基于巨噬细胞自噬探讨中医药干预糖尿病动脉粥样硬化的调控机制与策略

宁宇[1]，程艺豪[1]，许迅佳[1]，朱蓉[1]，张清燕[2*]，符宇[2*]
（1. 河南中医药大学 第一临床医学院，郑州 450046；2. 河南中医药大学 第一附属医院，郑州 450000）

［摘要］ 糖尿病动脉粥样硬化（DM-AS）是糖尿病大血管病变的病理基础，也是糖尿病患者发生心血管事件的主要病因。持续高血糖可损伤血管内皮并加剧脂质代谢紊乱与炎症反应，推动斑块由形成向易损演变，从而增加破裂与血栓风险，因此维持斑块稳定性对预防心血管事件具有重要意义。巨噬细胞泡沫化程度与巨噬细胞促炎型（M1）/抗炎修复型（M2）极化失衡直接影响斑块稳定性。自噬是维持巨噬细胞内稳态的关键通路，可通过调控脂质代谢与炎症相关信号、维持自噬流通量，影响斑块炎性负荷与坏死核心扩展，从而参与维持斑块稳定性。中医药具有多成分、多靶点、整体调节的优势，已有研究表明多种中药活性成分及复方对调控自噬网络、干预DM-AS斑块进展有明显优势。该文围绕巨噬细胞自噬，系统梳理腺苷酸活化蛋白激酶/哺乳动物雷帕霉素靶蛋白（AMPK/mTOR）、磷脂酰肌醇3-激酶/蛋白激酶B（PI3K/Akt）、过氧化物酶体增殖物激活受体（PPAR）、晚期糖基化终产物受体/核转录因子-κB（RAGE/NF-κB）等关键通路靶向调控巨噬细胞自噬介导极化平衡在DM-AS不同阶段发挥作用的机制，对中药化合物、中药复方调控自噬进而抑制斑块演进的研究现状进行总结，以期为DM-AS机制研究及临床转化提供新的研究思路。

［关键词］ 糖尿病；动脉粥样硬化；巨噬细胞自噬；巨噬细胞极化；斑块稳定性；信号通路；中医药
［中图分类号］ R242；R256；R587.1 ［文献标识码］ A ［文章编号］ 1005-9903（2026）12-0353-10
［doi］ 10.13422/j.cnki.syfjx.20260361
［网络出版地址］ https://link.cnki.net/urlid/11.3495.r.20260321.1530.005
［网络出版日期］ 2026-03-23 14:55:17 ［增强出版附件］ 内容详见http://www.syfjxzz.com或http://cnki.net

Regulatory Mechanisms and Strategies of Traditional Chinese Medicine Intervention in Diabetic Atherosclerosis Based on Macrophage Autophagy: A Review

NING Yu[1], CHENG Yihao[1], XU Xunjia[1], ZHU Rong[1], ZHANG Qingyan[2*], FU Yu[2*]
(1. *The First Clinical Medical College of Henan University of Chinese Medicine*, *Zhengzhou* 450046, *China*; 2. *The First Affiliated Hospital of Henan University of Chinese Medicine*, *Zhengzhou* 450000, *China*)

［**Abstract**］ Diabetic atherosclerosis (DM-AS) is the pathological basis of diabetic macrovascular complications and is a major cause of cardiovascular events in patients with diabetes. Persistent hyperglycemia can damage the vascular endothelium and exacerbate lipid metabolic disorders and inflammatory responses, promoting the transition of plaques from formation to vulnerability, thereby increasing the risk of rupture and thrombosis. Therefore, maintaining plaque stability is of great importance for the prevention of cardiovascular events. The degree of macrophage foam cell formation and the imbalance between pro-inflammatory M1 polarization and anti-inflammatory reparative M2 polarization directly affect plaque stability. Autophagy is a key pathway for maintaining macrophage homeostasis. By regulating lipid metabolism, inflammation-related signaling, and autophagic flux, autophagy influences the inflammatory burden of plaques and the expansion of the necrotic core, thereby contributing to plaque stabilization. Traditional Chinese medicine (TCM) has the advantages of multi-component, multi-target, and holistic regulation. Previous studies showed that active compounds derived from Chinese materia medica and TCM formulas exhibit notable advantages in modulating the autophagy network and intervening in the progression of DM-AS plaques. Focusing on macrophage

［收稿日期］ 2025-12-12
［基金项目］ 国家自然科学基金面上项目（82474493）；河南省自然科学基金项目（232300420053）
［第一作者］ 宁宇，在读硕士，从事中西医结合防治内分泌疾病研究，E-mail：1121976739@qq.com
［通信作者］ *符宇，副主任医师，博士生导师，从事中西医结合内分泌疾病基础与临床研究，E-mail：kybfuyu@126.com；
*张清燕，博士，助理研究员，从事生物化学与分子生物研究，E-mail：hnaidszqy@163.com

autophagy, this review systematically summarizes the mechanisms by which key pathways, including adenosine monophosphate-activated protein kinase/mammalian target of rapamycin (AMPK/mTOR), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), peroxisome proliferator-activated receptor (PPAR), and receptor for advanced glycation end-product/nuclear factor-κB (RAGE/NF-κB), target macrophage autophagy to mediate polarization balance and exert effects at different stages of DM-AS. It also summarizes current research on TCM compounds and formulas that regulate autophagy and thereby inhibit plaque progression, with the aim of providing new insights for mechanistic studies and clinical translation in DM-AS.

[**Keywords**] diabetes; atherosclerosis; macrophage autophagy; macrophage polarization; plaque stability; signaling pathway; traditional Chinese medicine

动脉粥样硬化(AS)是糖尿病大血管病变的核心病理基础,也是糖尿病患者发生心血管事件的主要病因[1],研究显示,糖尿病患者心血管事件中,约40%与冠心病有关,15%与心力衰竭有关,10%与脑卒中有关[2]。相较于非糖尿病人群,持续的高血糖状态不仅直接损伤血管内皮功能,还会加剧脂质代谢紊乱[3],从而促进糖尿病动脉粥样硬化(DM-AS)斑块的形成与发展,并增加心血管事件发生风险[4]。自噬在AS中发挥重要作用,其功能状态直接影响斑块稳定性[5-6]。作为维持巨噬细胞稳态的关键机制,自噬不仅通过清除受损细胞器与脂滴参与斑块调控[7],更是细胞应对代谢压力、调控免疫应答的重要方式[8]。自噬活性可动态调控巨噬细胞M1/M2极化转化,适度自噬有助于抑制炎症并增强修复功能,而自噬失衡则会破坏表型平衡,进而影响斑块进展与稳定性[9]。中医药在防治DM-AS方面具有多靶点、整体调节的优势。前期研究已证实部分中药活性成分及复方可通过调节自噬相关信号通路、影响巨噬细胞功能,进而干预斑块发展[10]。本文围绕巨噬细胞自噬在DM-AS中的作用机制,系统梳理中药单体及复方通过调控自噬网络干预疾病的相关研究,创新性地从自噬调控与免疫稳态整合的视角,系统阐释中医药在多层次、多通路上协调巨噬细胞功能与斑块微环境的作用模式,以期为中医药在DM-AS中的机制研究与临床转化提供更具系统性的理论依据。

1 巨噬细胞自噬调控DM-AS斑块的发生发展

1.1 巨噬细胞自噬贯穿DM-AS斑块阶段性演进 在DM-AS斑块形成中,巨噬细胞自噬是重要的胞内降解与维持稳态机制,可通过调控脂质代谢和炎症反应影响斑块稳定性。巨噬细胞在AS的发生与发展中发挥重要作用[11-12]。在斑块形成过程中,巨噬细胞可通过吞噬脂质形成泡沫细胞,并分泌多种炎症因子,进而加剧局部脂质沉积、炎症反应及斑块结构重塑。根据功能状态不同,巨噬细胞可分为M1型和M2型,两者之间的动态转化对维持炎症与修复平衡具有重要意义。在DM-AS状态下,巨噬细胞极化平衡常发生失调,表现为M1型比例增加而M2型功能受限,导致炎症反应持续增强并促进斑块进展。自噬通过降解脂质、清除受损细胞器和脂滴,调控炎症相关信号,影响巨噬细胞泡沫化及炎症反应,从而参与斑块的形成与维持稳定性[8-13]。在斑块形成早期,适度自噬有助于胆固醇降解与外排,减轻脂质堆积和氧化应激,并在炎症信号中形成制衡[14-15]。然而,在糖尿病病程中,自噬活性下降或自噬流受阻会限制脂质清除,导致脂质积聚,促进泡沫细胞形成和脂质条纹发展[16-17]。斑块进入纤维斑块阶段后,自噬通过清除活性氧(ROS)和促炎介质,缓解局部炎症并维持巨噬细胞存活[18]。若自噬受损,则凋亡细胞和脂质清除减少,坏死核心扩大,使斑块向易损表型转化[19]。随着病程进一步发展,自噬抑制伴随炎症加剧和细胞焦亡,损伤相关分子模式释放放大炎症反应[20]。在破裂高危阶段,细胞死亡调控失衡可促进白细胞介素(IL)-1β和组织因子释放,增加血栓形成风险,而抗炎表型不足会削弱炎症控制能力[21-23]。

