

姜黄素在糖尿病防治中的作用机制与生物利用度提升策略研究进展

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摘 要

糖尿病的发生与进展涉及氧化应激、炎症、胰岛素信号异常及 β 细胞功能受损等多重机制。姜黄素具有抗氧化、抗炎、调节葡萄糖代谢及保护 β 细胞等多靶点作用, 但其口服生物利用度极低严重限制其应用。本综述概述姜黄素的主要降糖机制, 并总结比较辅助吸收、纳米脂质载体等提升其利用度策略的效果。新型递送策略虽能显著提高姜黄素体内暴露与降糖效果, 但安全性与临床证据仍不足, 未来需加强相关研究以推动其转化。

关键词

姜黄素, 糖尿病, 生物利用度, 纳米脂质载体

Advances in the Mechanisms of Curcumin in the Prevention and Treatment of Diabetes and Strategies to Enhance Its Bioavailability

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Abstract

The onset and progression of diabetes involve multiple mechanisms, including oxidative stress,

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inflammation, impaired insulin signaling, and dysfunction of pancreatic β cells. Curcumin exerts multi-target actions—antioxidant, anti-inflammatory, glucose-regulatory, and β -cell-protective—but its extremely low oral bioavailability severely limits clinical application. This review summarizes the primary antidiabetic mechanisms of curcumin and compares the effectiveness of bioavailability-enhancing strategies such as co-administration with adjuvants and nanostructured lipid carriers. Although these advanced delivery approaches markedly increase systemic exposure and glycemic benefits, their safety profiles and clinical evidence remain insufficient. Further research is needed to support translational development.

Keywords

Curcumin, Diabetes, Bioavailability, Nanostructured Lipid Carriers

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1. 引言

1.1. 2 型糖尿病的病理特征与流行现状

2 型糖尿病(Type 2 Diabetes Mellitus, T2DM)是由胰岛素分泌不足和胰岛素抵抗共同作用引起的慢性代谢性疾病,其主要病理表现为胰岛素分泌功能受损、胰岛素作用不良、葡萄糖代谢异常[1]-[3]。当前糖尿病的主要治疗策略包括口服降糖药和外源性胰岛素替代等,然而这些方法存在一定局限性,例如药物副作用、长期依赖性等[4]-[6]。寻找新的治疗策略具有重大意义,而天然植物活性成分因其对糖尿病的良好干预效果和安全性逐渐成为研究热点[7]-[9]。

1.2. 姜黄素的理化性质与生物活性

姜黄素(Curcumin)是姜黄根茎中的主要活性成分,其呈橙黄色结晶粉末,水溶解度极低,碱性条件或光下易降解[10]-[12]。已有研究表明,姜黄素具有抗氧化、抗炎、降低空腹血糖(Fasting Blood Glucose, FBG)、降低糖化血红蛋白(Glycated Hemoglobin, HbA1c)等作用,因此也被视为糖尿病防治研究的有力候选者[13]-[22]。生物利用度较低是姜黄素作为营养补充剂应用的核心瓶颈,严重阻碍其从实验研究向临床应用的转化[16] [23]。

本综述总结姜黄素防治糖尿病的分子机制,并介绍微乳(Microemulsion, ME)、自乳化体系(Self-Emulsifying Drug Delivery System, SEDDS)、固体分散体(Solid Dispersion, SD)及纳米脂质载体(Nanostructured Lipid Carriers, NLC)等提升姜黄素生物利用度的主要递送策略的设计理念与优势,分析比较其潜力与局限,为姜黄素临床转化及功能食品开发提供理论支撑与优化思路。

2. 姜黄素防治糖尿病作用的研究证据

2.1. 体外模型研究进展

在体外研究中,已有多条轨迹揭示了姜黄素在细胞模型中的防治糖尿病潜能。在胰岛 β 细胞模型中,姜黄素可显著增强胰岛素分泌与 β 细胞功能。Rouse 等发现,姜黄素能提高胰岛 β 细胞 cAMP 水平,促进胰岛素释放[24]。其他研究亦提示姜黄素能够减轻炎症与氧化应激造成的细胞损伤,改善 β 细胞活性

