

Dysfunctional glucose metabolism triggers oxidative stress to induce kidney injury in diabetes

Meng Gao, Meng-Ting Dai, Guo-Hua Gong

Specialty type: Endocrinology and metabolism

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade A, Grade B, Grade C, Grade C

Novelty: Grade B, Grade B, Grade B, Grade B

Creativity or Innovation: Grade B, Grade B, Grade B, Grade C

Scientific Significance: Grade B, Grade B, Grade B, Grade B

P-Reviewer: Correa TL; Hu WG; Kehinde SA

Received: October 22, 2024

Revised: January 14, 2025

Accepted: February 5, 2025

Published online: April 15, 2025

Processing time: 129 Days and 23 Hours



Meng Gao, Meng-Ting Dai, Guo-Hua Gong, School of Laboratory Medicine and Life Sciences, Wenzhou Medical University, Wenzhou 325035, Zhejiang Province, China

Meng Gao, Institute for Regenerative Medicine, Shanghai East Hospital, School of Life Sciences and Technology, Tongji University, Shanghai 200092, China

Corresponding author: Guo-Hua Gong, PhD, Professor, School of Laboratory Medicine and Life Sciences, Wenzhou Medical University, Chashan Higher Education Park, Wenzhou 325035, Zhejiang Province, China. guohgong@wmu.edu.cn

Abstract

In this editorial, we discussed the article published in the recent issue of the *World Journal of Diabetes*. To understand the effect of mizagliflozin on kidney injury induced by diabetes, we focused on the mechanisms by which high glucose triggers oxidative stress and contributes to kidney injury in diabetes. The high level of unmetabolized glucose reaching the kidney triggers glucose reabsorption by renal tubules, which elevates the cellular glucose level of renal cells. High glucose induces lactate dehydrogenase overexpression and thus shifts glucose metabolism, which causes mitochondrial dysfunction. Mitochondria generate approximately 90% of the reactive oxygen species in cells, whose dysfunction further alters glucose metabolism and enhances reactive oxygen species generation. Oxidative stress stimulates proinflammatory factor production and kidney inflammatory injury. Mizagliflozin decreases glucose reabsorption and thus ameliorates diabetes-induced kidney injury.

Key Words: Glucose metabolism; Sodium-D-glucose cotransporter 1; Glucose reabsorption; Mitochondrial dysfunction; Reactive oxygen species; Inflammation

©The Author(s) 2025. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: In diabetes, insulin resistance and insufficient insulin release lead to a decrease in glucose uptake by muscles and fat tissues, resulting in elevated blood glucose levels, which are dangerous to human organs. The tolerance of high glucose switches the metabolism of glucose, which causes mitochondrial dysfunction. Oxidative stress induced by excess reactive oxygen species generated by dysfunctional mitochondria causes cell damage and thus stimulates proinflammatory factor production and tissue injury. Therefore, antidiabetic therapies are aimed at decreasing blood glucose and oxidative stress.

Citation: Gao M, Dai MT, Gong GH. Dysfunctional glucose metabolism triggers oxidative stress to induce kidney injury in diabetes. *World J Diabetes* 2025; 16(4): 102554

URL: <https://www.wjgnet.com/1948-9358/full/v16/i4/102554.htm>

DOI: <https://dx.doi.org/10.4239/wjd.v16.i4.102554>

INTRODUCTION

Diabetes mellitus is defined as hyperglycemia in both the fasting and postprandial states[1]. Insulin serves as the primary regulator of blood glucose levels. Insufficient insulin release and suppressed insulin action (named insulin resistance) lead to increased glucose production in the liver and decreased glucose uptake by muscles and fat tissues, resulting in elevated blood glucose concentrations, which are dangerous to human health[2,3]. Hyperglycemia can contribute to increased reactive oxygen species (ROS) generation and upregulate markers of inflammation, which ultimately cause tissue dysfunction. Conversely, increased oxidative stress and inflammation further increase insulin resistance and impair insulin secretion[2,4,5]. Diabetes can cause serious health complications. In patients with diabetes, persistent hyperglycemia and disorders of metabolic pathways cause damage to various tissues and organs, which increases the risk of cardiovascular disease and can result in disorders such as diabetic retinopathy, neuropathy, and nephropathy (Figure 1) [6-8]. The complications of diabetes are far more harmful than those of diabetes itself[7].

