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糖酵解对糖尿病及其并发症影响的研究进展

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摘　要

糖尿病(Diabetes Mellitus, DM)是全球高发的代谢性疾病，严重影响患者的生活质量并导致了一系列并发症。糖酵解作为细胞主要的能量生产途径之一，与DM及其并发症的发生和发展密切相关。近年来，糖酵解在DM中的研究取得了重要进展，研究表明糖酵解途径中关键酶的异常表达可能是DM及其并发症的核心病理机制之一。糖酵解的异常不仅破坏了能量代谢的平衡，还可能通过毒性代谢产物的积累加剧糖尿病肾病(DN)、糖尿病心肌病(DCM)、糖尿病视网膜病变(DR)、糖尿病神经病变(DPN)、糖尿病脑血管病(DCVD)等并发症的进展。靶向糖酵解关键酶的治疗策略，展现出对DM及其并发症治疗的巨大潜力，并为新的治疗方法提供了理论依据。

关键词

糖尿病，糖尿病并发症，糖酵解，靶向治疗

Research Progress on the Impact of Glycolysis on Diabetes and Its Complications

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Abstract

Diabetes mellitus (DM) is a globally prevalent metabolic disorder that significantly affects patients' quality of life and leads to various complications. As one of the primary energy-producing pathways in cells, glycolysis is closely associated with the onset and progression of DM and its complications. In recent years, substantial progress has been made in understanding the role of glycolysis in DM. Studies have demonstrated that abnormal expression of key enzymes in the glycolytic pathway may

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be a fundamental pathological mechanism underlying DM and its complications. Dysregulated glycolysis not only disrupts energy metabolism homeostasis but also contributes to the accumulation of toxic metabolic byproducts, thereby exacerbating diabetic nephropathy (DN), diabetic cardiomyopathy (DCM), diabetic retinopathy (DR), diabetic peripheral neuropathy (DPN), and diabetic cerebrovascular disease (DCVD). Therapeutic strategies targeting key glycolytic enzymes have shown great potential in the treatment of DM and its complications, providing a theoretical basis for novel therapeutic approaches.

Keywords

Diabetes Mellitus, Diabetic Complications, Glycolysis, Targeted Therapy

1. 引言

糖尿病(Diabetes Mellitus, DM)是一种以糖代谢紊乱和胰岛素抵抗为特征的慢性代谢性疾病。据统计，2021 年全球 20~79 岁人群中 DM 的患病率约为 10.5% (5.366 亿人)，预计到 2045 年这一数字将上升至 12.2% (7.832 亿人)，表明全球 DM 负担的持续加重[1]。长期高血糖状态会引发多种靶器官损伤，进而导致 DM 相关并发症的发生，如糖尿病肾病(DKD)、糖尿病心肌病(DCM)、糖尿病视网膜病变(DR)、糖尿病周围神经病变(DPN)和糖尿病脑血管病(DCVD)等，严重影响患者的生活质量并增加临床治疗负担。鉴于 DM 及其并发症的高发对人类健康产生巨大威胁，相关的防治研究已成为全球关注的重点。近年来，随着代谢组学的不断发展，糖代谢相关的靶向代谢组学研究已逐渐成为治疗 DM 及其并发症的重要方向之一。糖代谢是体内关键的能量供应途径，包括糖酵解、氧化磷酸化(OXPHOS)、磷酸戊糖代谢、糖原合成与分解、糖异生等多个重要过程。有研究表明，糖酵解途径中关键酶的异常表达可能与 DM 及其并发症的发病机制密切相关，这些酶因此成为潜在的治疗靶点。本文将综述糖酵解在 DM 及其并发症中的作用，以望为相关的靶向防治策略和进一步的机制研究提供理论依据。