[25][26]。在肝细胞模型中，姜黄素可改善高糖或脂毒性条件下的胰岛素抵抗。相关研究显示，其能够调节关键代谢信号、缓解氧化与炎症应激，并抑制糖异生相关酶活性，从而改善肝细胞葡萄糖代谢与脂质累积[27]-[29]。在肌细胞中，姜黄素能够改善胰岛素抵抗，研究证实其可促进葡萄糖转运蛋白 4 (Glucose Transporter Type 4, GLUT4)转位、增强葡萄糖摄取，并与胰岛素产生协同效应，改善骨骼肌对葡萄糖的利用[30]-[32]。综合来看，体外证据显示姜黄素可作用于胰岛 β 细胞、肝细胞及肌细胞，通过调节胰岛素分泌及促进葡萄糖摄取来改善代谢，为动物及临床研究提供坚实基础。

2.2. 动物模型研究进展

在糖尿病动物模型中，姜黄素可改善葡萄糖代谢，降低血糖并减轻胰腺损伤[25] [33] [34]。Alsulaim 等发现其可显著降低血糖、甘油三酯和总胆固醇，同时抑制 $TNF-\alpha$ 与 IL-6 表达，减轻胰岛病理改变[35]。Na 等报道姜黄素剂量依赖性降低血糖和血脂，改善葡萄糖耐量，并激活骨骼肌葡萄糖代谢信号通路，缓解胰岛素抵抗[36]。Xia 等亦证实其可改善高血糖与高脂血症[34]。Özsan 等证实其可减轻海马氧化应激与炎症，改善糖尿病神经损伤[37]。Abdulmalek 等发现低剂量姜黄素纳米粒即可显著降低 FBG、改善胰岛素抵抗并调节血脂与肝脏氧化应激[38]。总体而言，动物研究一致表明姜黄素可调节代谢稳态，降低血糖血脂、改善胰岛素信号，并减轻氧化应激与炎症，为临床给药方案和制剂优化提供实验依据。

2.3. 临床试验研究进展

近年来，多项随机对照临床试验(Randomized Controlled Trial, RCT)系统评估了姜黄素在糖尿病及相关代谢异常人群中的干预价值(见表 1)。Panahi 等采用姜黄素联合胡椒碱干预 T2DM 患者，观察到 FBG、HbA1c、C 肽及肝酶水平均显著下降[39]。Lamichhane 等发现姜黄素可显著降低糖尿病前期老年人群的 HbA1c 水平，改善血糖稳态，提示其潜在预防价值[40]。Shafabakhsh 等证实姜黄素可显著降低患者体内丙二醛(malondialdehyde, MDA)水平，提高谷胱甘肽水平与总抗氧化能力(TAC)，改善代谢状态[41]。Yaikwawong 等证明姜黄素可显著降低肥胖合并 T2DM 患者 FBG 和 HbA1c，改善胰岛 β 细胞功能[42]。Thota 等发现姜黄素可改善患者多项代谢指标与胰岛素抵抗，保护胰岛功能[43]。Adab 等报道姜黄素可降低患者体重指数(BMI)，改善甘油三酯、低密度脂蛋白胆固醇(LDL-C)和总胆固醇水平[44]。El-Rakabawy 等研究显示，姜黄素可降低患者的 LDL-C、 $TNF-\alpha$ 、MDA 水平及动脉粥样硬化风险等级[45]。Rahimi 等表明负载姜黄素的纳米胶束可以显著降低 T2DM 患者 HbA1c、FBG、TG 和 BMI 等指标，部分降低血清 LDL-C，提示纳米化姜黄素的良好干预效果[46]。

Table 1. Summary of RCTs on curcumin formulations in patients with type 2 diabetes mellitus
表 1. 姜黄素类制剂用于 T2DM 患者的 RCTs 研究概览表