1.2 巨噬细胞自噬介导极化状态调控DM-AS斑块 在DM-AS状态下,巨噬细胞极化并非孤立发生,而是受到细胞内稳态调控网络的约束,其中自噬状态是决定极化方向的关键。自噬通过清除受损线粒体并调节能量代谢稳态,进而影响巨噬细胞向M1或M2表型极化。自噬抑制可诱导炎症信号持续激活,促进M1型优势与M2型不足的极化失衡。巨噬细胞功能同时受自噬流强度显著调控,自噬流强度反映自噬从启动、自噬体形成、与溶酶体融合直至底物降解全过程的整体通量与效率,其变化直接影响细胞稳态的维持能力。

在斑块启动及脂质条纹形成阶段,通常以M1型巨噬细胞的早期激活为主导[24]。若自噬流强度下降,M1型巨噬细胞可在脂多糖和γ干扰素等刺激下极化,并释放IL-1β、IL-6、肿瘤坏死因子-α(TNF-α)、ROS及一氧化氮等介质,从而加剧炎症反应。在纤维斑块形成阶段,自噬流通畅是M2抗炎修复与胞葬功能稳态的基础,若M2型极化不足,则组织修复与炎症损伤之间动态失衡[25]。此外,晚期糖基化终产物受体(AGEs)与其受体晚期糖基化终产物受体(RAGE)结合可损害与M2型相关的胞葬功能,降低凋亡细胞清除效率,促进坏死核心进一步扩大[26]。在斑块高危破裂阶段,自噬流进一步受损,斑块内凋亡或坏死细胞及其碎片的清除效率进一步降低[27],坏死核心持续扩展,并与斑块不稳定性增加密切相关[28]。综上,巨噬细胞极化受自噬流强度显著影响,贯穿斑块从形成到破裂的全过程,并通过调控炎症强度、脂质代谢及组织修复等关键环节,最终影响斑块稳定性及疾病结局。具体机制见图1。

1.2.1 腺苷酸活化蛋白激酶/哺乳动物雷帕霉素靶蛋白(AMPK/mTOR)信号通路在巨噬细胞自噬介导极化中的调控作用 AMPK/mTOR信号通路是调控巨噬细胞自噬的关键通路。AMPK激活后可抑制mTOR信号通路中调控自噬的核心节点(mTORC1)并促进自噬起始激酶1(ULK1)活化,从而增强自噬启动并改善自噬通量,该过程有助于维持自噬-溶酶体系统对脂滴、受损细胞器和氧化应激产物的清

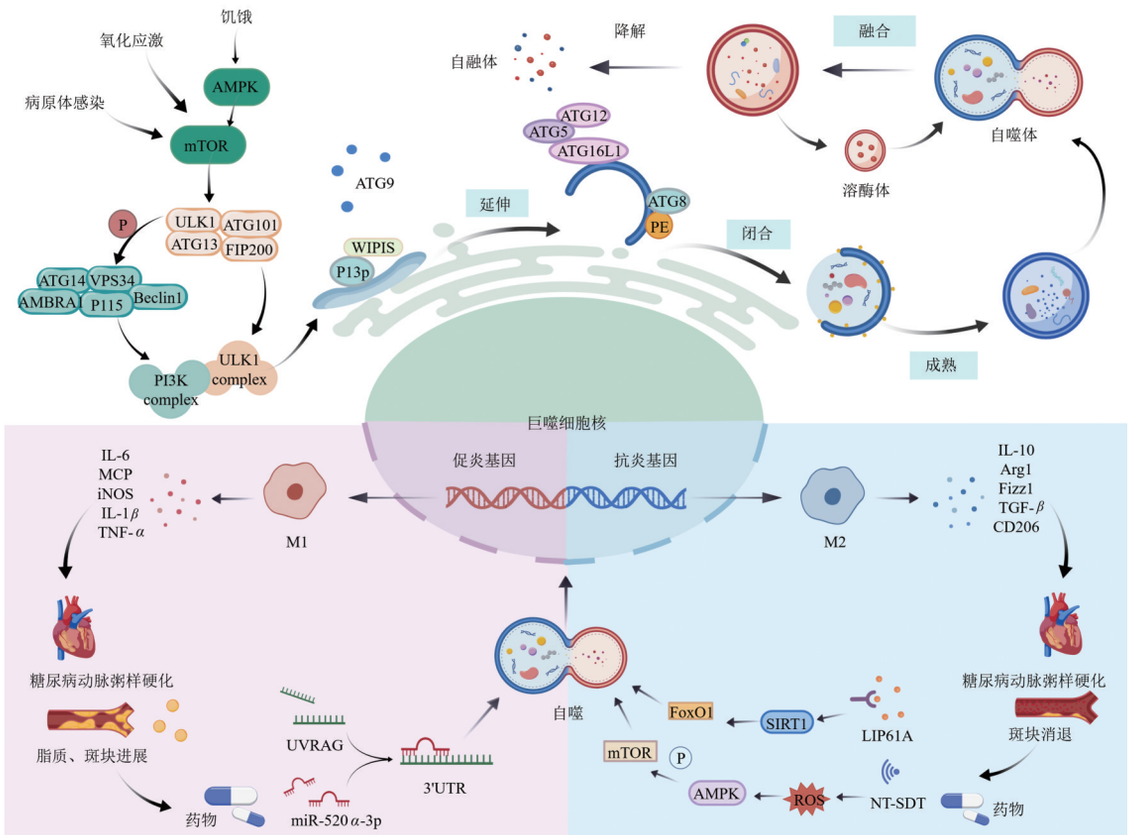

图 1　DM-AS 状态下巨噬细胞自噬调控极化介导斑块发生发展的机制

Fig. 1　Mechanism by which macrophage autophagy regulation polarization regulates plaque formation and development in DM-AS state

除能力，进而抑制炎症放大[29-30]。相反，当 AMPK 活性下降，或 mTOR 异常激活时，自噬体与溶酶体融合及底物降解过程受阻，脂质和受损细胞器积聚，推动巨噬细胞向 M1 表型偏移，加重斑块炎症负荷与不稳定性[31]。在 DM-AS 相关代谢应激条件下，线粒体 ROS 升高可进一步损伤溶酶体功能，加重自噬阻滞，并推动巨噬细胞向促炎表型偏移[32]。已有研究表明，激活 AMPK 或选择性抑制 mTOR 可恢复巨噬细胞自噬通量，减轻泡沫化及斑块炎症负荷。青蒿素及骨髓间充质干细胞来源的细胞外囊泡均可通过调控该通路发挥抗 AS 作用。然而，当 AMPK 或自噬被抑制时，这种保护作用明显减弱[33]。因此，AMPK/mTOR 信号通路是连接代谢应激、自噬失衡与巨噬细胞极化重塑的重要枢纽。