Diabetic nephropathy (DN), one of the most important long-term complications of diabetes, is the major cause of end-stage renal disease and high mortality in patients with diabetes[9,10]. Thus, protecting the kidney is very important for patients with diabetes. High blood glucose and oxidative stress are the major contributors to kidney injury; therefore, anti-DN is aimed at inhibiting excess blood glucose and ROS overproduction[1,4].

Glucose is taken up in the kidney *via* sodium-D-glucose cotransporters (SGLTs), which further maintain high levels of serum glucose to play an important role in diabetic kidney injury. The two most well-known members of the SGLT family are SGLT1 and SGLT2[11]. SGLT1 is located on the apical side of the proximal tubule and facilitates the reabsorption of urinary glucose from the glomerular filtrate. SGLT1 accounts for most of the dietary glucose absorption in the intestine and the renal reabsorption of glucose in the kidney, especially in patients with uncontrolled diabetes and those receiving SGLT2 inhibitors[12,13]. Inhibiting SGLT1 can reduce the risk of cardiovascular death and improve nonalcoholic steatohepatitis by reducing glycogen accumulation and decreasing the production of mitochondrial ROS[13-15]. Currently, novel antidiabetic drugs aimed at lowering blood glucose through the inhibition of SGLT in the intestine and kidney have been developed. Mizagliflozin (MIZ) is a potent, orally active, and selective SGLT1 inhibitor that has been used as an antidiabetic agent that can modify postprandial blood glucose excursion[16-18].

MECHANISMS OF HIGH GLUCOSE TRIGGER OXIDATIVE STRESS AND KIDNEY INFLAMMATORY INJURY

Oxidative stress, which is defined by a disturbance in the balance between ROS production and antioxidant defenses, plays a critical role in cellular physiology and pathophysiology and is associated with the initiation and progression of numerous diseases[19,20]. Chronic oxidative stress induces lipid peroxidation, protein modifications, and DNA damage[21]. Increased ROS generation plays a crucial role in the pathogenesis of diabetes, including DN[2]. Mitochondria, as the power plants of cells, play pivotal roles in adenosine triphosphate production and ROS generation. They are extremely sensitive to environmental stimuli, including hypoxia, drugs, toxicity, and changes in nutrient supply[22,23]. Mitochondrial alterations serve as the primary driving force for cellular malfunction before and after insulin resistance[24]. Dysfunctional mitochondria-produced ROS overwhelm intrinsic antioxidant defenses, causing oxidative stress, which can lead to deleterious oxidative damage to DNA, proteins, and membrane lipids and chronic inflammation[25]. Conversely, inflammation can lead to oxidative stress[26].

At present, there is strong evidence that the hyperglycemia-induced overproduction of superoxide by the extracellular matrix proteins and attenuated antioxidant defenses are recognized as major causes of the clinical complications associated with diabetes[2,27]. High blood glucose triggers lactate dehydrogenase (LDH) overexpression and enhances the rate of the anaerobic glycolytic pathway, reduces glucose oxidation, and decreases fatty acid β -oxidation[28,29]. Dysfunctional metabolism causes mitochondrial dysfunction, which augments ROS generation. Moreover, long-chain free fatty acid accumulation can inactivate mitochondrial enzymatic activity and hinder electron transport, thus further increasing ROS production, and saturated free fatty acids can also induce chronic inflammation[30-32]. Other metabolic pathways are also involved in oxidative stress development, including the enhanced formation of advanced glycation end products,

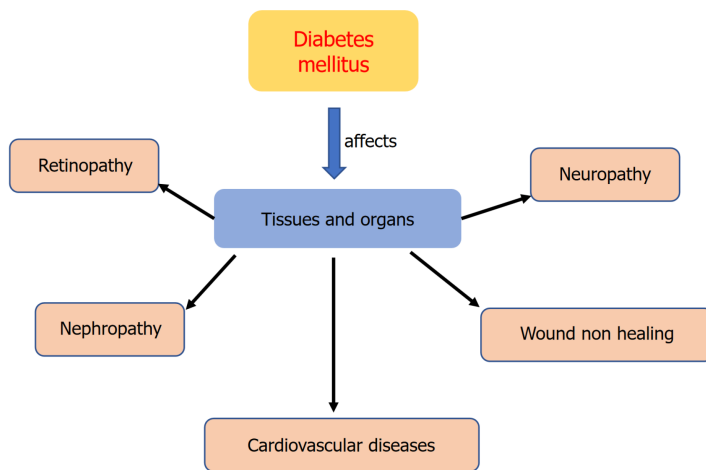


Figure 1 Common complications of diabetes mellitus. Chronic hyperglycemia stimulates tissues and organs, which causes multiple problems and pathological changes including retinopathy, neuropathy, nephropathy, cardiovascular diseases, and chronic healing.