参考	受试者特征	剂型	剂量	时长	主要结局指标	不良事件
Panahi 等[39]	18~65 岁的 T2DM 患者	姜黄素类药物	姜黄素 500 mg/d，与胡椒碱 5 mg/d 联合服用	8 周	相比于基线水平，两组患者的主要结局指标有以下改变：安慰剂组：FBG：-3 ± 11 mg/dL；C 肽：0.02 ± 0.6 ng/mL；HbA1c：-0.2 ± 0.5%；ALT：-1 ± 5 U/L；AST：-0.3 ± 4 U/L。姜黄素干预组：FBG：-9 ± 16 mg/dL；C 肽：-0.6 ± 0.8 ng/mL；HbA1c：-0.9 ± 1.1%；ALT：-2 ± 6 U/L；AST：-3 ± 5 U/L。	部分受试者出现轻微胃肠不适

续表

Lamichhane 等[40]	年龄 ≥ 60 岁的糖尿病前期或超重/肥胖的老年人	含姜黄素胶囊	80 mg/d	12 周	相比于基线水平，两组患者的主要结局指标有以下改变：姜黄素干预组 HbA1c 降低 0.25%，AST 水平升高；安慰剂组 ALT 水平降低；ALT/AST 比值两组均降低，菌群的 α 多样性和 β 多样性均未发生显著变化但姜黄素干预组肠道有益菌群丰度略有增加；BMI、血脂谱和身体成分无显著变化。	未报告严重不良反应
Shafabakhsh 等[41]	45~85 岁且患有冠心病的 T2DM 患者	姜黄素片剂	1000 mg/d	12 周	相比于安慰剂组，姜黄素干预组的主要结局指标有以下改变：匹兹堡睡眠质量指数：降低 1.27，MDA：降低 0.20 $\mu\text{mol/L}$ ，TAC：升高 75.82 mmol/L，还原型谷胱甘肽 (GSH)：升高 63.48 $\mu\text{mol/L}$ ，PPAR- γ ：显著降低。	未报告严重不良反应
Yaikwawong 等[42]	年龄 ≥ 35 岁且 BMI ≥ 23 kg/m ² 的 T2DM 患者	含姜黄素胶囊	1500 mg/d	12 月	相比于基线水平，两组患者的主要结局指标有以下改变：安慰剂组：FBG：130.71 mg/dL，HbA1c：6.47%，HOMA- β ：105.19，HOMA-IR：6.04，脂联素：10.36 $\mu\text{g/mL}$ ，瘦素：20.66 ng/mL，BMI：29.34 kg/m ² 。姜黄素干预组：FBG：115.49 mg/dL，HbA1c：6.12%，HOMA- β ：136.20，HOMA-IR：4.86，脂联素：14.51 $\mu\text{g/mL}$ ，瘦素：9.42 ng/mL，BMI：25.94 kg/m ² 。	未报告严重不良反应
Thota 等[43]	30~70 岁、BMI 为 25~45 kg/m ² 、澳大利亚 2 型糖尿病风险问卷得分 ≥ 12 分的患者	姜黄素片剂	180 mg/d	12 周	相比于基线水平，两组患者的主要结局指标有以下改变：安慰剂组：糖原合成酶 3 β (GSK-3 β)：-0.3 ± 0.6 ng/mL，胰岛淀粉样多肽(IAPP)：0.4 ± 0.6 ng/mL，HOMA-IR：0.01 ± 0.05。姜黄素干预组：GSK-3 β ：-2.4 ± 0.4 ng/mL，IAPP：-2.0 ± 0.7 ng/mL，HOMA-IR：-0.3 ± 0.1。	未报告严重不良反应
Adab 等[44]	30~70 岁、BMI 为 20~35 kg/m ² 且患有高脂血症的 T2DM 患者	含姜黄素胶囊	2100 mg/d	8 周	相比于基线水平或安慰剂组，姜黄素干预组的主要结局指标有以下改变：体重、BMI、TG、LDL-C 和总胆固醇显著降低(p < 0.05)；FBG、高敏 C 反应蛋白(hs-CRP) 和 TAC 无显著变化。	未报告严重不良反应