1.2.2　磷脂酰肌醇 3-激酶/蛋白激酶 B（PI3K/Akt）相关信号通路在巨噬细胞自噬介导极化中的调控作用　PI3K/Akt 信号通路是连接胰岛素信号、炎症刺激与巨噬细胞脂质代谢的重要分子通路。在 DM-AS 状态下，高胰岛素血症、胰岛素抵抗及炎症刺激可激活 PI3K/Akt 及其下游 mTOR 信号，促进巨噬细胞脂质摄取和胆固醇酯沉积，从而加速泡沫细胞形成[34-36]。Akt 持续活化可抑制自噬起始并削弱溶酶体清除功能，导致巨噬细胞对脂滴和受损细胞器的降解能力下降[31]。因此，PI3K/Akt 信号异常激活可导致自噬通量下降和脂质处理受限，巨噬细胞更易维持 M1 表型并促进斑块进展；而抑制 PI3K/Akt/mTOR 信号通路有助于恢复巨噬细胞自噬水平并改善斑块稳定性[37]。此外，不同来源巨噬细胞对氧化低密度脂蛋白（ox-LDL）刺激的反应及 M1/M2 标志物表达存在差异，提示 PI3K/Akt 介导的自噬与极化调控具有一定细胞背景依赖性[25]。药物干预研究进一步表明，瑞舒伐他汀在 ApoE$^{-/-}$小鼠及 ox-LDL 刺激的巨噬细胞模型中抑制 PI3K/Akt 信号，提升自噬活性并恢复自噬流，减少泡沫细胞形成，并促进 M1 向 M2 转化，发挥抗 AS 作用[38]。

1.2.3　巨噬细胞自噬介导极化在沉默信息调节因子 1（SIRT1）相关转录调控网络中的作用　SIRT1 是调控巨噬细胞自噬-溶酶体稳态的重要去乙酰化酶，其可通过调节转录因子 EB（TFEB）等转录因子的活性，影响自噬相关基因表达及溶酶体生物发生。在巨噬细胞中，小檗碱可促进 SIRT1 介导的 TFEB 去乙酰化，增强自噬相关蛋白表达并改善溶酶体功能，即 SIRT1/TFEB 信号通路参与自噬过程与溶酶体生成的协同调控[39]。当该调控网络受损时，自噬末端降解受限，脂滴及受损细胞器易于堆积，从而促进泡沫细胞表型维持，加重病灶内炎症反应[40-41]。除 TFEB 外，SIRT1 还可通过调控叉头框蛋白 O3a（FoxO3a）等转录因子参与炎症调控。研究表明，激活 SIRT1/FoxO3a 信号可诱导巨噬细胞自噬，并降低炎症刺激下 TNF-α 等促炎因子的表达[42]。在 DM-AS 进展过程中，SIRT1 表达下降与血管衰老、氧化应激及 AS 加重密切相关[43-44]。因此，SIRT1 相关转录调控网络通过维持巨噬细胞自噬-溶酶体功能，影响脂质代谢、炎症反应及表型重

塑，从而参与斑块进展。

2 中药化合物多通路调控巨噬细胞自噬并稳定斑块

2.1 过氧化物酶体增殖物激活受体α/γ（PPARα/γ）促进脂质自噬并抑制炎症放大 PPARα/γ信号通路在巨噬细胞脂质代谢调控及脂质自噬过程中发挥核心调节作用，是连接脂质处理、自噬转录调控与炎症表型转换的重要分子节点[45]。通过调节胆固醇外排、脂滴代谢及自噬相关基因表达，PPARα/γ通路在维持巨噬细胞脂质稳态及抑制泡沫细胞形成中具有关键作用。近年来研究表明，中医药干预可通过调控PPAR信号通路影响巨噬细胞自噬水平，进而改善AS病变进程。小檗碱作为从黄连中提取的生物碱类化合物[46]，可通过上调克鲁佩尔样因子16（KLF16）表达并促进线粒体自噬，激活PPARα介导的脂肪酸氧化，从而抑制泡沫细胞形成，并减少小鼠主动脉根部斑块面积，同时增加纤维帽厚度[47]。此外，小檗碱通过激活PPARγ亦可增强自噬流，提升AS斑块稳定性[48]。人参皂苷Rg_3通过激活PPARγ信号增强巨噬细胞自噬，逆转AGEs诱导的M1型极化倾向，并抑制核转录因子-κB（NF-κB）通路活化。同时，下调IL-6、TNF-α等促炎因子的表达，并上调抗炎因子IL-10与转化生长因子-β（TGF-β）的水平[49-50]。人参皂苷Rg_3亦可显著减轻糖尿病$ApoE^{-/-}$小鼠主动脉斑块负担，减少斑块内脂质沉积[51]。此外，姜黄素衍生物L3作为一种酚类活性化合物[52]，可通过调控PPAR信号通路减轻氧化应激并修复受损的自噬功能，降低胰腺组织中ROS生成及主动脉弓部氧化低密度脂蛋白受体-1（LOX-1）表达水平，最终改善主动脉脂质沉积与AS病理改变[53]。

2.2 抑制NF-κB解除自噬抑制并降低炎症负荷 炎症反应是推动斑块形成与不稳定的重要病理基础，其中NF-κB信号通路被认为是调控巨噬细胞炎症反应的核心分子通路[54]。NF-κB持续活化不仅促进多种促炎因子表达，还可干扰自噬相关基因转录及信号调控，抑制自噬活性，导致受损细胞器及炎症介质在细胞内积聚。白藜芦醇作为一种天然多酚类化合物，主要通过调节NF-κB通路发挥抗炎及抗血小板聚集作用[54-55]。研究发现，白藜芦醇可显著下调NF-κB蛋白表达水平，减少TNF-α、IL-6及单核细胞趋化蛋白-1（MCP-1）等炎症因子的释放，其抗炎作用与维持巨噬细胞自噬稳态密切相关[56]。丹酚酸A同样表现出较强的抗炎活性，其可降低大鼠主动脉组织中磷酸化NF-κB的表达，并抑制NOD样受体蛋白3（NLRP3）炎症小体的活化，从而延缓疾病进展[57-58]。梓醇通过多靶点途径发挥抗AS作用[59]。动物实验表明，梓醇不仅能够降低血脂水平[60-62]，更能够抑制NF-κB信号通路降低血浆炎症因子水平，通过逆转自噬受抑状态维持血管壁结构的稳定[63]。此外，来源于大黄等药材的番泻苷A可引起转录谱重塑，通路富集显示其可能与NF-κB炎性通路相关，通过调节血管张力及改善代谢紊乱，间接减轻炎症介导的血管损伤[64]，但具体分子节点仍待进一步验证。灵芝多糖作为具有免疫调节与抗氧化作用的活性成分[65]，可降低斑块内脂蛋白相关磷脂酶A2（Lp-PLA2）活性并改善血脂异常，通过抑制NF-κB介导的炎症反应减少组织缺血损伤，从而稳定斑块[66-67]。

2.3 阻断AGEs/RAGE信号通路可修复自噬受损并减轻糖尿病相关血管炎症 AGEs/RAGE信号通路是连接高糖内环境、氧化应激与炎症放大的重要信号通路。AGEs持续积聚并激活RAGE信号后，可进一步放大炎症反应并干扰自噬通量，从而加重巨噬细胞脂质沉积及泡沫化[68]。甘草中的活性成分甘草酸具有显著的抗炎作用，在预防血管并发症方面展示出一定潜力[69-70]。研究表明，甘草酸可有效抑制RAGE及其下游NF-κB信号通路激活，在一定程度上解除炎症反应对自噬系统的抑制作用，经甘草酸干预后，DM-AS大鼠模型中斑块数量明显减少，巨噬细胞泡沫化水平下降，脂质代谢紊乱亦得到改善[71]。

2.4 激活AMPK/mTOR/ULK1信号通路提升自噬通量并抑制泡沫化 在自噬调控网络中，AMPK/mTOR/ULK1信号通路是整合能量代谢信号并调控自噬通量的重要分子中枢，通过协调自噬启动及脂质降解过程，在巨噬细胞脂质稳态维持及斑块形成调控中发挥关键作用[72]。多项研究表明，中药活性成分能够对AMPK介导的代谢-自噬信号通路进行精准调节。槲皮素作为侧柏叶、高良姜等药材的重要活性成分，可通过调控AMPK、SIRT1及NF-κB等构成的信号网络，抑制高脂饮食诱导的炎症反应与氧化应激水平[73-74]。此外，银杏叶提取物通过靶向mTOR信号并修复受损的自噬通量，显著减少斑块面积及脂质沉积[75-76]。冬虫夏草素在增强自噬活性及改善巨噬细胞功能方面表现突出[77]，可通过提高AMPK磷酸化水平并抑制mTOR活性，使主动脉斑块面积减少约42%，同时显著降低斑块内巨噬细胞浸润程度[77-78]。此外，川芎嗪也可通过激活AMPK/mTOR信号通路来促进巨噬细胞自噬功能，进而抑制脂质积累。实验结果显示，经川芎嗪干预8周后，主动脉斑块面积减少约35%，表明其可能在抗炎及抗氧化方面的潜在应用价值[79-80]。