2. 糖酵解的定义及作用

在体内，细胞主要利用糖酵解和 OXPHOS 途径进行能量产生和生物合成，两者间的平衡是保障细胞正常代谢的基础，对维持机体生命活动至关重要。在葡萄糖及氧气充足的条件下，细胞倾向于选择 OXPHOS 途径。葡萄糖被摄取后，首先通过糖酵解转化为丙酮酸，然后丙酮酸被转运至线粒体，进入三羧酸循环(TCA)和电子传递链(ETC)生成 ATP。相反，在无氧或缺氧条件下，细胞利用厌氧糖酵解，将丙酮酸转化为乳酸，以更快但效率更低的方式产生 ATP。特别注意的是，某些细胞(如肿瘤细胞)即使是在有氧的情况下，仍主要利用糖酵解产能，这一现象由德国科学家奥托·瓦尔堡(Otto Warburg)首次报道，故将这种特殊的糖酵解现象称为瓦尔堡效应(Warburg effect)，也称有氧糖酵解[2]。具体而言，糖酵解是依靠一系列糖酵解酶协同作用从而产生 ATP 的酶促过程[3]，可分为两个阶段：一是由葡萄糖分解成丙酮酸的过程，称之为酵解途径；二是丙酮酸转变成乳酸的过程。第一阶段又可分为三个步骤，即葡萄糖的磷酸化、磷酸己糖的裂解及 ATP 和丙酮酸的生成，共 10 步酶促反应，净生成 2 个 ATP 和 NADH。在第二阶段，丙酮酸结合第一阶段产生的 NADH，在乳酸脱氢酶(LDH)催化下形成乳酸。

在生理状态下，糖酵解通过产生丙酮酸辅助 OXPHOS 途径，并为生物合成提供中间产物(如乙酰辅

酶 A、磷酸戊糖等)，支持细胞生长和增殖[4]，但在一些病理条件下，糖酵解的异常表达可能会加剧疾病的严重程度。在肿瘤疾病中，糖酵解的上调为肿瘤细胞的生长提供更多能量[5]，促进肿瘤转移，3-溴丙酮酸(3-BrPA)通过抑制己糖激酶(Hexokinase, HK)从而抑制癌细胞增殖[6]；在感染性疾病中，糖酵解的持续活化会导致免疫细胞发生 ATP 耗竭和乳酸酸中毒，最终引发多器官功能障碍[7]，2-脱氧-D-葡萄糖(2-DG)通过抑制糖酵解，减少中性粒细胞募集，达到缓解炎症的目的[8]；在神经退行性疾病中，促进糖酵解途径可提升线粒体质量，为神经元提供大量 ATP，罗沙司他(roxadustat)通过激活 HIF 通路上调糖酵解，以提高神经元缺血耐受性[9]。因此，糖酵解不仅是细胞能量代谢的基本途径，也在多种疾病中展现出重要的治疗潜力。深入研究糖酵解的调控机制及其在疾病中的作用，将为开发新的治疗策略提供理论基础和实践指导。

3. 糖酵解在 DM 及其并发症中的作用

3.1. 糖酵解与 DM

DM 的本质是胰岛素作用的缺陷，按胰岛素分泌的情况 DM 可分为 1 型和 2 型[10]。1 型糖尿病(Type 1 Diabetes Mellitus, T1DM)是一类自身免疫性疾病，常见于儿童和青少年，在自身免疫系统攻击下，胰岛 β 细胞发生不可逆破坏，导致胰岛素分泌绝对不足，需要终生使用外源胰岛素治疗。2 型糖尿病(Type 2 Diabetes Mellitus, T2DM)主要以胰岛素抵(IR)和胰岛素分泌缺陷为特征，通常发生在成年后期，先表现为糖耐量受损，随后胰岛 β 细胞功能进行性减退，导致分泌的胰岛素量减少，血糖水平升高。

胰岛素抵抗、高血糖与糖酵解之间的相互作用在 DM 的发生发展中占据核心地位。慢性高血糖状态会导致糖酵解代谢通量异常增加，尤其通过稳定己糖激酶-2 (Hexokinase 2, HK2)活性，导致糖酵解途径在未受调控的情况下持续进行[11]。这种代谢失衡在胰腺 β 细胞中表现为磷酸果糖激酶(Phosphofructokinase, PFK)与甘油醛-3-磷酸脱氢酶(GAPDH)之间的中间产物异常蓄积，并伴有 GAPDH 活性降低。GAPDH 活性抑制不仅造成糖酵解途径阻滞，更直接导致线粒体 OXPHOS 受损及 ATP 合成减少[12]，使得 β 细胞胰岛素分泌功能显著下降，最终发展为不可逆的糖毒性介导的 β 细胞衰竭[13]。在胰岛素敏感组织(如骨骼肌和脂肪组织)中，糖酵解超负荷会干扰胰岛素信号通路，进一步加剧胰岛素抵抗[14]-[16]。此外，高血糖通过促进糖酵解过程从而激活肝脏糖异生途径，形成肝源性葡萄糖输出的恶性循环，进一步加重高血糖状态[17]。特别的是，不同组织间的糖酵解调控存在异质性，如 β 细胞的糖酵解亢进与功能衰竭相关，而骨骼肌的糖酵解抑制则与葡萄糖摄取障碍相关，这种组织特异性差异共同推动了 DM 进展[18]。