续表

El-Rakabawy 等[45]	50~74 岁、10 年 ASCVD 风险评 分 ≥5%且患有高 血压和血脂异常 的 T2DM 患者	含姜黄素 胶囊	1500 mg/d	14 周	相比于安慰剂组，姜黄素干预组的主要结局指标有以下改变：收缩压和舒张压降低，动脉粥样硬化性心血管疾病(ASCVD)风险分级降低，LDL-C、TNF- α 和 MDA 水平降低，HDL-C 水平升高(p 均< 0.05)；HbA1c、FBG、TC 或 TG 水平无显著差异(p > 0.05)。	部分受试者出现轻微不良反应：恶心、头痛、黄便和腹泻
Rahimi 等[46]	年龄 > 18 岁的 T2DM 患者	负载姜黄素的 纳米胶束	80 mg/d	3 月	相比于基线水平或安慰剂组，姜黄素干预组的主要结局指标有以下改变：BMI、FBG、HbA1c、估算平均血糖(eAG)、TG、TC、LDL-C 降低，HDL-C 升高，其中 HbA1c、eAG、LDL-C 和 BMI 存在显著差异(p < 0.05)。	未报告严重不良反应

现有临床证据显示，姜黄素在糖尿病及高危人群中的疗效与递送剂型密切相关，传统粉末姜黄素需高剂量才能发挥降糖效果，且效果波动较大，反应吸收和体内暴露不足。辅助吸收型制剂在中等剂量下即可显著改善胰岛素抵抗指数(HOMA-IR)等指标，显示更高体内稳定性。纳米化姜黄素制剂则在 BMI、HbA1c、LDL-C 等多重指标上均表现显著改善，为临床证据中疗效较优的剂型。总体来看，递送系统从传统粉末到辅助吸收再到纳米化的逐级改良，提升了姜黄素代谢改善幅度与稳定性，表明提高生物利用度是实现临床价值的关键。

3. 姜黄素防治糖尿病作用机制

3.1. 抑制氧化应激机制

在糖尿病的病理过程中，持续高血糖及脂代谢紊乱可诱导活性氧(reactive oxygen species, ROS)过量生成，引起代谢器官的氧化损伤，姜黄素可显著提高实验动物体内抗氧化水平，缓解氧化应激状态。Hou 等研究表明，姜黄素可通过调控胰腺 β 细胞中的 C/EBP 同源蛋白等关键分子，减轻氧化应激，改善 β 细胞功能[47]。Li 等在体内外实验中证实，姜黄素可降低 ROS 的生成，抑制 NADPH 酶活性，并恢复超氧化物歧化酶和过氧化氢酶水平，减少胰岛细胞凋亡并改善其功能[48]。在糖尿病动物模型中，姜黄素上调肝脏抗氧化酶的表达并激活抗氧化通路，增强机体抗氧化能力[26] [49]。综上，姜黄素通过多靶点提升抗氧化酶活性、抑制 ROS 生成并激活相关信号通路，从而有效缓解糖尿病相关氧化应激损伤。

3.2. 抑制炎症反应机制

慢性低度炎症是糖尿病发生与胰岛素抵抗的重要机制之一。姜黄素可通过多靶点抑制炎症因子的表达与相关信号通路的活化。在高糖诱导的细胞及糖尿病动物模型中，姜黄素显著降低血清 TNF- α 、IL-6 水平，并抑制核因子 κ B (nuclear factor- κ B, NF- κ B)及 c-Jun 氨基末端激酶/p38 丝裂原活化蛋白激酶通路的磷酸化活性，从而有效减轻组织炎症反应[50] [51]。临床研究同样发现，补充姜黄素可改善糖尿病患者炎症标志物，提高过氧化物酶体增殖物激活受体 γ (peroxisome proliferator-activated receptor γ , PPAR- γ)表达水平[41]。这些结果表明，姜黄素通过抑制炎症信号和调节代谢相关核受体，发挥系统性抗炎作用。