2.5 调节B细胞淋巴瘤-2（Bcl-2）/自噬关键分子酵母Atg6同系物（Beclin-1）可恢复自噬起始并减轻血管壁损伤 在自噬起始阶段，Bcl-2与Beclin-1之间的相互作用构成调控自噬启动的重要分子开关。该复合物的解离可促进自噬起始复合体形成，启动自噬程序，并在调控巨噬细胞脂质清除及血管壁损伤修复过程中发挥重要作用[81]。在临床前研究中，多种天然活性成分可通过调控该通路发挥抗AS作用。黄芪甲苷可通过调节Bcl-2家族蛋白表达平衡增强自噬活性，在糖尿病合并高脂饮食动物模型中显著降低血清IL-6与C反应蛋白水平，从而缓解早期AS病变[81-82]。此外，木通皂苷D也可通过干预Bcl-2及其下游胱天蛋白酶（Caspase）-3信号通路，在抑制脂质沉积的同时延缓斑块形成与进展[83]。见增强出版附加材料[84-85]。

3 中药复方多靶点协同恢复自噬稳态并延缓斑块进展

3.1 调节NF-κB通路类复方 以NF-κB通路为靶点的中药复方干预DM-AS的研究广泛，涉及多种具有化痰、活血、补气等功效的经典方剂。NF-κB活化可促进促炎细胞因子释放，干扰巨噬细胞内稳态，导致受损细胞器及代谢产物积聚，进而加重巨噬细胞泡沫化和促炎极化，加重斑块进展。益糖

康、降糖消脂方、丹栝方、加味温胆汤均可通过下调NF-κB及其相关炎症信号，减轻炎症反应并改善巨噬细胞稳态调节功能。其中，益糖康通过调控胸主动脉组织中Toll样受体3（TLR3）及NF-κB的基因转录与蛋白表达水平，从源头抑制炎症反应并延缓斑块形成[86]。降糖消脂方可抑制TNF-α、IL-6等炎症因子的分泌，促进巨噬细胞由M1型向M2型极化，发挥血管保护作用[87-90]。丹栝方通过下调NF-κB的mRNA转录水平及蛋白活性，有效减轻高血糖诱导的细胞毒性并促进细胞周期的恢复[91-92]；丹瓜方则通过下调炎症因子表达并调节氧化应激反应，从而改善血管超微结构损伤[93-94]。此外，加味温胆汤可通过调控NF-κB/NLRP3信号通路降低血清IL-18及TNF-α水平[95-96]。活血解毒降糖方通过纠正异常自噬状态以修复血管病理损伤[97]。此外，健脾消渴方通过调节血糖（GLU）水平并降低总胆固醇（TC）、甘油三酯（TG）含量，有效延缓颈动脉斑块的进展[98-99]。综上，调节NF-κB相关通路、修复巨噬细胞自噬功能是中药复方延缓DM-AS斑块进展的关键通路之一。

3.2 调节SIRT1通路类复方　黄芪葛根汤出自《证治汇补》，具有健脾、益气养阴生津等功效[100]。瓜蒌汤出自《三因极一病证方论》，瓜蒌、枳壳具有增加冠状动脉流量等作用[101]。黄芪葛根汤瓜蒌汤合方通过多层次激活SIRT1/AMPK与SIRT1/FoxO1信号通路，上调凋亡关键蛋白Bcl-2，下调Beclin-1，提高细胞自噬水平，降低血脂水平，改善DM-AS大鼠的内皮功能障碍[102]。

3.3 调节TGF-β/Smad通路类复方　TGF-β通路在调控糖脂代谢及抑制上皮-间质转化过程中具有重要作用。关于黄芪葛根汤与远志汤合方的研究表明，该方在干预过程中呈现出多通路、多分子协同参与的作用特点[103]。机制研究显示，其可通过调控TGF-β相关信号级联反应，上调HDL-C水平及AMPK蛋白表达，同时下调固醇调节元件结合蛋白1c（SREBP-1c）等脂质代谢相关转录因子的表达[103]。相关实验结果表明，该干预可改善糖脂代谢紊乱状态，并在一定程度上减轻DM-AS病理进展。

3.4 调节NLRP3/凋亡相关斑点样蛋白（ASC）/Caspase-1通路类复方　当归补血汤体现了中医“气血双补则脉道通利”的治疗理念，通过补气养血以改善痰瘀互结的病理状态。在分子机制层面，研究显示该方可抑制NLRP3/ASC/Caspase-1炎性小体相关信号通路的表达与活化，从而阻断下游炎症级联反应发生[104]。炎症反应减弱在动物实验中表现为动脉斑块面积的缩小与病理损伤程度的改善。

3.5 调节其他通路类复方　除核心信号通路外，部分经验效方也可通过多靶点协同调节发挥干预作用。例如，知葛通脉颗粒能够下调斑块组织中TNF-α、基质金属蛋白酶（MMP）-9及细胞间黏附分子-1（ICAM-1）等蛋白的表达，改善斑块局部炎性微环境，减轻血管内皮的慢性炎症损伤[105]。相关研究表明，中药复方在糖尿病大动脉病变的病理过程中，呈现出多途径、多靶协同干预的特点[106-108]。见增强出版附加材料。

4　结语

DM-AS是一个多因素、多机制参与的复杂病理过程，其发病机制涉及代谢紊乱、炎症反应、表观遗传改变等多个层面[109]。其中，AGEs形成、TG升高、高密度脂蛋白胆固醇降低及小而致密的低密度脂蛋白颗粒增多共同导致糖脂代谢异常，加速AS进程[106]。同时，胰岛素抵抗导致代谢紊乱加速内皮祖细胞（EPCs）功能受损，导致血管修复能力下降，推动DM-AS疾病进展。再者，血管壁慢性炎症反应及免疫细胞浸润与活化造成免疫功能紊乱，改变斑块微环境，影响斑块的稳定性。磷脂酶A2、NLRP3炎症小体、环状RNA（circRNAs）等分子功能的阐释及验证推动病理过程研究，也为新药研发和治疗策略提供新思路。

DM-AS复杂的发病机制引导更多的研究者将关注点转向较为宏观的基因多态性、表观遗传调控[107]。以DDAH2基因-449G/C多态性、非对称性二甲基精氨酸（ADMA）等为代表的发现为DM-AS发生与发展的预测分子提供研究基础。而DNA甲基化和组蛋白修饰等表观遗传改变为疾病进展提供了新的分子机制阐释。前期大量核酸蛋白分子功能的深入研究及多组学的宏观综合阐释提示DM-AS的发病机制需关注病理动态过程的调控机制。笔者以DM-AS斑块形成的核心调控免疫细胞“巨噬细胞”为研究对象，聚焦其极化动态平衡对免疫微环境及斑块稳定性的影响，深入剖析自噬流强度介导极化平衡的分子机制，全面综述自噬调控极化平衡的分子网络，综合阐明DM-AS的复杂发病机制。同时，总结槲皮素、虫草素、小檗碱及黄芪葛根汤等中药活性成分与复方，通过AMPK、SIRT1、PPARα、NF-κB等信号通路，多环节、多层次调控巨噬细胞自噬、脂质代谢与炎症反应，维持极化动态平衡，缓解免疫紊乱，从而抑制斑块进展并增强其稳定性的潜在机制。

虽然中药干预巨噬细胞自噬治疗DM-AS方面有一定的研究成果，但仍存在一些不足。首先是本文机制阐释主要基于动物实验模型，中药活性成分在病程长、进展慢的代谢性疾病过程中的生物安全性仍有待通过临床前研究加以阐明。其次，尽管强调了“多成分-多通路”协同，但中药复方中各活性成分如何有序地作用于自噬的动态过程，并使其调控效应精准适应DM-AS斑块的不同发展阶段，其内在的动态调控逻辑仍是当前研究的重点与难点。未来研究应聚焦于开展规范的临床前安全性及长周期药效评价，观察中药干预对斑块演进全过程的动态影响，为临床给药方案提供实验依据；此外，可整合化学物质组、转录组、蛋白组及代谢组等多组学技术，结合网络药理学与分子对接，系统性解析复方中主要成分群作用于巨噬细胞自噬相关靶点的时序关系与交互效应。

［利益冲突］ 本文不存在任何利益冲突

［参考文献］

［1］ 尹经霞，余丽，蒲丹岚，等.《中国糖尿病防治指南（2024版）》解读[J]. 重庆医科大学学报，2025，50（5）：557-564.
YIN J X，YU L，PU D L，et al. Interpretation of Chinese

guidelines for the prevention and treatment of diabetes (2024 edition)[J]. J Chongqing Med Univ, 2025, 50(5): 557-564.

