International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 23s, 2025
https://theaspd.com/index.php

Evaluation Of The Protective Role Of Empagliflozin In Inflammation-Triggered Kidney Disease In Preclinical Settings

Meenu[1], Mohd Aqil[2], Syed Ehtaisham Ul Haque[3], Mohd Akhtar[4], Abul Kalam Najmi[5*]
[1,2,3,4,5*]School of Pharmaceutical Education and Research (SPER), Jamia Hamdard, New Delhi 110062, India.

Abstract
Inflammation has a critical part in the occurrence of diabetes mellitus (DM) and diabetic nephropathy (DN). DN, if not adequately controlled, is the principal basis for progression to end-stage renal disease. DN, existing with albuminuria, glomerulosclerosis, and decreased glomerular filtration rate, is driven by complex pathophysiological mechanisms, including inflammation as a center of causative mechanisms. In DN, high glucose levels promote renal inflammation via NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) transcription factors activation. NF-κB after phosphorylation further triggers transcriptional up-regulation of NLRP3 (NLR family pyrin domain containing 3), upregulates inflammatory cytokines, and stimulates the inflammatory cascade leading to renal injury. Despite current therapies for DM, the progression of DN remains a challenge. Empagliflozin (EMP) is a sodium-glucose cotransporter 2 inhibitor. EMP has shown promising renoprotective effects beyond glycemic control in DN. Preclinical studies in animal models have demonstrated renoprotective effects of EMP beyond glycemic control, especially through its antiinflammatory properties. However, the role of EMP in the protection of DN via modulation of inflammatory pathways is still not clear. This review highlights the current evidence from preclinical animal studies that explore the effect of EMP in protecting against diabetic-associated kidney disease (DKD) through the inhibition of inflammatory pathways.
Keywords: *Diabetic nephropathy, empagliflozin, inflammation, NF-κB and NLRP3.*

INTRODUCTION

Diabetes mellitus (DM) is a metabolism related condition that have the features of high glucose levels in blood along with insulin resistance (Yang et al., 2020). If not adequately controlled then DM can progress to diabetic nephropathy (DN) (Bhattacharjee et al., 2016; Khanra et al., 2017). As per current estimates, worldwide, there are ~580 million peoples with diabetes and by 2050 this number will increase to ~850 million (IDF, 2025). DN is the principle basis for end-stage renal disease (ESRD). Most of the patents diagnosed with DM are of type 2 diabetes (~90%) and 20-50% of these patents may progress to ESRD (Aboismaiel et al., 2024; Gao et al., 2021; Hoogeveen, 2022).

DN, existing with albuminuria, glomerulosclerosis, and decrease glomerular filtration rate, is driven by complex pathophysiological mechanisms including glomerular hyperfiltration, oxidative stress, fibrosis, hemodynamic changes, and inflammation (Habli, 2024). Amongst these mechanisms inflammation has emerged as a central contributor to DN progression (Bhattacharjee et al., 2016).

Despite current therapies for DM, the progression of DN remains a challenge. Sodium-glucose cotransporter protein 2 (SGLT2) is present on the epithelial lining of proximal tubule. SGLT2 inhibitors (SGLT2i) can successfully lower high blood glucose (via enhanced glucose excretion) without raising the risk of hypoglycemia as they are not insulin dependent. Several studies indicates that SGLT2i could counteract inflammation associated with DM conditions in kidney and liver of metabolic disease models (Benetti, 2016; Hsia, 2017). Dapagliflozin, canagliflozin, and empagliflozin (EMP) are some of the currently available SGLT-2i; with EMP being highly selective for SGLT2 compared to SGLT1. EMP, originally developed as a hypoglycemic agent targeting SGLT2 in the renal proximal tubules, has been shown antiinflammatory effects, making it a potential disease-modifying agent for diabetic kidney disease (DKD). However, its role on the protection of DKD via modulation of inflammatory signals is still not clear.

Therefore, the present review evaluated the preclinical data on the role of EMP in protection of DKD via modulation of inflammatory triggers.

LITERATURE REVIEW

Literature search was performed in PubMed to provide a complete and current update on the published literature, aiming to identify preclinical data on the protective role of EMP in kidney disease. Several search terms, “inflammation”, “diabetes”, “nephropathy”, “kidney disease” or “renal injury” along with “empagliflozin”

were used to identify relevant literature. Additionally, data from ScienceDirect and Google Scholar was also searched. The potentially relevant articles were identified for the role of EMP in protection of kidney disease via modulation of inflammatory triggers. These articles are summarized in this review.

Empagliflozin and inhibition of inflammation in kidney disease: Evidence from animal studies

Inflammation has a critical part in the occurrence of DN (Dua et al., 2021). In DKD, high glucose levels promotes renal inflammation by activating transcription factors like NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) and upregulating inflammatory cytokines (Aboismaiel et al., 2024; Sahakyan et al., 2022). These mediators recruit immune cells to renal tissue, resulting in tubular injury, and glomerular damage (Donate-Correa et al., 2021). Modulation of inflammatory pathways is key area for inhibiting disease progression. EMP has shown promising results in progression of DKD via inhibition of inflammatory signaling pathways (Table 1).