3.2. 糖酵解与 DM 并发症

DM 往往会引发一系列并发症，糖酵解在这些并发症中同样起着重要作用，以下是糖酵解与一些 DM 常见并发症的联系。

3.2.1. 糖尿病肾病

糖尿病肾病(Diabetic Nephropathy, DN)是 DM 最常见的并发症之一，通常表现为肾小球基底膜增厚、足细胞足突融合、肾小管上皮间质纤维化及进行性蛋白尿等病理特征[16]。高血糖诱发的糖酵解紊乱通过多种机制参与 DN 发生发展，该过程涉及了肾小球内皮细胞(GECs)、足细胞等关键细胞类型及复杂的信号调控网络[17] [18]。研究揭示，高糖微环境显著激活 GECs 的糖酵解通路，糖酵解相关蛋白的上调不仅促进了血管生成，还破坏了肾小球滤过屏障，加速了 DN 进程[19]。足细胞作为肾小球的关键结构细胞，对糖酵解能量供给具有高度依赖性。研究表明，DN 患者足细胞糖酵解通量异常，这使足细胞产生更高水平的毒性葡萄糖代谢物、线粒体功能障碍和细胞凋亡[20]。这种“能量饥饿”状态引发足细胞骨架蛋白结

构重塑，促使足突融合与脱落，最终发展为不可逆的蛋白渗漏[21]。另外，作为糖酵解副产物，甲基乙二醛(MGO)通过促进氧化应激和蛋白质修饰，直接损伤肾小球基底膜并诱导足细胞凋亡[22]。

3.2.2. 糖尿病心肌病

糖尿病心肌病(Diabetic Cardiomyopathy, DCM)是 DM 特有的心脏损伤表现，其主要病理特征包括心室扩张、心肌肥大、心肌纤维化和心脏功能障碍[23]，DCM 发病机制涉及心肌能量代谢异常、氧化应激、细胞凋亡及纤维化等多方面因素。正常心脏具有代谢灵活性，可根据能量需求动态调节葡萄糖和脂肪酸的利用[24]，但 DM 心脏表现为糖酵解抑制和脂肪酸氧化增强的代谢失衡现象[25] [26]。这种代谢失衡不仅通过抑制糖酵解相关酶活性降低果糖-2,6-二磷酸(F-2,6-P)水平，进而削弱糖酵解通量对能量需求的动态响应能力[27]，还直接阻碍了缺氧诱导因子(HIF)介导的适应性糖酵解代偿途径，进一步加重了心肌能量危机与缺血损伤[28]。值得注意的是，糖酵解代谢产物(如乳酸)的生成减少虽在慢性病程中加重能量代谢缺陷，但在急性缺血期可能通过减轻质子蓄积和细胞内酸中毒发挥保护作用，这也部分解释了 DM 心脏对特定缺血刺激的耐受现象[29]。这种矛盾效应与糖毒性损伤交织存在，表现为 MGO 通过形成 AGEs 直接损伤心肌细胞结构和功能，造成进行性心功能衰竭[30]。

3.2.3. 糖尿病视网膜病变

糖尿病视网膜病变(Diabetic Retinopathy, DR)作为 DM 特异性微血管并发症，其病理进程涵盖血管损伤、神经退行性变与代谢紊乱的交互作用[31] [32]。临床特征呈现从早期血视网膜屏障(BRB)破坏、慢性炎症进展至晚期病理性微动脉瘤形成的动态演变[33] [34]，其中糖酵解代谢异常通过时空特异性调控机制贯穿疾病全程。在 DR 早期，高糖微环境驱动视网膜内皮细胞(RECs)糖酵解过度活化，其副产物乳酸或晚期糖基化终末产物(AGEs)将会破坏内皮细胞屏障功能[35]；视网膜微胶质细胞启动代谢重编程，实现从氧化磷酸化向有氧糖酵解转换，促进其 M1 型极化并释放促炎因子，进一步放大神经炎症和神经元损伤[36]。而在光感受器细胞中，糖酵解关键酶表达下降，从而影响参与调节光感受器功能的磷酸二酯酶 6β (PDE6β)，导致光感受器功能障碍[37]。在 DR 晚期，糖酵解产生的乳酸在玻璃体中过度沉积，加剧视网膜缺血微环境，激活炎症反应并最终促进了病理性新生血管形成[38]。