[2] MARX N, FEDERICI M, SCHÜTT K, et al. 2023 ESC guidelines for the management of cardiovascular disease in patients with diabetes[J]. Eur Heart J, 2023, 44(39): 4043-4140.

[3] YUN J S, KO S H. Current trends in epidemiology of cardiovascular disease and cardiovascular risk management in type 2 diabetes[J]. Metabolism, 2021, 123: 154838.

[4] 赵依婷, 秦合伟, 魏霞. 自噬在心血管疾病中的作用及中医药治疗进展[J]. 中国实验方剂学杂志, 2025, 31(7): 284-292.
ZHAO Y T, QIN H W, WEI X. Role of autophagy in cardiovascular diseases and research progress of traditional Chinese medicine treatment[J]. Chin J Exp Tradit Med Form, 2025, 31(7): 284-292.

[5] 杨茜雅, 顾嘉静, 毛若馨, 等. 巨噬细胞在动脉粥样硬化发生机制中的作用[J]. 心脑血管病防治, 2025, 25(9): 41-45.
YANG Q Y, GU J J, MAO R X, et al. Role of macrophages in the pathogenesis of atherosclerosis[J]. Prev Treat Cardio-Cereb Vasc Dis, 2025, 25(9): 41-45.

[6] 熊建龙, 许滔, 向怡, 等. 中医药调控斑块稳定性对急性冠脉综合征的作用机制研究进展[J]. 陕西中医, 2025, 46(7): 1006-1009.
XIONG J L, XU T, XIANG Y, et al. Research progress on the mechanism of traditional Chinese medicine in regulating plaque stability in acute coronary syndrome[J]. Shaanxi J Tradit Chin Med, 2025, 46(7): 1006-1009.

[7] 王宇洁, 邱红梅, 杨婷, 等. ATF3 通过抑制 ATG5 和 ATG16L1 表达调控巨噬细胞自噬与炎症反应[J]. 陆军军医大学学报, 2025, 47(19): 2351-2364.
WANG Y J, QIU H M, YANG T, et al. ATF3 regulates macrophage autophagy and inflammatory response by inhibiting the expression of ATG5 and ATG16L1[J]. J Army Med Univ, 2025, 47(19): 2351-2364.

[8] DOS SANTOS B G, GOEDEKE L. Macrophage immunometabolism in diabetes-associated atherosclerosis[J]. Immunometabolism, 2023, 5(4): e00032.

[9] 陈志超, 林巧妮, 孙立亚, 等. 巨噬细胞激活与极化在糖尿病及其相关并发症的作用及中医药干预[J]. 中国实验方剂学杂志, 2025, 31(6): 311-320.
CHEN Z C, LIN Q N, SUN L Y, et al. Role of macrophage activation and polarization in diabetes and its related complications and intervention of traditional Chinese medicine[J]. Chin J Exp Tradit Med Form, 2025, 31(6): 311-320.

[10] 王欢欢, 郑成瑶, 刘佳蕊, 等. 基于动脉粥样硬化病理基础探讨中药复方的防治特点[J/OL]. 中国动脉硬化杂志, 1-16[2026-03-19]. https://link. cnki. net/urlid/43. 1262. R. 20250928. 1257. 012.
WANG H H, ZHENG C Y, LI J R, et al. Prevention and treatment characteristics of traditional Chinese medicine compounds based on the pathological basis of atherosclerosis[J/OL]. Chin J Arterioscler, 1-16[2026-03-19]. https://link. cnki. net/urlid/43. 1262. R. 20250928. 1257. 012.

[11] 王浩然, 于金. 动脉粥样硬化发生机制及治疗药物的研究进展[J]. 首都医科大学学报, 2010, 31(6): 828.
WANG H R, YU J. Research progress on the pathogenesis and therapeutic drugs of atherosclerosis[J]. J Capital Med Univ, 2010, 31(6): 828.

[12] 丁士芳, 张运, 张梅, 等. 斑块稳定性与炎症反应在急性冠状动脉综合征中作用的研究[J]. 中华心血管病杂志, 2006, 34(6): 512-514.
DING S F, ZHANG Y, ZHANG M, et al. Study on the role of plaque stability and inflammatory response in acute coronary syndrome[J]. Chin J Cardiol, 2006, 34(6): 512-514.

[13] 时佳, 陶慧娴, 郭艳, 等. 自噬在脂多糖诱导的 A549 细胞炎症反应中的作用及机制研究[J]. 中国当代儿科杂志, 2022, 24(10): 1161-1170.
SHI J, TAO H X, GUO Y, et al. Role and mechanism of autophagy in lipopolysaccharide-induced inflammatory response in A549 cells[J]. Chin J Contemp Pediatr, 2022, 24(10): 1161-1170.

[14] KOELWYN G J, CORR E M, ERBAY E, et al. Regulation of macrophage immunometabolism in atherosclerosis[J]. Nat Immunol, 2018, 19(6): 526-537.

[15] LIBBY P, RIDKER P M, HANSSON G K. Progress and challenges in translating the biology of atherosclerosis[J]. Nature, 2011, 473(7347): 317-325.

[16] REDDY M A, CHEN Z, PARK J T, et al. Regulation of inflammatory phenotype in macrophages by a diabetes-induced long noncoding RNA[J]. Diabetes, 2014, 63(12): 4249-4261.

[17] RAHAMAN S O, LENNON D J, FEBBRAIO M, et al. A CD36-dependent signaling cascade is necessary for macrophage foam cell formation[J]. Cell Metab, 2006, 4(3): 211-221.

[18] WU J, HE S, SONG Z, et al. Macrophage polarization states in atherosclerosis[J]. Front Immunol, 2023, 14: 1185587.

[19] 刘哲, 方杰. 巨噬细胞在下肢动脉硬化闭塞症病理机制中的研究进展[J]. 新医学, 2018, 49(6): 382-385.
LIU Z, FANG J. Research progress of macrophages in the pathological mechanism of arteriosclerosis obliterans of lower extremities[J]. J New Med, 2018, 49(6): 382-385.

[20] SHU F, XIAO H, LI Q N, et al. Epigenetic and post-translational modifications in autophagy: biological functions and therapeutic targets[J]. Signal Transduct Target Ther, 2023, 8(1): 32.

[21] KAVURMA M M, RAYNER K J, KARUNAKARAN D. The walking dead: Macrophage inflammation and death in atherosclerosis[J]. Curr Opin Lipidol, 2017, 28(2): 91-98.

[22] PUYLAERT P, ZUREK M, RAYNER K J, et al. Regulated necrosis in atherosclerosis[J]. Arterioscler Thromb Vasc Biol, 2022, 42(11): 1283-1306.

[23] KHATANA C, SAINI N K, CHAKRABARTI S, et al. Mechanistic insights into the oxidized low-density lipoprotein-induced atherosclerosis[J]. Oxid Med Cell Longev, 2020, 2020(1): 5245308.

[24] KHALLOU-LASCHET J, VARTHAMAN A, FORNASA G, et al. Macrophage plasticity in experimental atherosclerosis[J].