the hexosamine pathway, the polyol metabolism pathway, and the activation of protein kinase C, which are thought to be involved in the pathogenesis of DN[2,33,34]. Mitochondrial metabolic reprogramming is characterized by mitochondrial biosynthesis dysfunction, increased glycolysis, and abnormal lipid and amino acid metabolism, which significantly influences the pathophysiological progression of DN. Increased fatty acid oxidation in diabetes leads to an increase in the level of oxidized low-density lipoproteins, which activates the nuclear factor kappa B signaling pathway[35]. Once activated, it translocates to the nucleus and is bound to a specific section of DNA that triggers the expression of various proinflammatory cytokines, such as interleukin (IL)-6, tumor necrosis factor (TNF)- α , and transforming growth factor beta, and chemokines (Figure 2)[36].

Glucose levels and metabolite-generated ROS play major roles in the development of various diabetes-related complications. Therefore, antidiabetic therapies are aimed at decreasing blood glucose and oxidative stress[2,37]. Numerous studies have demonstrated the effectiveness of various antioxidants (Q10, α -lipoic acid, coenzymes, and glutathione are the principal intracellular antioxidant buffers against oxidative stress) in the treatment of diabetes mellitus[38,39].

MIZ TARGETS SGLT2 TO DECREASE GLUCOSE REABSORPTION IN THE KIDNEY

MIZ, a potent selective SGLT1 inhibitor, can decrease glucose reabsorption in the kidney. Lin *et al*[40] reported that “mizagliflozin ameliorates diabetes induced kidney injury by inflammation and oxidative stress”. High glucose increased the expression of SGLT1, LDH, TNF- α/β , and IL-1 β and the levels of superoxide dismutase and malondialdehyde and decreased the levels of catalase and glutathione peroxidase. MIZ treatment decreased the protein expression of SGLT1, which decreased glucose reabsorption under high-glucose conditions. It would be better if these effects were supported with SGLT1 knockdown studies. Decreased cellular glucose can normalize glucose metabolism and thus reverse LDH expression and ROS generation[40]. If mitochondrial functions were measured, the authors could see the restoration of those functions. For oxidative stress, it is necessary to analyze the level of ROS, which are the major mediators of oxidative stress, *via* confocal microscopy or spectrophotometer *via* the use of mitochondrial ROS or 2’7’-dichlorofluorescein diacetate dye. The decreased ROS restored antioxidant defenses and deactivated the nuclear factor kappa B signaling pathway, which reduced TNF- α/β and IL-1 β expression and apoptosis (should be analyzed in cells). Thus, MIZ effectively ameliorated kidney injury in patients with diabetes (Figure 2).

Compared with canagliflozin, MIZ resulted in greater improvement in LDH levels caused by high glucose. In addition to reducing serum glucose and kidney protection, most SGLT1 and SGLT2 inhibitors provide cardiovascular and liver protection[41]. However, SGLT2 has rarely been detected in human hearts, whereas SGLT1 is highly expressed in the myocardium. As SGLT2 inhibitors also have a moderate inhibitory effect on SGLT1, the cardiovascular protection of SGLT2 inhibitors may be due to SGLT1 inhibition[42].

CONCLUSION

High glucose-induced cellular metabolism triggers mitochondrial dysfunction, oxidative stress, and inflammation in diabetes. Thus, restoring glucose metabolism and mitochondrial function is important for diabetic therapy. Inhibiting glucose absorption and reabsorption through the suppression of SGLT1 plus antioxidants represents a potentially new therapeutic approach in the diabetic mellitus therapeutic process. Given the role of mitochondria in metabolism and ROS generation, future efforts should focus on validating mitochondrial protection mechanisms in DN.