3.3. 胰岛 β 细胞保护与再生机制

多项基础研究证实, 姜黄素可在糖尿病环境下保护胰岛 β 细胞并促进胰岛结构修复。其主要作用体现在增强 β 细胞的增殖能力、维持胰岛结构完整性及促进组织再生。Badr 等在糖尿病小鼠中观察到, 姜黄素处理可显著扩大胰岛面积并增加 β 细胞数量, 提示其通过改善细胞内应激环境, 有助于促进受损胰岛的结构重建[52]。Weisberg 等进一步报道, 姜黄素可提高 db/db 小鼠胰岛中 Ki-67 阳性细胞比例, 表明其具备促进 β 细胞增殖的能力, 并可能通过调控蛋白酶体相关途径增强细胞修复与再生[53]。此外, Abdel 等的研究显示, 部分姜黄素衍生物同样能够促进胰岛组织再生并改善胰岛素分泌功能, 提示结构优化可能进一步增强其 β 细胞保护效应[54]。综上, 姜黄素在维持胰岛结构、促进 β 细胞增殖和修复方面具有重要潜力。

3.4. 改善胰岛素抵抗机制

胰岛素抵抗是 2 型糖尿病的关键病理基础, 姜黄素在多条代谢信号通路中展现出改善胰岛素抵抗的潜力。Kim 等研究表明姜黄素可促进腺苷酸活化蛋白激酶(AMPK)活化, 抑制糖异生关键酶的表达, 从而改善肝细胞和肌细胞的糖代谢[13] [31]。Na 等证实姜黄素干预可显著降低骨骼肌胰岛素抵抗指数, 并上调胰岛素受体底物-1、磷脂酰肌醇-3-激酶(phosphoinositide 3-kinase, PI3K)和 GLUT4 的表达, 从而提高骨骼肌对葡萄糖的摄取能力[36]。Mohiti 等通过细胞研究表明, 姜黄素可通过激活 AMPK 与蛋白激酶 B (protein kinase B, Akt) 双通路, 改善肌细胞对胰岛素的反应性[30]。Song 等发现姜黄素能够激活 PI3K/Akt/GLUT2 信号通路, 减轻高糖环境导致的胰岛 β 细胞功能损伤[55]。综上, 姜黄素通过调控代谢关键节点, 从多层面恢复胰岛素信号转导, 有助于改善外周组织胰岛素抵抗并维持糖代谢稳态。

3.5. 肠道菌群调节机制

近年来研究发现, 姜黄素还可通过调节肠道菌群与宿主代谢互作通路, 间接改善糖代谢状态。Zhong 等研究显示, 其可通过重塑肠道菌群改善胰岛素抵抗, 粪菌移植实验进一步证明菌群变化在其中具有因果作用[56]。Huang 等证实, 姜黄素在糖尿病大鼠模型中可提高紧密连接蛋白表达、降低 LPS 水平并重塑菌群结构, 改善低度炎症与胰岛素抵抗[57]。Xiao 等则在糖尿病合并结肠炎模型中发现, 姜黄素可同时调节免疫细胞比例与菌群多样性, 相关改善伴随血糖与炎症指标下降[58]。总体而言, 姜黄素通过菌群调控参与葡萄糖稳态、炎症缓解与能量代谢重塑, 这可能构成其改善糖代谢失衡的重要的作用途径。