PLoS One, 2010, 5(1): e8852.
[25] BISGAARD L S, MOGENSEN C K, ROSENDAHL A, et al. Bone marrow-derived and peritoneal macrophages have different inflammatory response to oxLDL and M1/M2 marker expression: implications for atherosclerosis research[J]. Sci Rep, 2016, 6(1): 35234.
[26] EVANS T D, JEONG S J, ZHANG X, et al. TFEB and trehalose drive the macrophage autophagy-lysosome system to protect against atherosclerosis[J]. Autophagy, 2018, 14(4): 724-726.
[27] SEIFERT R, KUHLMANN M T, ELIGEHAUSEN S, et al. Molecular imaging of MMP activity discriminates unstable from stable plaque phenotypes in shear-stress induced murine atherosclerosis[J]. PLoS One, 2018, 13(10): e0204305.
[28] LUAN G, PAN F, BU L, et al. Butorphanol promotes macrophage phenotypic transition to inhibit inflammatory lung injury via κ receptors[J]. Front Immunol, 2021, 12: 692286.
[29] CUI Y, CHEN J, ZHANG Z, et al. The role of AMPK in macrophage metabolism, function and polarisation[J]. J Transl Med, 2023, 21(1): 892.
[30] CAO Q, DU H, FU X, et al. Artemisinin attenuated atherosclerosis in high-fat diet-fed ApoE mice by promoting macrophage autophagy through the AMPK/mTOR/ULK1 pathway[J]. J Cardiovasc Pharmacol, 2020, 75(4): 321-332.
[31] ZHAI C, CHENG J, MUJAHID H, et al. Selective inhibition of PI3K/Akt/mTOR signaling pathway regulates autophagy of macrophage and vulnerability of atherosclerotic plaque[J]. PLoS One, 2014, 9(3): e90563.
[32] YUAN Y, CHEN Y, PENG T, et al. Mitochondrial ROS-induced lysosomal dysfunction impairs autophagic flux and contributes to M1 macrophage polarization in a diabetic condition[J]. Clin Sci, 2019, 133(15): 1759-1777.
[33] LIU L, AN Z, ZHANG H, et al. Bone marrow mesenchymal stem cell-derived extracellular vesicles alleviate diabetes-exacerbated atherosclerosis via AMPK/mTOR pathway-mediated autophagy-related macrophage polarization[J]. Cell Death Dis, 2025, 24(1): 48.
[34] PARK Y M, KASHYAP S R, MAJOR J A, et al. Insulin promotes macrophage foam cell formation: Potential implications in diabetes-related atherosclerosis[J]. Lab Invest, 2012, 92(8): 1171-1180.
[35] BANERJEE D, SINHA A, SAIKIA S, et al. Inflammation-induced mTORC2-Akt-mTORC1 signaling promotes macrophage foam cell formation[J]. Biomaterials, 2018, 151: 139-149.
[36] LIANG C P, HAN S, SENOKUCHI T, et al. The macrophage at the crossroads of insulin resistance and atherosclerosis[J]. Circ Res, 2007, 100(11): 1546-1555.
[37] VERGADI E, IERONYMAKI E, LYRONI K, et al. Akt signaling pathway in macrophage activation and M1/M2 polarization[J]. J Immunol, 2017, 198(3): 1006-1014.
[38] ZHANG X, QIN Y, WAN X, et al. Rosuvastatin exerts anti-atherosclerotic effects by improving macrophage-related foam cell formation and polarization conversion via mediating autophagic activities[J]. J Transl Med, 2021, 19(1): 62.
[39] ZHENG Y, KOU J, WANG P, et al. Berberine-induced TFEB deacetylation by SIRT1 promotes autophagy in peritoneal macrophages[J]. Aging (Albany NY), 2021, 13(5): 7096.
[40] SERGIN I, EVANS T D, ZHANG X, et al. Exploiting macrophage autophagy-lysosomal biogenesis as a therapy for atherosclerosis[J]. Nat Commun, 2017, 8(1): 15750.
[41] EMANUEL R, SERGIN I, BHATTACHARYA S, et al. Induction of lysosomal biogenesis in atherosclerotic macrophages can rescue lipid-induced lysosomal dysfunction and downstream sequelae[J]. Arterioscler Thromb Vasc Biol, 2014, 34(9): 1942-1952.
[42] TILIJA PUN N, SUBEDI A, KIM M J, et al. Globular adiponectin causes tolerance to LPS-induced TNF-α expression via autophagy induction in RAW 264. 7 macrophages: Involvement of SIRT1/FoxO3A axis[J]. PLoS One, 2015, 10(5): e0124636.
[43] KITADA M, OGURA Y, KOYA D. The protective role of Sirt1 in vascular tissue: Its relationship to vascular aging and atherosclerosis[J]. Aging (Albany NY), 2016, 8(10): 2290.
[44] ZHAO Y, LIU Y S. Longevity factor FOXO3: A key regulator in aging-related vascular diseases[J]. Front Cardiovasc Med, 2021, 8: 778674.
[45] CHANG E, ZHU Y, WEI W, et al. Chiglitazar, a PPAR pan-agonist: Impacts on type 2 diabetes mellitus and multi-system metabolic regulation: A review[J]. Biomed Pharmacother, 2025, 193: 118850.
[46] FENG X, SUREDA A, JAFARI S, et al. Berberine in cardiovascular and metabolic diseases: From mechanisms to therapeutics[J]. Theranostics, 2019, 9(7): 1923.
[47] MAN B, HU C, YANG G, et al. Berberine attenuates diabetic atherosclerosis via enhancing the interplay between KLF16 and PPARα in ApoE mice[J]. Biochem Biophys Res Commun, 2022, 624: 59-67.
[48] LI H, HE C, WANG J, et al. Berberine activates peroxisome proliferator-activated receptor gamma to increase atherosclerotic plaque stability in Apoe mice with hyperhomocysteinemia[J]. J Diabetes Investig, 2016, 7(6): 824-832.
[49] MAO L, YIN R, YANG L, et al. Role of advanced glycation end products on vascular smooth muscle cells under diabetic atherosclerosis[J]. Front Endocrinol (Lausanne), 2022, 13: 983723.
[50] SRIRANGAN P, SABINA E P. Protective effects of herbal compounds against cyclophosphamide-induced organ toxicity: A pathway-centered approach[J]. Drug Chem Toxicol, 2025, 48(5): 972-1014.
[51] GUO M, XIAO J, SHENG X, et al. Ginsenoside Rg_3 mitigates atherosclerosis progression in diabetic ApoE mice by skewing macrophages to the M2 phenotype[J]. Front Pharmacol, 2018, 9: 464.
[52] DEVI K P, MALAR D S, NABAVI S F, et al. Kaempferol and inflammation: From chemistry to medicine[J]. Pharmacol Res, 2015, 99: 1-10.

[53] ZHENG B, YANG L, WEN C, et al. Curcumin analog L3 alleviates diabetic atherosclerosis by multiple effects[J]. Eur J Pharmacol, 2016, 775: 22-34.

[54] HUO X, ZHANG T, MENG Q, et al. Resveratrol effects on a diabetic rat model with coronary heart disease[J]. Med Sci Monit, 2019, 25: 540-546.

[55] HUANG D D, SHI G, JIANG Y, et al. A review on the potential of resveratrol in prevention and therapy of diabetes and diabetic complications[J]. Biomed Pharmacother, 2020, 125: 109767.

[56] GUO R, LI B, WANG K, et al. Resveratrol ameliorates diabetic vascular inflammation and macrophage infiltration in db/db mice by inhibiting the NF-κB pathway[J]. Diabetes Vasc Dis Res, 2014, 11(2): 92-102.

[57] HO J H, HONG C Y. Salvianolic acids: Small compounds with multiple mechanisms for cardiovascular protection[J]. J Biomed Sci, 2011, 18(1): 30.

[58] MA Q, YANG Q, CHEN J, et al. Salvianolic acid A ameliorates early-stage atherosclerosis development by inhibiting NLRP3 inflammasome activation in Zucker diabetic fatty rats[J]. Molecules, 2020, 25(5): 1089.

[59] ZHANG Z, DAI Y, XIAO Y, et al. Protective effects of catalpol on cardio-cerebrovascular diseases: A comprehensive review[J]. J Pharm Anal, 2023, 13(10): 1089-1101.

[60] CHEN Q, QI X, ZHANG W, et al. Catalpol inhibits macrophage polarization and prevents postmenopausal atherosclerosis through regulating estrogen receptor alpha[J]. Front Pharmacol, 2021, 12: 655081.

[61] REN H, WANG D, ZHANG L, et al. Catalpol induces autophagy and attenuates liver steatosis in ob/ob and high-fat diet-induced obese mice[J]. Aging (Albany NY), 2019, 11(21): 9461.