3.2.4. 糖尿病周围神经病变

糖尿病周围神经病变(Diabetic Peripheral Neuropathy, DPN)作为 DM 最具致残性的并发症之一，其核心病理特征为周围神经纤维的“逆向死亡”现象——从远端轴突逐渐向近端神经胞体发展的退行性改变，伴随雪旺细胞去分化和神经内膜微血管病变[39]。近年研究揭示，DN 致病机制与糖酵解–线粒体代谢失衡密切相关[40]。DM 状态下，高血糖通过抑制神经元及雪旺细胞的线粒体 OXPHOS，迫使其转向糖酵解功能，导致能量代谢紊乱[41]。糖酵解异常导致了 MGO 及乳酸的积累，引发局部缺氧和氧化应激，进一步损害线粒体功能并抑制 TCA 循环[42] [43]。长期的代谢失衡导致神经生长锥能量匮乏，从而抑制轴突再生和侧支发芽能力，加速了 DPN 发展[44]。也有研究表明，在糖酵解代偿性升高的同时，伴随了糖酵解中间体的显著减少，提示糖酵解通路可能仍处于受阻状态[45]，胰岛素样生长因子-1 (IGF-1)通过提升糖酵解能力，缓解了 DM 大鼠背根神经节(DRG)神经元的能量不足[46]。

3.2.5. 糖尿病脑血管病

糖尿病脑血管病(Diabetic Cerebrovascular Disease, DCVD)是 DM 常见的大血管并发症之一，主要表现为动脉粥样硬化、血栓形成或出血等脑血管病，并最终可能引发缺血性或出血性脑血管事件[47]。糖酵解途径异常及其毒性代谢产物 MGO 在这一过程中发挥着关键作用。高血糖通过增强糖酵解通量促使 MGO 生成增加，而 DM 患者乙二醛酶系统(Glo1)功能受损导致 MGO 清除障碍，形成病理性蓄积[48]。

过量 MGO 通过非酶糖基化反应生成晚期糖基化终末产物(AGEs)，沉积于脑血管中破坏内皮细胞功能并激活 RAGE 受体，引发炎症反应和氧化应激，加剧血脑屏障通透性增加及微血管功能障碍。同时，MGO 可剂量依赖性地激活内质网应激反应中的 PERK、IRE1α 和 ATF6 通路，诱导血管平滑肌细胞凋亡并促进动脉粥样硬化斑块形成，进一步加速 DM 引发的脑血管重构[49]。有趣的是，性别差异在 DCVD 中呈现独特代谢代偿现象，表现为雌性 DM 小鼠的血糖和乳酸水平较高，但它们对缺血的耐受性显著优于雄性。其原因之一可能是雌激素通过上调糖酵解通路，提供了保护效应，从而增强了雌性小鼠对缺血的耐受能力[50]。

4. 糖酵解的治疗靶点及其靶向药物

以上研究结果提示，糖酵解在 DM 及其并发症的发生发展中具有重要作用，对糖酵解关键节点进行靶向调控可能成为治疗 DM 及其并发症的新策略。接下来，本文将围绕糖酵解关键酶作为 DM 及其并发症治疗靶点的研究展开探讨。

4.1. 葡萄糖转运蛋白

葡萄糖转运蛋白(Glucose Transporters, GLUT)家族通过易化扩散方式介导葡萄糖跨膜运输，其表达水平和活性直接调控细胞内葡萄糖供应量，从而影响糖酵解速率[51]。在肌肉和脂肪组织中，胰岛素通过促进 GLUT4 从细胞内囊泡向质膜转位，显著增强葡萄糖摄取，进而为糖酵解提供底物。研究显示，胰岛素抵抗状态下，DM 患者骨骼肌细胞膜上 GLUT4 数量减少，导致葡萄糖流入受阻，这可能与 DM 引起的高血糖有直接关系[52]。长期高血糖还会导致血管内皮细胞 GLUT 亚型表达异常，具体表现为冠状动脉内皮中 GLUT1、3、4、5 显著下调而 GLUT2 异常上调，而 GLUT2 的异常上调可能通过增强葡萄糖毒性加速微血管病变发展[53]。在肝脏中，GLUT-2 的表达及膜转位受损会导致肝糖输出调节异常，现已有研究发现 DM 大鼠肝细胞膜 GLUT-2 易位减少，而牛磺酸可通过激活 PI3K/Akt 通路增强其膜定位，改善糖代谢紊乱[54]。同时，有研究发现肝细胞 GLUT-2 的转录水平受 HCV 病毒复制抑制，而干扰素治疗可恢复其启动子活性，提示抗病毒治疗在调控 GLUT 的过程中可能对 DM 具有潜在益处[55]。另外，脑内 GLUT 异常表达或分布可能加剧神经元功能损伤或 β 淀粉样蛋白生成，表明 GLUT 在 DPN 中的重要作用[56] [57]。这些发现共同表明，通过精准调控特定组织中 GLUT 亚型的表达和分布，可为 DM 及其并发症的治疗提供新的干预策略。