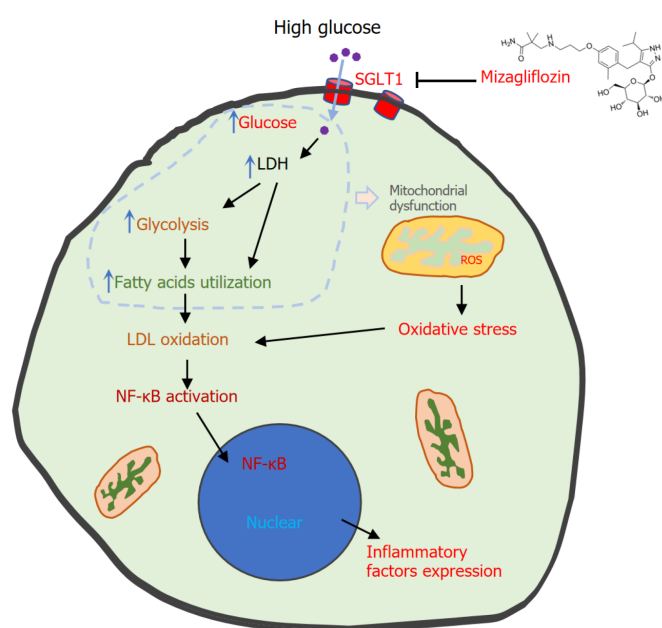


Figure 2 High glucose induces kidney cell injury and the protective effect of mizagliflozin. High glucose is absorbed into the cytosol and induces lactate dehydrogenase overexpression and thus shifts metabolism (glycolysis and fatty acid oxidation), which causes mitochondrial dysfunction. Dysfunctional mitochondria generate excessive reactive oxygen species, causing oxidative stress. Low-density lipoprotein oxidation leads to nuclear factor kappa B activation, which further triggers the expression of inflammatory factors. Oxidative stress and inflammation contribute to kidney cell injury. Mizagliflozin inhibits sodium-D-glucose cotransporter 1 and changes these processes, thus protecting cells. LDH: Lactate dehydrogenase; LDL: Low-density lipoproteins; NF-κB: Nuclear factor kappa B; ROS: reactive oxygen species; SGLT1: Sodium-D-glucose cotransporter 1.

FOOTNOTES

Author contributions: Gao M and Dai MT contributed to the discussion of the literature and design of the manuscript; Gao M and Gong GH contributed to the writing and editing of the manuscript; Gong GH designed the overall concept and outline of the manuscript; All authors read and approved the final version of the manuscript to be published.

Supported by The Basic Research Project of Wenzhou Municipal Science and Technology Bureau, No. Y20240008; The Medical Health Science and Technology Project of Zhejiang Provincial Health Commission, No. 2024KY138; and The Key Laboratory of School of Laboratory Medicine and Life Sciences, Wenzhou Medical University of China, No. JS2023003.

Conflict-of-interest statement: All authors declare no conflict of interest in publishing the manuscript.

Open Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country of origin: China

ORCID number: Guo-Hua Gong 0000-0002-9652-1040.

S-Editor: Luo ML

L-Editor: Filipodia

P-Editor: Xu ZH

REFERENCES

- Wang L, Peng W, Zhao Z, Zhang M, Shi Z, Song Z, Zhang X, Li C, Huang Z, Sun X, Wang L, Zhou M, Wu J, Wang Y. Prevalence and Treatment of Diabetes in China, 2013-2018. *JAMA* 2021; **326**: 2498-2506 [PMID: 34962526 DOI: 10.1001/jama.2021.22208]
- Darenskaya MA, Kolesnikova LI, Kolesnikov SI. Oxidative Stress: Pathogenetic Role in Diabetes Mellitus and Its Complications and Therapeutic Approaches to Correction. *Bull Exp Biol Med* 2021; **171**: 179-189 [PMID: 34173093 DOI: 10.1007/s10517-021-05191-7]
- Amiel SA. The consequences of hypoglycaemia. *Diabetologia* 2021; **64**: 963-970 [PMID: 33550443 DOI: 10.1007/s00125-020-05366-3]
- Luc K, Schramm-Luc A, Guzik TJ, Micolajczyk TP. Oxidative stress and inflammatory markers in prediabetes and diabetes. *J Physiol Pharmacol* 2019; **70** [PMID: 32084643 DOI: 10.26402/jpp.2019.6.01]
- Hernandez LF, Eguchi N, Whaley D, Alexander M, Tantisattamo E, Ichii H. Anti-Oxidative Therapy in Diabetic Nephropathy. *Front Biosci*