Table 1: Pharmacological data of empagliflozin in DKD

References	Model	Key Findings	Inflammatory Markers Affected
Al-Wakeel et al. 2022	CAF-induced insulin resistance in rats	Hypoglycemic, renoprotective, hepatoprotective, antiinflammatory, and antiapoptotic effect	NF-κB and TNF-α
Awad and Younis 2023	STZ-induced DN in albino rats	Antioxidative and antiinflammatory effect	TNF-α, IL-1β, and IL-6
Badreldin et al. 2024	AF-induced AKI in rats	Modulation of the Nrf2/HO-1 and NF-κB/TNF-α signaling pathways, and antiinflammatory effect	TNF-α and IL-6
Fang et al. 2024	HFD and STZ-induced diabetes in C57BL/6J mice	Improvement of renal function by reducing inflammation	NF-κB, NLRP3, and IL-1β
Gembardt et al. 2014	BTBR ob/ob T2D mice	Antihyperglycemic, renoprotective, and antiinflammatory effect	MCP-1, RANTES and IL-6
Guo et al. 2020	db/db mice	Inhibition of renal SGLT2 and activation of p-AMPK, and antiinflammatory effect	IL-6 and MCP-1
Huang et al. 2024	C57BLKS/J-db/m and C57BLKS/J-db/db induced by EndMT	Suppression of VEGF-C/VEGFR3 pathway and reduction of lymphangiogenesis	TNF-α, IL-1β, TGF-β1, and VEGF-C
Madhag and Al-Isawi 2024	STZ and fructose-induced DM in Sprague Dawley rats	Improved renal function, decreased apoptosis and inflammation	IL-6 and TNF-α
Mujalli et al. 2023	HF/HFD-induced obesity and insulin resistance in C57BL/6J mice	Improved glucose status, renoprotective and antiinflammatory effect	IL-1β, IL-6, TNF-α, and IL10
Ojima et al. 2015	STZ-induced DN in Sprague-Dawley rats	Suppression of the AGE-RAGE Axis, block of glucose uptake into renal proximal tubular cells, and antiinflammatory effect	MCP-1, ICAM-1, PAI-1, TGB-β, and CTGF
Ramadan et al. 2025	STZ-induced DN in albino rats	Antidiabetic, antioxidative, and antiinflammatory effect	TNF-α, IL-1β, and IL-6
Said and Abdallah 2021	STZ-induced DN in albino Wistar rats	Glucose lowering effect, antioxidative, antiinflammatory and antifibrotic effect	TNF-α, IL-6, and TGF-β1
Shelke et al. 2023	STZ and bilateral IR-induced AKI in Wistar rats	Antihyperglycemic, reduced apoptosis, and inflammation	HMGB1/TLR4/MyD88/IK-βα/NF-κB pathway

Vallon et al. 2014	T1D Akita mice	Reduced markers of kidney growth, gluconeogenesis, and inflammation	NF-κB, CCL2, CD14, TIMP2, and IL-6
Wu et al. 2021	HFD, high-sugar and STZ-induced DM in Sprague Dawley rats	Reduction of inflammation and renal fibrosis	TNF-α, IL-1β, and IL-6
Yang et al. 2024	DKD in Sprague Dawley rats	Protection of kidney function, structural integrity, and antiinflammatory effect	NF-κB, TNF-α, and MMP-9

AF: Atrial fibrillation; AKI: Acute kidney injury; CAF: Cafeteria diet; CCL2: Chemokine (C-C motif) ligand 2; CD14: Cluster of differentiation 14; DKD: Diabetic kidney disease; DM: Diabetes mellitus; EndMT: Endothelial-to-mesenchymal transition; HF: High-fructose; HFD: High-fat diet; ICAM-1: Intercellular adhesion molecule-1; IL-1β: Interleukin-1beta; IL-6: Interleukin-6; IR: Ischemia-reperfusion; MCP-1: Monocyte chemoattractant protein-1; MMP-9: Matrix Metallopeptidase 9; NF-κB: Nuclear factor κB; NRF2: Nuclear factor erythroid 2-related factor; HO-1: Hemoxygenase 1 (HO-1); PAI-1: Plasminogen activator inhibitor-1; p-AMPK: Phosphorylated AMP-activated protein kinase; RANTES: Regulated on activation normal T cell expressed and secreted; SGLT2: Sodium glucose transport protein 2; STZ: Streptozotocin; TGB-β: Transforming growth factor-beta; TGB-β1: Transforming growth factor-beta1; T1D: Type 1 diabetes; T2D: Type 2 diabetes; TIMP2: Tissue inhibitor of metalloproteinases 2; TNF-α: Tumor necrosis factor-alpha; VEGF-C: Vascular endothelial growth factor-C.