3.6. 姜黄素主要代谢物的活性及其防治糖尿病的作用机制

姜黄素在体内迅速代谢为四氢姜黄素(Tetrahydrocurcumin, THC)等还原产物及葡萄糖醛酸化、硫酸化结合物[59]。THC 在自由基清除能力及抗炎、抗氧化效应上显示较强活性, 是姜黄素药效的重要执行者[60]-[62]。结合代谢物抗氧化能力较弱, 但可作为可逆“储存库”, 调节姜黄素及还原代谢物的再分布与再活化[63]。多项研究揭示姜黄素代谢物在调节糖代谢与保护胰岛功能方面的关键作用。Kim 等在离体胰岛模型中发现, THC 可减轻 β 细胞凋亡, 改善胰岛功能[64]。Tsai 等在糖尿病小鼠中发现 THC 上调脂联素-受体信号, 增强胰岛素传导[65]。Yuan 等发现, THC 可重塑肠道菌群组成, 上调胰腺 GLP-1 表达, 降低 FBG, 增强血糖调控能力[66]。总体来看, 姜黄素还原代谢物不仅直接保护胰岛 β 细胞, 还通过改善胰岛素抵抗及调节肠道菌群参与系统性代谢调控, 是其体内效应的重要组成部分。

4. 姜黄素生物利用度受限因素及提升策略

4.1. 姜黄素生物利用度受限的关键因素

姜黄素口服后系统暴露极低, 主要受限其水溶性差、肠道吸收率低及体内快速代谢。多项药代研

究表明,即使口服高剂量姜黄素,其在血浆中仍呈极低或难检状态,仅能检测到少量结合代谢物,凸显其生物利用度极低[67]-[70]。

4.2. 姜黄素生物利用度提升策略

4.2.1. 化学结构修饰

多项研究通过化学结构修饰提升姜黄素的理化性质与体内稳定性,显著改善其溶解度,并提高细胞摄取和大鼠口服暴露[71][72]。合理结构修饰可改善姜黄素的吸收与代谢稳定性,为口服制剂优化提供思路。

4.2.2. 物理配方优化

在提升姜黄素口服生物利用度的策略中,物理配方优化尤为实用,主要包括 ME、SEDDS、SD 和 NLC,旨在改善溶解度、稳定性、胃肠道释放及吸收,从而提升系统暴露。

ME、SEDDS 和 SD 可显著提高水系溶出速率与肠道可用性,不同研究中构建的负载姜黄素的 ME、SEDDS、SD 等均显著提高姜黄素暴露量与口服生物利用度[73]-[76]。上述配方主要通过提高溶解度、抑制结晶与改善稳定性发挥作用。

NLC 由固态与液态脂质组成,载药量高、结构稳定、吸收良好,可改善脂溶性药物的生物利用度[77][78]。Madane 等发现鼻用姜黄素纳米粒可显著提高脑组织分布[79]。Fang 等证实姜黄素纳米粒缓释特性,可延长消化道停留时间,提升其生物利用度[80]。Liu 等采用共轭亚油酸构建姜黄素纳米粒,极大提高姜黄素在模拟消化中的生物可及率[81]。Elkhateeb 等发现姜黄素纳米粒可增加其在皮肤各层滞留量以提升药物暴露,而 Sun 等将姜黄素纳米粒融入水凝胶珠,在模拟消化通透中表现出良好稳定性且保留抗氧化活性,为其营养保健制剂应用提供新思路[82][83]。这类基于脂质或高分子材料的纳米载体,已成为姜黄素递送研究的主流方向。

4.2.3. 辅助吸收策略

在不改变化学结构前提下,共用辅剂与代谢抑制是提升姜黄素口服暴露的有效策略。胡椒碱可抑制肠肝葡萄糖醛酸化及 UDP-葡萄糖醛酸转移酶(UGT)等外排蛋白,显著提高血浆暴露[67][84][85]。姜黄素与槲皮素共服可改变姜黄素白蛋白结合、细胞摄取及组织分布,但伴随血浆浓度下降与胆汁外排增加[86]。

4.3. 提升利用度策略对姜黄素代谢谱的影响

生物利用度提升策略可通过改变姜黄素吸收、首过代谢及组织分布,从而影响疗效。药代学研究表明,纳米粒可保护原型分子免受胃肠降解,改善溶解性与肠道转运,并使部分药物经淋巴或脂质通路进入循环,减少首过代谢,可能会改变血浆中结合物与还原代谢物比例[87]-[89]。辅剂如胡椒碱可抑制 UGT 等转运通路,延长原型半衰期[67]。