4.2. 己糖激酶

HK 是糖酵解途径的起始关键酶，催化葡萄糖磷酸化生成葡萄糖-6-磷酸(G6P)，这一反应不仅是糖酵解的限速步骤[58]，还决定了葡萄糖代谢的后续分流方向(如糖酵解、磷酸戊糖途径或糖原合成)。HK 家族包括 HK1、HK2、HK3 和葡萄糖激酶(GCK/HK4)，这些亚型在不同组织中具有特定的表达模式和功能差异。HK2 作为存在于胰岛素敏感组织(骨骼肌、脂肪)及胰岛 β 细胞的核心亚型[59]，在高血糖环境下因底物结合稳定性增强而逃避蛋白酶降解，导致持续性激活引发“计划外糖酵解”(unscheduled glycolysis)，进而引发胰岛素抵抗、β 细胞糖毒性及血管并发症[60]。此外，HK 具备的线粒体膜定位特性使其通过调节氧化还原信号和能量代谢进一步影响 DM 病理进程[61]。研究发现，抑制 HK2 活性可减少糖酵解超载从而缓解 DM 及其并发症[62]，提示 HK 可作为治疗 DM 的潜在靶点。临床药物如二甲双胍通过重构 HK 与 PFK 的酶活性分布，恢复了 DM 小鼠模型中的糖酵解节律[63]。此外，SGLT2 抑制剂(如恩格列净)通过抑制 HK2 介导的糖酵解副产物积累，阻止了 DN 中的上皮－间质转化(EMT)进程[3。更具启发意义的是，HK 在不同器官中的功能异质性为精准干预提供依据。例如，心肌组织中 HK2 表达下调引发的能量

危机可通过 HIF-1α 激活实现代谢补偿[64]，而视网膜病变中 HK2 活性抑制可减少病理性新生血管形成[65]。基因组学研究进一步揭示 HK 多态性的临床价值：HK1-rs201626997 与 HK3-rs143604141 位点变异显著影响南亚人群 DM 易感性[66]，而 HK2 基因突变可能导致外周组织特异性胰岛素抵抗，这为基于代谢酶基因型的个体化治疗指明了方向[67]。

4.3. 磷酸果糖激酶

PFK 作为糖酵解网络的中央调控枢纽，存在多种亚型(如 PFKM、PFKL、PFKP)，负责催化果糖-6-磷酸(F6P)不可逆转化为 F-1,6-BP，构建了葡萄糖代谢的速率决定屏障。PFK 在骨骼肌、心肌等组织中活性降低，且其与细胞骨架的结合能力受损，这可能是加剧 DM 患者胰岛素抵抗和糖代谢障碍的原因之一[68]。在 DCM 患者中，PFK 的同工酶 PFK-2 发生降解打乱了糖酵解与糖异生的平衡，使心肌代谢灵活性丧失，加速了 DCM 发展[69]。动物模型证实，在增加 PFK-2 活性后，DCM 小鼠心脏功能得以增强[70]。当前，针对 PFK 作为 DM 治疗靶点的研究已陆续出现。小分子 PhAM 抵消了原钒酸钠与 PFK-1 的结合，提升了 PFK-1 活性从而降低了血糖水平[71]；而 PFK-3 抑制剂 3PO 通过阻断内皮细胞糖酵解流，减少了视网膜病理性新生血管的形成[72]；PFK15 通过抑制 PFK-3 下调 CD4+ T 细胞的糖酵解速率，缓解了 T 细胞对 β 细胞抗原的反应，延缓了 DM 的发作[73]。特别的是，经典降糖药物二甲双胍被证明对 DM 心脏具有保护作用，该治疗效果与其对 PFK-3 等糖酵解限速酶具有调节作用有关[74]。这些研究进一步验证了 PFK 作为多靶点治疗枢纽的临床价值。