[62] ZHU H F, WANG Y, LIU Z Q, et al. Antidiabetic and antioxidant effects of catalpol extracted from *Rehmannia glutinosa* (Di Huang) on rat diabetes induced by streptozotocin and high-fat, high-sugar feed[J]. Chin Med, 2016, 11(1): 25.

[63] LIU J Y, ZHENG C Z, HAO X P, et al. Catalpol ameliorates diabetic atherosclerosis in diabetic rabbits[J]. Am J Transl Res, 2016, 8(10): 4278.

[64] 刘美志, 王子杨, 姜雅宁, 等. 番泻苷 A 对 2 型糖尿病小鼠动脉粥样硬化斑块形成及 5-羟色胺信号分子表达的影响[J]. 上海交通大学学报: 医学版, 2024, 44(8): 991-998.
LIU M Z, WANG Z Y, JIANG Y N, et al. Effects of sennoside A on atherosclerotic plaque formation and expression of serotonin signaling molecules in type 2 diabetic mice[J]. J Shanghai Jiaotong Univ: Med Sci, 2024, 44(8): 991-998.

[65] LU J, HE R, SUN P, et al. Molecular mechanisms of bioactive polysaccharides from *Ganoderma lucidum* (Lingzhi): A review[J]. Int J Biol Macromol, 2020, 150: 765-774.

[66] WIHASTUTI T A. Lowering inflammation level by Lp-PLA2 inhibitor (Darapladib) in early atherosclerosis development: *In vivo* rat type 2 diabetes mellitus model[J]. J Clin Diagn Res, 2017, 8(2): 50-55.

[67] WIHASTUTI T A, AMIRUDDIN R, CESA F Y, et al. Decreasing angiogenesis vasa vasorum through Lp-PLA2 and H2O2 inhibition by PSP from *Ganoderma lucidum* in atherosclerosis: *In vivo* diabetes mellitus type 2[J]. J Basic Clin Physiol Pharmacol, 2019, 30(6): 20190349.

[68] TAGUCHI K, FUKAMI K. RAGE signaling regulates the progression of diabetic complications[J]. Front Pharmacol, 2023, 14: 1128872.

[69] TAN D, TSENG H H, ZHONG Z, et al. Glycyrrhizic acid and its derivatives: Promising candidates for the management of type 2 diabetes mellitus and its complications[J]. Int J Mol Sci, 2022, 23(19): 10988.

[70] FENG L, ZHU M M, ZHANG M H, et al. Protection of glycyrrhizic acid against AGEs-induced endothelial dysfunction through inhibiting RAGE/NF-κB pathway activation in human umbilical vein endothelial cells[J]. J Ethnopharmacol, 2013, 148(1): 27-36.

[71] ZHAO Y, LI W, ZHANG D. Glycyrrhizic acid alleviates atherosclerotic lesions in rats with diabetes mellitus[J]. Mol Med Rep, 2021, 24(5): 755.

[72] AL-KURAISHY H M, SULAIMAN G M, MOHSIN M H, et al. Targeting of AMPK/MTOR signaling in the management of atherosclerosis: Outmost leveraging[J]. Int J Biol Macromol, 2025, 309: 142933.

[73] XU J, HU H, JIANG H, et al. The therapeutic mechanisms of quercetin on inflammatory diseases: An update[J]. Inflammation, 2025, 33(6): 3015-3049.

[74] ZHANG F, FENG J, ZHANG J, et al. Quercetin modulates AMPK/SIRT1/NF-κB signaling to inhibit inflammatory/oxidative stress responses in diabetic high fat diet-induced atherosclerosis in the rat carotid artery[J]. Exp Ther Med, 2020, 20(6): 280.

[75] VAN BEEK T A. Chemical analysis of *Ginkgo biloba* leaves and extracts[J]. J Chromatogr A, 2002, 967(1): 21-55.

[76] TIAN J, POPAL M S, LIU Y, et al. *Ginkgo biloba* leaf extract attenuates atherosclerosis in streptozotocin-induced diabetic ApoE mice by inhibiting endoplasmic reticulum stress via restoration of autophagy through the mTOR signaling pathway[J]. Oxid Med Cell Longev, 2019, 2019(1): 8134678.

[77] LI X, ZHOU Y, ZHANG X, et al. Cordycepin stimulates autophagy in macrophages and prevents atherosclerotic plaque formation in ApoE mice[J]. Oncotarget, 2017, 8(55): 94726.

[78] MIHAYLOVA M M, SHAW R J. The AMPK signalling pathway coordinates cell growth, autophagy and metabolism[J]. Nat Cell Biol, 2011, 13(9): 1016-1023.

[79] 李四, 刘萍, 冯雪, 等. 川芎嗪对动物模型动脉粥样硬化作用及机制的系统评价和荟萃分析[J]. 公共科学图书馆综合, 2022, 17(5): e0267968.
LI S, LIU P, FENG X, et al. The role and mechanism of tetramethylpyrazine for atherosclerosis in animal models: A systematic review and Meta-analysis[J]. PLoS One, 2022, 17(5): e0267968.

[80] 李文婷, 郑舒宁, 张琪, 等. 基于网络药理学探讨黄芪-川芎药对对糖尿病周围神经病变作用机制的研究[J]. 上海中医药杂

志,2022,55(1):6-12,34.
LI W T,ZHENG S N,ZHANG Q,et al. Mechanism of Astragalus-Chuanxiong herb pair on diabetic peripheral neuropathy based on network pharmacology[J]. Shanghai J Tradit Chin Med,2022,55(1):6-12,34.

[81] XIA D,LI W,TANG C,et al. Astragaloside Ⅳ,as a potential anticancer agent[J]. Front Pharmacol,2023,14:1065505.

[82] ZHU H,ZHENG L,ZHANG K,et al. Astragaloside Ⅳ improves diabetic kidney disease by regulating NLRP3 inflammasome[J]. J Diabetes Res,2025,2025(1):3340719.

[83] YANG S,ZHANG W,XUAN L L,et al. Akebia saponin D inhibits the formation of atherosclerosis in ApoE mice by attenuating oxidative stress-induced apoptosis in endothelial cells[J]. Atherosclerosis,2019,285:23-30.

[84] LIU X,LIANG Q,JIANG W,et al. Curcumin and its novel formulations for diabetes mellitus and its complications:A review[J]. Food Funct,2025,16(18):6965-6999.

[85] NI H X,YU N J,YANG X H. The study of ginsenoside on PPARγ expression of mononuclear macrophage in type 2 diabetes[J]. Mol Biol Rep,2010,37(6):2975-2979.

[86] 张冰冰,朱爱松,石岩. 从 Toll 受体 3 介导的信号传导通路探讨中药益糖康对糖尿病小鼠动脉粥样硬化的影响[J]. 中华中医药杂志,2019,34(10):4885-4888.
ZHANG B B,ZHU A S,SHI Y. Influence of traditional Chinese medicine Yitangkang on atherosclerosis in diabetic mice based on Toll receptor 3-mediated signaling pathway[J]. China J Tradit Chin Med Pharm,2019,34(10):4885-4888.

[87] WANG M,JIN L,ZHANG Q,et al. Curcumin analog JM-2 alleviates diabetic cardiomyopathy inflammation and remodeling by inhibiting the NF-κB pathway[J]. Biomed Pharmacother,2022,154:113590.

[88] 李冬方,顾宁,黄娟. 黄芪多糖对 THP-1 巨噬细胞 HSP60 诱导下 IL-6,TNF-α 表达的影响[J]. 时珍国医国药,2015,26(12):2830-2832.
LI D F,GU N,HUANG J. Effects of Astragalus polysaccharides on the expression of IL-6 and TNF-α induced by HSP60 in THP-1 macrophages[J]. Lishizhen Med Mater Med Res,2015,26(12):2830-2832.

[89] 朱文举,左菁. 糖尿病肾病患者 TyG,SAA 与动脉粥样硬化的相关性研究[J]. 临床医学进展,2022,12(4):2535-2540.
ZHU W J,ZUO J. Study on the correlation between TyG,SAA and atherosclerosis in patients with diabetic nephropathy[J]. Adv Clin Med,2022,12(4):2535-2540.

