不愈，逐渐伤及阴津，导致阴血亏虚，无法濡养四肢筋脉，气虚则使推动血行的力量减弱，导致血液运行不畅，脉络痹阻，进而使经脉失去滋养，导致肢体出现隐痛、刺痛、麻木等症状，属于"本虚标实"之证，气阴两虚和瘀血阻络是DPN典型病变特征，病情的发生与发展往往与气虚、阴血亏损及瘀血阻滞密切相关[39-40]。中药单体是指从中药材中提取出来的单一化合物成分，是中药复杂体系中的基本组成单元。与传统的中药复方相比，中药单体具有成分明确、结构清楚、作用机制相对单一等特点。近年来，随着现代科学技术的不断发展，中药单体的研究通过利用先进技术手段，深入地揭示中药单体的作用机制和药效物质基础，为中医药学科提供科学依据和技术支撑。中医以整体观念与辨证论治为治疗核心，具有多靶点、多层次的特点，其中，中药单体以多通路、双向调节在DPN中发挥作用。因此，对于DPN的中药单体治疗分析有利于治疗DPN的可能[41-81]。中药单体与铁死亡总结表见增强出版附加材料。

2.1 皂苷类 皂苷类化合物是一类广泛存在于植物中的次生代谢产物，近年被证实在降糖[41]、治疗神经系统疾病[42]及改善铁死亡[43]中发挥着显著作用。芍药苷是从芍药中提取的活性成分，能够通过降低ROS和MDA水平，增加GSH和GPX4活性，上调Nrf2及其相关通路，抑制HG诱导的大鼠SCs系RSC96细胞的氧化应激[44]。此外，HG能显著影响RSC96细胞线粒体内硫氧还蛋白2(Trx2)及线粒体外膜转位酶复合体的亚基线粒体外膜转位酶20(TOM20)蛋白的表达量，芍药苷通过上调SCs中TOM20蛋白的表达，促进Trx2的线粒体输入从而降低氧化应激，改善DPN[45]。此外，ZHAI等[46]研究指出，芍药苷能够降低淀粉样前体蛋白/早老素1(APP/PS1)小鼠铁离子、ROS和MDA水平，提高抗氧化酶SOD的表达，从而抑制铁死亡。黄芪甲苷Ⅳ(AS-Ⅳ)源自中药黄芪。通过调控沉默调节蛋白1(SIRT1)/肿瘤抑制蛋白p53与蛋白激酶B(Akt)/糖原合成酶激3β(GSK3β)/Nrf2信号通路，上调胰岛β细胞系大鼠胰岛素瘤细胞(INS-1)中GSH和SOD的表达，清除ROS，下调铁离子、MDA和p53水平，达到抑制铁死亡的目的[47]。此外，黄芪甲苷Ⅳ显著降低高糖环境下RSC96细胞内ROS，修复线粒体损伤，延缓DPN进展[48]。LYU等[49]实验证实，黄芪甲苷Ⅳ减少糖尿病小鼠体内铁死亡标志物及脂质过氧化产物，上调GPX4，显著减轻铁死亡对细胞的损伤。三七皂苷R_1(Notoginsenosides R_1)源于中药三七，能够改善$ApoE^{-/-}$小鼠脂代谢紊乱，减少铁离子累积，激活Nrf2/SLC7A11/GPX4信号通路减少脂质过氧化，抑制其铁死亡的发生[50]。WANG等[51]研究证实，三七皂苷R_1通过减少ROS生成，以及调节相关RNA及信号通路表达，改善RSC96细胞的氧化应激反应，改善DPN。