代谢谱改变可能双向调控药效:原型药物暴露增加可增强直接效应,而 THC 等还原代谢物富集则可能成为主要效应物,放大或改变治疗谱系[90]。尽管已有综述和药代学研究支持该机制,但缺乏系统实证,未来可通过代谢组学技术、药代动力学及药效动力学分析,探索制剂对姜黄素代谢谱及疗效的完整关联[87]。

4.4. 提升利用度策略在糖尿病模型中的应用比较

在糖尿病动物模型中,多种提升姜黄素利用度的策略均显示出代谢改善效应。

化学结构修饰能够增强姜黄素在糖尿病模型中的体内活性,姜黄素三酮改造物在糖尿病大鼠中更有

效地抑制基质金属蛋白酶活性、改善炎症与伤口愈合，并在糖尿病相关骨丧失模型中促进炎症消退、减轻骨质退化[91][92]。Abdel Aziz 等构建的水溶性姜黄素衍生物能提高体内暴露，在糖尿病大鼠中降低血糖、改善胰岛结构并缓解氧化应激[93]。

SEDDS 和 SD 能提高姜黄素在体内溶解度与吸收率，改善血浆暴露和生物利用度，同时对糖尿病相关组织损伤具有保护作用[94]。Khursheed 等研究显示，将负载姜黄素 SEDDS 应用于糖尿病大鼠，可显著改善血糖、血脂水平，并改善胰腺和肝脏组织结构[95]。

NLC 能在提高生物利用度的同时增强降糖与胰岛保护作用，减轻胰岛炎症与 β 细胞凋亡[96]-[98]。Sharma 等证实姜黄素纳米粒可提高血浆暴露并改善血糖与胰岛功能[99]。Abdulmalek 等构建的姜黄素纳米粒能通过激活 Akt、抑制 MAPK 途径，缓解氧化应激与炎症，延缓并发症进展[38]。

辅助吸收策略可提升姜黄素生物利用度并改善部分代谢指标[67][86]。细胞与动物研究显示该策略可抑制高糖诱导的氧化应激与炎症，改善血糖与胰、肝、肾组织功能[100]-[102]。临床研究证实姜黄素-胡椒碱组合可改善 T2DM 患者 FBG、HbA1c 及炎症[39][103]。然而其协同效果并不恒定，部分研究过量胡椒碱可能削弱姜黄素的抗氧化与降糖效应[104]。

化学结构修饰通过优化位点选择性提升稳定性与靶向性，可根本性改善体内暴露，适配长期可控干预需求，但合成复杂且需评估代谢毒性[72][105]。SEDDS 和 SD 能快速改善溶解度与首过吸收，制备简便，适合快速调糖场景，但体内持续性不足[106][107]。NLC 兼具溶解性提升、肠道吸收增加与靶器官递送优势，长期给药潜力突出，但制备及规模化成本高、稳定性需严格控制[108]。胡椒碱等辅助吸收策略廉价易行，可显著抑制姜黄素代谢并已显现临床降糖获益，然而药物相互作用风险需警惕[39][67][104]。化学修饰聚焦改变药物内在性质以实现长期可控疗效，SEDDS/SD、NLC 等递送系统侧重优化吸收与组织分布以放大原药效应，辅助吸收手段则以低成本快速增效为核心，因此策略选择需结合起效时间、给药频次、靶器官需求及生产复杂度综合判定。

5. 未来展望

未来，姜黄素糖尿病防治研究应聚焦机制、制剂优化与临床验证，需提升递送体系效率与安全性，明确活性形式及组织分布，为剂型优化提供依据。临床上应评估其在糖尿病高危人群及代谢共病患者中的干预潜力，探索联合用药应用价值，并开展大样本、多中心研究。随着机制解析与技术完善，姜黄素有望成为糖尿病辅助干预的潜在候选成分，为精准营养与代谢管理提供新方向。

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