- (Schol Ed) 2022; **14**: 14 [PMID: 35730439 DOI: 10.31083/j.fbs1402014]
- 6 **Zhang Q**, Lu L, Wang J, Lu M, Liu D, Zhou C, Liu Z. Metabolomic profiling reveals the step-wise alteration of bile acid metabolism in patients with diabetic kidney disease. *Nutr Diabetes* 2024; **14**: 85 [PMID: 39384774 DOI: 10.1038/s41387-024-00315-0]
 - 7 **Yu MG**, Gordin D, Fu J, Park K, Li Q, King GL. Protective Factors and the Pathogenesis of Complications in Diabetes. *Endocr Rev* 2024; **45**: 227-252 [PMID: 37638875 DOI: 10.1210/endrev/bnad030]
 - 8 **Wang Y**, Jin M, Cheng CK, Li Q. Tubular injury in diabetic kidney disease: molecular mechanisms and potential therapeutic perspectives. *Front Endocrinol (Lausanne)* 2023; **14**: 1238927 [PMID: 37600689 DOI: 10.3389/fendo.2023.1238927]
 - 9 **Reutens AT**. Epidemiology of diabetic kidney disease. *Med Clin North Am* 2013; **97**: 1-18 [PMID: 23290726 DOI: 10.1016/j.mcna.2012.10.001]
 - 10 **Sagoo MK**, Gnudi L. Diabetic Nephropathy: An Overview. *Methods Mol Biol* 2020; **2067**: 3-7 [PMID: 31701441 DOI: 10.1007/978-1-4939-9841-8_1]
 - 11 **Lv Y**, Cheng X, Dong Q. SGLT1 and SGLT2 inhibition, circulating metabolites, and cerebral small vessel disease: a mediation Mendelian Randomization study. *Cardiovasc Diabetol* 2024; **23**: 157 [PMID: 38715111 DOI: 10.1186/s12933-024-02255-6]
 - 12 **Rieg T**, Vallon V. Development of SGLT1 and SGLT2 inhibitors. *Diabetologia* 2018; **61**: 2079-2086 [PMID: 30132033 DOI: 10.1007/s00125-018-4654-7]
 - 13 **Tsimihodimos V**, Filippas-Ntekouan S, Elisaf M. SGLT1 inhibition: Pros and cons. *Eur J Pharmacol* 2018; **838**: 153-156 [PMID: 30240793 DOI: 10.1016/j.ejphar.2018.09.019]
 - 14 **Tran BAC**, White RT, Bullers K, Cornelio CK. A Review of the Potential Role of Sotagliflozin: A Dual SGLT2 and SGLT1 Inhibitor-in the Treatment of Heart Failure. *J Pharm Technol* 2024; **40**: 248-256 [PMID: 39391325 DOI: 10.1177/87551225241261040]
 - 15 **Harrison SA**, Manghi FP, Smith WB, Alpenidze D, Aizenberg D, Klarenbeek N, Chen CY, Zuckerman E, Ravussin E, Charatcharoenwitthaya P, Cheng PN, Katchman H, Klein S, Ben-Ari Z, Mendonza AE, Zhang Y, Martic M, Ma S, Kao S, Tanner S, Pachori A, Badman MK, He Y, Ukomadu C, Sicard E. Licogliflozin for nonalcoholic steatohepatitis: a randomized, double-blind, placebo-controlled, phase 2a study. *Nat Med* 2022; **28**: 1432-1438 [PMID: 35725922 DOI: 10.1038/s41591-022-01861-9]
 - 16 **Inoue T**, Takemura M, Fushimi N, Fujimori Y, Onozato T, Kurooka T, Asari T, Takeda H, Kobayashi M, Nishibe H, Isaji M. Mizagliflozin, a novel selective SGLT1 inhibitor, exhibits potential in the amelioration of chronic constipation. *Eur J Pharmacol* 2017; **806**: 25-31 [PMID: 28410751 DOI: 10.1016/j.ejphar.2017.04.010]
 - 17 **Ishida N**, Saito M, Sato S, Tezuka Y, Sanbe A, Taira E, Hirose M. Effects of mizagliflozin, a selective SGLT1 inhibitor, on chronic hypoperfusion-induced vascular cognitive impairment. *Proceedings for Annual Meeting of The Japanese Pharmacological Society* 2022; **95**: 3-P [DOI: 10.1254/jpsuppl.95.0_3-p-195]
 - 18 **Fukudo S**, Kaku K. Effect of Mizagliflozin on Postprandial Plasma Glucose in Patients With Functional Constipation. *J Neurogastroenterol Motil* 2019; **25**: 332-333 [PMID: 30982244 DOI: 10.5056/jnm19010]
 - 19 **Liu B**, Chen L, Gao M, Dai M, Zheng Y, Qu L, Zhang J, Gong G. A comparative study of the efficiency of mitochondria-targeted antioxidants MitoTEMPO and SKQ1 under oxidative stress. *Free Radic Biol Med* 2024; **224**: 117-129 [PMID: 39178922 DOI: 10.1016/j.freeradbiomed.2024.08.022]