2.2 黄酮类 黄酮类化合物作为植物中丰富的多酚类化合物具有多样生物活性，其作为铁死亡抑制剂在治疗铁死亡相关疾病方面广泛被研究[52]。槲皮素是一种黄酮类强效抗氧化剂，在治疗糖尿病及其并发症方面具有巨大潜力[53]。槲皮素能够通过抗氧化和促进细胞增殖等途径，改善HG诱导的RSC96细胞损伤及SD大鼠SCs损伤，抑制DPN的发生发展[54]。近期ZHANG等[55]研究显示，槲皮素下调SD大鼠体内的铁水平和MDA，上调GSH、GPX4和Nrf2的表达，改善脂质过氧化，抑制铁死亡，进一步证实了槲皮素抑制SCs铁死亡和改善DPN中的潜在作用。葛根素是一种从葛根中分离得到的异黄酮类衍生物，临床上治疗DPN疗效已得到证实[56]。葛根素能够通过抑制细胞凋亡和调节自噬相关蛋白的表达，对HG诱导的RSC96细胞损伤发挥保护作用[57]，还能减少ROS，减轻线粒体去极化和DNA损伤等机制抗氧化，对HG诱导的RSC96细胞损伤有保护作用[58]。当前YANG等[59]研究表明，葛根素能够下调C57BL/6J小鼠体内铁浓度、MDA和ROS，上调GSH、GPX4和Nrf2的表达，抑制铁死亡，并且还能够改善小鼠葡萄糖代谢。柚皮素(Naringenin)常见于陈皮、橘皮等中药中。研究证实，柚皮素能够通过抑制Wistar大鼠核转录因子-κB(NF-κB)信号通路，降低ROS、促炎性细胞因子和MDA水平，提升SOD活性，从而通过抑制氧化应激及炎症来抑制HG环境下SCs的损伤[60]。近期XU等[61]研究证实，柚皮素激活Nrf2/SLC7A11/GPX4轴，降低ROS、铁积累，改善脂质过氧化来抑制铁死亡的发生。

2.3 多酚类 白藜芦醇是一种多酚化合物，主要存在于藜芦、虎杖等中药中。其优异的抗氧化性能和促进神经再生的能力，使其在治疗DPN领域备受关注并被广泛研究[62-64]。白藜芦醇能够在HG环境下促进SCs的Nrf2核转位，增强SOD、血红素加氧酶-1(HO-1)、谷胱甘肽S-转移酶(GST)和NAD(P)H:醌氧化还原酶1(NQO1)等抗氧化酶的表达，从而减少ROS的生成，改善DPN的发生和发展[65]。当前NI等[66]研究证实，白藜芦醇能够通过激活小鼠的Nrf2/GPX4信号通路，降低铁含量和脂质过氧化水平，抑制MDA和ROS的生成，同时上调GSH、GPX4及多种抗氧化酶的表达，减少脂质过氧化，从而有效抑制铁死亡的发生。厚朴酚(HNK)是一种从中药厚朴中提取的多酚类木脂素类化合物。HU等[67]研究证实，厚朴酚通过体内外实验激活SD大鼠及RSC96细胞腺苷酸活化蛋白激酶(AMPK)/SIRT1/过氧化物酶体增殖物激活受体γ辅激活因子-1α(PGC-1α)通路，降低了铁离子积累并恢复了抗氧化基因的表达，减轻了HG引起的氧化应激，降低ROS和MDA水平，提高了GSH含量，改善HG引起的线粒体功能障碍，从而抑制铁死亡发生，显著改善了HG诱导的SCs损伤和DPN。丹酚酸A是一种从丹参中提取的天然多酚化合物，XU等[68]研究指出，丹酚酸A能防止HG诱导RSC96细胞损伤，上调Nrf2，促进SCs、髓鞘和线粒体再生，改善DPN。YANG等[69]研究证实，丹酚酸A上调