4.4. 丙酮酸激酶

丙酮酸激酶(Pyruvate Kinase, PK)作为糖酵解终末能量转化枢纽，通过催化磷酸烯醇式丙酮酸(PEP)向丙酮酸的不可逆转化，不仅直接决定 ATP 生成效率，更通过调控代谢中间产物分布影响糖异生与糖酵解的代谢平衡[75]。PK 具有四种亚型(PKM1、PKM2、PKL、PKR)，而 PKM2 因其在胰岛素敏感组织及内皮细胞中呈现出独特的可塑性[76]，是 PK 相关研究领域的重点。DM 状态下，PKM2 的四聚体解离导致丙酮酸生成减少，严重影响 ATP 生成和胰岛素分泌，削弱了胰岛 β 细胞对血糖水平的响应能力，从而加剧 DM 的代谢异常[77]。同样，有研究证实在肾脏组织中，PKM2 的 Cys358 位点发生氧化，PKM2 四聚体减少促使足细胞凋亡，而靶向激活剂 TEPP-46 可通过稳定四聚体构象逆转高血糖对足细胞产生的毒性作用[20]。然而，PKM2 二聚体作为蛋白激酶发挥非代谢性作用的过程仍不可忽视。相关研究提示，PKM2 二聚体通过调控磷酸二酯酶 6β (PDE6β)的降解速率，提升环磷鸟嘌呤核苷(cGMP)水平，导致光感受器细胞凋亡，参与 DR 早期病变[37]，并通过磷酸化 STAT3 等信号分子加剧 DN 的纤维化进程[78]，而 TEPP-46 的使用逆转了这一现象。由此可见，PK 亚型构象的多能性为 DM 及其并发症提供了新型“构象靶向”治疗策略。

4.5. 乳酸脱氢酶

乳酸脱氢酶(Lactate Dehydrogenase, LDH)是由两种亚基(M 亚基和 H 亚基)组成的四聚体。作为糖酵解终末酶，主要通过催化丙酮酸与乳酸的可逆转化维持 NAD^+再生循环，其活性动态平衡对缺氧条件下细胞能量代谢至关重要[79]。研究显示，在 DR 及 DN 患者体内 LDH 水平显著提高，提示 LDH 或可作为 DR 及 DN 进展的生物标志物[80] [81]。在神经系统并发症中，DM 模型海马区乳酸水平随病程持续上升，并伴随 LDH-A 表达及酶活性全面上调，这种糖酵解代偿亢进通过破坏神经元氧化还原稳态诱发认知功能障碍，而 LDH 特异性抑制剂草酸盐可显著改善 DM 相关的记忆损伤[82]。关于 LDH 抑制剂治疗 DM 的研究中，发现天然活性成分如丹皮酚通过下调 LDH 活性联合抗氧化机制，显著降低 DR 的氧化应激水

平[83]；二苯基二硒化物(DPDS)通过抑制 LDH 活性同步改善高血糖与氧化损伤。除此之外，LDH 抑制剂在联合二甲双胍治疗 DM 中表现出显著效果。草酸酯作为 LDH 的一种抑制剂，与二甲双胍联用的过程中可减低其引发的高血乳酸，协同增强抗炎及胰岛素增敏作用，这为代谢－炎症联合干预提供了新思路[84]。

5. 展望

糖酵解在 DM 及其并发症中的作用已经得到了广泛关注。研究发现，糖酵解异常通过破坏能量代谢、积累有害代谢产物和引发氧化应激，推动了 DM 的发生和发展。糖酵解不仅在 DM 的代谢失调中起着关键作用，还在 DM 并发症的形成过程中扮演着重要角色。因此，调控糖酵解已成为 DM 及其并发症治疗中的一个热点研究方向，靶向糖酵解关键酶的治疗策略展现出了显著潜力。尽管已有许多研究表明糖酵解关键酶作为潜在治疗靶点具有可行性，但糖酵解在 DM 不同组织中的调控机制存在差异。各个组织对糖酵解的依赖性及其调节方式不同，这为 DM 的治疗提出了新的挑战和机会。未来的研究应聚焦于深入理解糖酵解在不同组织中的调控模式，探索如何针对特定组织的糖酵解异常进行个性化干预，以更有效地防治 DM 及其并发症。

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