 - 20 **Li A**, Gao M, Liu B, Qin Y, Chen L, Liu H, Gong G. Inhibition of mitochondrial superoxide promotes the development of hiPS-CMs during differentiation. *Free Radic Biol Med* 2022; **190**: 94-104 [PMID: 35952922 DOI: 10.1016/j.freeradbiomed.2022.08.005]
 - 21 **Kaarniranta K**, Uusitalo H, Blasiak J, Felszeghy S, Kannan R, Kauppinen A, Salminen A, Sinha D, Ferrington D. Mechanisms of mitochondrial dysfunction and their impact on age-related macular degeneration. *Prog Retin Eye Res* 2020; **79**: 100858 [PMID: 32298788 DOI: 10.1016/j.preteyeres.2020.100858]
 - 22 **Gao M**, Qin Y, Li A, Wei S, Liu B, Tian X, Gong G. Mitoflash generated at the Qo site of mitochondrial Complex III. *J Cell Physiol* 2021; **236**: 2920-2933 [PMID: 32930405 DOI: 10.1002/jcp.30059]
 - 23 **Li A**, Qin Y, Gong G. The Changes of Mitochondria during Aging and Regeneration. *Adv Biol (Weinh)* 2024; **8**: e2300445 [PMID: 38979843 DOI: 10.1002/adbi.202300445]
 - 24 **Townsend LK**, Brunetta HS, Mori MAS. Mitochondria-associated ER membranes in glucose homeostasis and insulin resistance. *Am J Physiol Endocrinol Metab* 2020; **319**: E1053-E1060 [PMID: 32985254 DOI: 10.1152/ajpendo.00271.2020]
 - 25 **Hussain T**, Tan B, Yin Y, Blachier F, Tossou MC, Rahu N. Oxidative Stress and Inflammation: What Polyphenols Can Do for Us? *Oxid Med Cell Longev* 2016; **2016**: 7432797 [PMID: 27738491 DOI: 10.1155/2016/7432797]
 - 26 **Wang P**, Xie K, Wang C, Bi J. Oxidative stress induced by lipid peroxidation is related with inflammation of demyelination and neurodegeneration in multiple sclerosis. *Eur Neurol* 2014; **72**: 249-254 [PMID: 25277682 DOI: 10.1159/000363515]
 - 27 **Catherwood MA**, Powell LA, Anderson P, McMaster D, Sharpe PC, Trimble ER. Glucose-induced oxidative stress in mesangial cells. *Kidney Int* 2002; **61**: 599-608 [PMID: 11849402 DOI: 10.1046/j.1523-1755.2002.00168.x]
 - 28 **Ding J**, Karp JE, Emadi A. Elevated lactate dehydrogenase (LDH) can be a marker of immune suppression in cancer: Interplay between hematologic and solid neoplastic clones and their microenvironments. *Cancer Biomark* 2017; **19**: 353-363 [PMID: 28582845 DOI: 10.3233/CBM-160336]
 - 29 **Zhao C**, Rutter GA. Overexpression of lactate dehydrogenase A attenuates glucose-induced insulin secretion in stable MIN-6 beta-cell lines. *FEBS Lett* 1998; **430**: 213-216 [PMID: 9688541 DOI: 10.1016/s0014-5793(98)00600-0]
 - 30 **Schönfeld P**, Wojtczak L. Fatty acids decrease mitochondrial generation of reactive oxygen species at the reverse electron transport but increase it at the forward transport. *Biochim Biophys Acta* 2007; **1767**: 1032-1040 [PMID: 17588527 DOI: 10.1016/j.bbabo.2007.04.005]
 - 31 **Qin Y**, Li A, Liu B, Gao M, Gong G. Letter to the editor: Compromised hepatic mitochondrial fatty acid oxidation and reduced markers of mitochondrial turnover in human NAFLD. *Hepatology* 2022; **76**: E104-E105 [PMID: 35491446 DOI: 10.1002/hep.32551]
 - 32 **Engin AB**. What Is Lipotoxicity? *Adv Exp Med Biol* 2017; **960**: 197-220 [PMID: 28585200 DOI: 10.1007/978-3-319-48382-5_8]
 - 33 **Fukami K**, Yamagishi S, Ueda S, Okuda S. Role of AGEs in diabetic nephropathy. *Curr Pharm Des* 2008; **14**: 946-952 [PMID: 18473844 DOI: 10.2174/138161208784139710]
 - 34 **Pham TK**, Nguyen THT, Yun HR, Vasileva EA, Mishchenko NP, Fedoreyev SA, Stonik VA, Vu TT, Nguyen HQ, Cho SW, Kim HK, Han J. Echinochrome A Prevents Diabetic Nephropathy by Inhibiting the PKC-Iota Pathway and Enhancing Renal Mitochondrial Function in db/db Mice. *Mar Drugs* 2023; **21**: 222 [PMID: 37103361 DOI: 10.3390/md21040222]
 - 35 **Noll C**, Carpentier AC. Dietary fatty acid metabolism in prediabetes. *Curr Opin Lipidol* 2017; **28**: 1-10 [PMID: 27870654 DOI: 10.1097/MOL.0000000000000369]