[90] 葛争艳,金龙,郭宇洁,等. 降糖消脂片对转基因小鼠降糖降脂作用的实验研究[J]. 中国中西医结合杂志,2012,32(8):1095-1098.
GE Z Y,JIN L,GUO Y J,et al. Experimental study on the hypoglycemic and hypolipidemic effects of Jiangtang Xiaozhi tablet on transgenic mice[J]. Chin J Integr Tradit West Med,2012,32(8):1095-1098.

[91] HENG X P,CHEN K J,HU Z F,et al. Glucose endothelial cytotoxicity and protection by Dan Gua-Fang,a Chinese herb prescription in HUVEC in hyperglycemia medium[J]. J Diabetes Complications,2009,23(5):297-303.

[92] HANNA R N,SHAKED I,HUBBELING H G,et al. NR4A1(Nur77)deletion polarizes macrophages toward an inflammatory phenotype and increases atherosclerosis[J]. Circ Res,2012,110(3):416-427.

[93] 黄苏萍,林如辉,陈文列,等. 丹瓜方对糖尿病大鼠胸主动脉超微结构影响的初步观察[J]. 福建中医药大学学报,2011,21(2):19-22.
HUANG S P,LIN R H,CHEN W L,et al. Preliminary observation on the effect of Dangua formula on the ultrastructure of thoracic aorta in diabetic rats[J]. J Fujian Univ Tradit Chin Med,2011,21(2):19-22.

[94] 衡先培,陈可冀,洪振丰,等. 高糖培养 ECV304 内 ROS 含量变化及丹瓜方影响的研究[J]. 光明中医,2008,23(5):551-555.
HENG X P,CHEN K J,HONG Z F,et al. Study on the change of ROS content in ECV304 cultured with high glucose and the influence of Dangua formula[J]. Guangming J Chin Med,2008,23(5):551-555.

[95] 刘超,王琳,姚凤云,等. 加味温胆汤调控 NF-κB/NLRP3 通路干预炎性反应抗大鼠糖尿病动脉粥样硬化的机制[J]. 中国实验方剂学杂志,2024,30(14):71-77.
LIU C,WANG L,YAO F Y,et al. Mechanism of modified Wendan decoction in regulating NF-κB/NLRP3 pathway to intervene inflammatory response against diabetic atherosclerosis in rats[J]. Chin J Exp Tradit Med Form,2024,30(14):71-77.

[96] 刘超,左铮云,王炳志,等. 加味温胆汤对雌性营养性肥胖大鼠 LEP,ACC 和 MCA 的影响[J]. 中国实验方剂学杂志,2020,26(1):87-91.
LIU C,ZUO Z Y,WANG B Z,et al. Effects of modified Wendan decoction on LEP,ACC and MCA in female nutritional obese rats[J]. Chin J Exp Tradit Med Form,2020,26(1):87-91.

[97] 符显昭,蒋晓凤,陈佳俊,等. 基于自噬理论探讨活血解毒降糖方对糖尿病动脉粥样硬化的影响[J]. 现代中西医结合杂志,2023,32(14):1899-1905,1977.
FU X Z,JIANG X F,CHEN J J,et al. Influence of Huoxue Jiedu Jiangtang formula on diabetic atherosclerosis based on autophagy theory[J]. Mod J Integr Tradit Chin West Med,2023,32(14):1899-1905,1977.

[98] 吴钧俊,叶军. 健脾益气方对初诊 2 型糖尿病患者胰岛β细胞功能的影响[J]. 中医学报,2015,30(4):490-492.
WU J J,YE J. Effect of Jianpi Yiqi formula on islet β-cell function in patients with newly diagnosed type 2 diabetes[J]. Acta Chin Med,2015,30(4):490-492.

[99] 邓龙飞,顾晶晶,黄珍祯,等. 健脾消渴方改善 2 型糖尿病大鼠药效学研究[J]. 辽宁中医药大学学报,2024,26(9):32-37.
DENG L F,GU J J,HUANG Z Z,et al. Pharmacodynamic study of Jianpi Xiaoke formula on improving type 2 diabetic rats[J]. J Liaoning Univ Tradit Chin Med,2024,26(9):32-37.

[100] 陆远凤,梁高敏,杨生. 浅析饮食疗法在消渴病中的重要性[J]. 现代诊断与治疗,2024,14:157.
LU Y F,LIANG G M,YANG S. Analysis of the importance of diet therapy in diabetes mellitus[J]. Mod Diagn Treat,2024,

14:157.

[101] 冯利,庄安琪,李轶维,等. 基于网络药理学和体外研究探究瓜蒌薤白半夏汤治疗动脉粥样硬化的机制[J]. 中国药理学通报,2022,38(6):904-912.
FENG L,ZHUANG A Q,LI Y W,et al. Exploring the mechanism of Gualou Xiebai Banxia decoction in the treatment of atherosclerosis based on network pharmacology and in vitro studies[J]. Chin Pharmacol Bull,2022,38(6):904-912.

[102] 毕东雨,范颖,李洪洲,等. 黄芪葛根汤与瓜蒌汤合方对糖尿病动脉粥样硬化大鼠主动脉 SIRT1/AMPK 信号通路的影响[J]. 中华中医药杂志,2024,39(2):951-956.
BI D Y,FAN Y,LI H Z,et al. Effect of Huangqi Gegen decoction combined with Gualou decoction on SIRT1/AMPK signaling pathway in aorta of diabetic atherosclerosis rats[J]. China J Tradit Chin Med Pharm,2024,39(2):951-956.

[103] 李茂宸,范颖,李洪洲,等. 黄芪葛根汤与远志汤合方抑制糖尿病动脉粥样硬化大鼠主动脉内皮细胞间质化的作用机制[J]. 安徽中医药大学学报,2023,42(4):61-66.
LI M C,FAN Y,LI H Z,et al. Mechanism of Huangqi Gegen decoction combined with Yuanzhi decoction in inhibiting aortic endothelial-to-mesenchymal transition in diabetic atherosclerosis rats[J]. J Anhui Univ Chin Med,2023,42(4):61-66.

[104] 李秋芳,王文恺,龚曼,等. 当归补血汤及其活性成分通过NLRP3/ASC/caspase-1通路调控糖尿病大鼠动脉粥样硬化及网络药理学研究[J]. 中成药,2022,44(6):1987-1992.
LI Q F,WANG W K,GONG M,et al. Danggui Buxue decoction and its active components regulate atherosclerosis in diabetic rats via NLRP3/ASC/Caspase-1 pathway and network pharmacology study[J]. Chin Tradit Pat Med,2022,44(6):1987-1992.

[105] 谢心,樊月月,吴坚. 知葛通脉颗粒对糖尿病动脉粥样硬化大鼠斑块组织炎症因子蛋白及mRNA表达影响的实验研究[J]. 上海中医药杂志,2022,56(4):72-78.
XIE X,FAN Y Y,WU J. Experimental study on the effects of Zhige Tongmai granules on the expression of inflammatory factor proteins and mRNA in plaque tissues of diabetic atherosclerosis rats[J]. Shanghai J Tradit Chin Med,2022,56(4):72-78.

[106] KATAKAMI N. Mechanism of development of atherosclerosis and cardiovascular disease in diabetes mellitus[J]. J Atheroscler Thromb,2018,25(1):27-39.

[107] KHAN A W,JANDELEIT-DAHM K A. Atherosclerosis in diabetes mellitus:Novel mechanisms and mechanism-based therapeutic approaches[J]. Nat Rev Cardiol,2025,22(7):482-496.

[108] 衡先培,黄苏萍,程心玲,等. 丹栝方干预糖尿病动脉粥样硬化大鼠糖脂代谢及氧化应激研究[J]. 中国中西医结合杂志,2013,33(2):244-251.
HENG X P,HUANG S P,CHENG X L,et al. Study on Dangua formula intervening glucose and lipid metabolism and oxidative stress in diabetic atherosclerosis rats[J]. Chin J Integr Tradit West Med,2013,33(2):244-251.

[109] KARAKASIS P,THEOFILIS P,PATOULIAS D,et al. Diabetes-driven atherosclerosis:Updated mechanistic insights and novel therapeutic strategies[J]. Int J Mol Sci,2025,26(5):2196.

[责任编辑　吕冬梅]