GSH、GPX4,下调MDA、铁含量和ROS,通过缺氧诱导因子-2α(HIF-2α)/双氧化酶1(DUOX1)/GPX4和铁稳态路径抑制铁死亡。

2.4 多糖类　多糖类化合物具有抗氧化、神经保护等药理作用[70]。枸杞多糖是从中药枸杞中提取的一种天然多糖,其抗氧化、免疫调节及神经保护等作用[71][72]。研究证实,枸杞多糖通过同轴静电纺丝掺入纳米纤维支架中,促进在支架上培养的SCs的增殖和神经分化,以及促进SCs的髓鞘形成[73]。当前张翠翠等[74]研究提出,枸杞多糖通过调节大鼠Nrf2/HO-1/GPX4信号通路,上调Nrf2、GPX4,抑制了铁死亡途径,同时改善大鼠氧化应激反应与胰岛素抵抗的情况。黄芪多糖是一种从传统中药黄芪中提取的活性成分,近年来其在治疗DPN方面已经得到证实[75]。研究指出,黄芪多糖能够有效抑制ROS的产生,从而减轻氧化应激对神经组织的损害,同时保护胰岛β细胞免受免疫性损害,维持其正常功能,还通过抗氧化和抑制炎症反应,促进体外培养的SCs增殖,维持神经纤维的正常结构和功能及神经元的存活,从而改善DPN的病理状态[76]。当前秦炜等[77]研究指出,黄芪多糖通过上调GPX4的表达,调节铁代谢及ROS,以及通过提高线粒体的膜电位和增加完整线粒体的比例,促进线粒体功能恢复,从而抑制铁死亡的发生。

2.5 其他类　天麻素是从中药天麻中提取的一种活性成分,属于苯酚类化合物。天麻素通过促进SCs的增殖,提高神经生长因子(NGF)的表达,抑制由HG引发的炎症反应,减少肿瘤坏死因子-α(TNF-α)、白细胞介素-1β(IL-1β)等的产生,减轻糖尿病引起的周围神经损伤[78]。当前JIANG等[79]研究指出,天麻素减少过氧化氢(H_2O_2)引起的氧化应激和脂质过氧化,提高GPX4活性和恢复GSH水平,同时降低MDA,增强了抗氧化蛋白Nrf2、HO-1和铁转运蛋白1(FPN1)的表达,减少了铁的积累和铁死亡。石蒜碱是一种生物碱,广泛存在于石蒜科植物中。胡乃华[80]研究证实,石蒜碱能够通过下调糖尿病小鼠坐骨神经中AMPK通路的激活和基质金属蛋白酶-9(MMP-9)的下调,促进了SCs的自噬,并且通过HG培养的RSC96细胞进行体外实验进一步证实石蒜碱能够促进SCs自噬,改善糖尿病引起的外周神经功能异常。当前DU等[81]研究指出,石蒜碱能够通过降低铁含量、ROS、MDA水平,上提GPX4活性和GSH水平,抑制铁死亡的发生。进一步证实了石蒜碱在通过抑制SCs铁死亡改善DPN的潜力。

3 小结

糖尿病是一种全球性慢性疾病,其并发症DPN给公共健康带来巨大威胁。DPN的发生与周围神经系统中的SCs发生铁死亡密切相关。铁死亡是一种由铁依赖性脂质过氧化驱动的特殊的新型程序性细胞死亡形式,是依赖于铁离子和磷脂多不饱和脂肪酸的过氧化损伤。HG环境导致铁过载和脂质过氧化等情况,引起的SCs发生铁死亡,进而加剧了神经损伤。皂苷类、黄酮类、多酚类、多糖类及其他中药单体成分,能通过上调抗氧化酶表达、减少脂质过氧化产物等途径,有效抑制SCs发生铁死亡,目前被认为在抑制SCs铁死亡方面具有一定潜力。

中药单体在抑制DPN如今仍在起步阶段,关于中药单体、DPN和铁死亡之间作用机制的研究有限,缺乏相关动物及临床实验支持。此外由于DPN的发病机制复杂,涉及代谢、血管及神经营养等多个相互作用的因素,导致治疗需针对多个靶点,但中药单体通常仅作用于特定靶点或信号通路,难以全面应对DPN的复杂性。因此,中药单体治疗DPN的作用机制尚待深入研究,提高对铁死亡相关信号通路和机制的理解,进一步通过临床研究提供高质量证据,从而为中医药治疗DPN提供新的策略与见解。

[利益冲突]　本文不存在任何利益冲突。

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