- 36 **Mengstie MA**, Abebe EC, Teklemariam AB, Mulu AT, Teshome AA, Zewde EA, Muche ZT, Azezew MT. Molecular and cellular mechanisms in diabetic heart failure: Potential therapeutic targets. *Front Endocrinol (Lausanne)* 2022; **13**: 947294 [PMID: [36120460](#) DOI: [10.3389/fendo.2022.947294](#)]
- 37 **Sun J**, Han J, Dong J, Zhai X, Zhang R. A kidney-targeted chitosan-melanin nanoplatfrom for alleviating diabetic nephropathy through modulation of blood glucose and oxidative stress. *Int J Biol Macromol* 2024; **264**: 130663 [PMID: [38453104](#) DOI: [10.1016/j.ijbiomac.2024.130663](#)]
- 38 **Ahmadvand H**, Tavafi M, Khosrowbeygi A. Amelioration of altered antioxidant enzymes activity and glomerulosclerosis by coenzyme Q10 in alloxan-induced diabetic rats. *J Diabetes Complications* 2012; **26**: 476-482 [PMID: [22795334](#) DOI: [10.1016/j.jdiacomp.2012.06.004](#)]
- 39 **Dludla PV**, Ziqubu K, Mabhida SE, Mazibuko-Mbeje SE, Hanser S, Nkambule BB, Basson AK, Pfeiffer C, Tiano L, Kengne AP. Dietary Supplements Potentially Target Plasma Glutathione Levels to Improve Cardiometabolic Health in Patients with Diabetes Mellitus: A Systematic Review of Randomized Clinical Trials. *Nutrients* 2023; **15**: 944 [PMID: [36839303](#) DOI: [10.3390/nu15040944](#)]
- 40 **Lin ZM**, Gao HY, Shi SH, Li YT. Mizagliflozin ameliorates diabetes induced kidney injury by inhibitor inhibit inflammation and oxidative stress. *World J Diabetes* 2025; **16**: 92711 [PMID: [39817219](#) DOI: [10.4239/wjd.v16.i1.92711](#)]
- 41 **Liang X**, Hou X, Bouhamdan M, Sun Y, Song Z, Rajagopalan C, Jiang H, Wei HG, Song J, Yang D, Guo Y, Zhang Y, Mou H, Zhang J, Chen YE, Sun F, Jin JP, Zhang K, Xu J. Sotagliflozin attenuates liver-associated disorders in cystic fibrosis rabbits. *JCI Insight* 2024; **9**: e165826 [PMID: [38358827](#) DOI: [10.1172/jci.insight.165826](#)]
- 42 **Zhao M**, Li N, Zhou H. SGLT1: A Potential Drug Target for Cardiovascular Disease. *Drug Des Devel Ther* 2023; **17**: 2011-2023 [PMID: [37435096](#) DOI: [10.2147/DDDT.S418321](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