Al-Wakeel et al. (2022) examined the renoprotective role of EMP in rats with insulin resistance-induced by a cafeteria diet (CAF). Treatment with EMP decreased kidney levels of high TLR-4 (toll-like receptor-4), NF-κB, and HMGB-1 (high mobility group box-1). It also decreased the TNF-α (tumor necrosis factor-alpha) concentrations and caspase-3. EMP exhibited antiinflammatory, anti-apoptotic, and renoprotective qualities.

EMP's effects were examined in ob/ob BTBR mice. In ob/ob BTBR mice without hypertension, EMP therapy had an impact on diabetes-related renal inflammatory markers (RANTES [regulated on activation normal T-cell expressed and secreted], MCP-1 [monocyte chemoattractant protein-1], and IL-6 [interleukin-6]), hypertrophy of glomerulus, and expansion of mesangial matrix. EMP improved the early symptoms of DN (Gembardt et al., 2014).

Madhag and Al-Isawi (2024) assessed the impact of EMP in rats with diabetes induced by streptozotocin (STZ). EMP therapy delayed the development of DN in diabetic Sprague Dawley rats by lowering tissue caspase-3 and serum TNF-α, IL-6, urea, creatinine, and glucose. It also enhanced kidney activity and decreased apoptosis and inflammation (Madhag and Al-Isawi, 2024).

Mujalli et al. (2023) assessed the role of paricalcitol and EMP in mice with DN. In treating DN, EMP was superior to paricalcitol monotherapy. Their combination demonstrated better nephroprotection, most likely due to improved glycemic management and increased kidney antiinflammatory and antioxidant effect. The treatment reduced kidney damage, apoptosis, oxidative stress, inflammatory markers (IL-6/TNF-α/interleukin-1beta [IL-1β]), renal sterol regulatory element-binding protein-1 (SREBP-1) lipogenic molecule, and adipokines (resistin/leptin).

In rats with ischemic acute kidney injury (AKI) and diabetes, the impact of EMP with as an adjuvant with phloretin (a TLR-4 inhibitor) was assessed. In addition to their antihyperglycemic action, phloretin and EMP both decrease apoptosis and inflammation by targeting the TLR-4/HMGB-1/myeloid differentiation primary response 88/IkappaBα/NF-κB pathway (Shelke et al., 2023).

The effects of EMP was assessed in diabetic type 1 Akita mice. EMP reduced or stopped the rise in glomerular size and markers of inflammation (chemokine ligand 2 [CCL2], cluster of differentiation 14 [CD14], tissue inhibitor of metalloproteinases 2 [TIMP2], IL-6 and NF-κB), gluconeogenesis, and kidney injury development (Vallon et al., 2014).

The effects of EMP and ursolic acid were investigated in DM rats. DM was generated by feeding of high-fat diet (HFD) along with high-sugar and injecting with STZ intraperitoneally. By lowering inflammatory markers (IL-6, TNF-α, and IL-1β), fibrosis in kidney and oxidative stress, the combination was observed to alleviate DN (Wu et al., 2021).

In DKD rats, Yang et al. (2024) examined the kidney protective efficacy of EMP and ADMSCs (mesenchymal stem cells derived from adipose) in combination. Combined ADMSCs-EMP were effective in protecting renal

function and structural integrity. The treatment decreased the levels of the markers of fibrosis, oxidative stress, apoptosis, inflammation (TNF-α/matrix metallopeptidase-9 [MMP-9]/NF-κB), and mitochondrial damaged.

Ojima et al. (2015) reported that treatment with EMP for 4 weeks significantly inhibited oxidative stress, inflammation (MCP-1, ICAM-1 [intercellular adhesion molecule-1], PAI-1 [plasminogen activator inhibitor-1], TGF-β [transforming growth factor-beta], CTGF [connective tissue growth factor]) and fibrotic reactions in the renal tissues of diabetic rats via modulation of advanced glycation end products (AGEs) and receptor for advanced glycation end products (RAGE).

In the study by Ramdan et al. (2025), EMP treatment attenuated the STZ-induced DN in male albino rats, via its antioxidative, antidiabetic, and antiinflammatory (TNF-α, IL-6, and IL-1β) effects.

Another study evaluated the renoprotective effect of EMP in STZ-induced diabetic rats. EMP showed kidney protective effect via its glucose reducing, antiinflammatory (TNF-α, IL-6 and TGF-β1) and antioxidative effect (Said and Abdallah, 2021).

Awad and Younis (2023) reported that EMP treatment in STZ-induced DN rats significantly decreased the serum urea, creatinine, and blood urea nitrogen (BUN), and showed reduction in inflammatory markers (TNF-α, IL-1β, and IL-6) and oxidative stress and fibrosis.

In C57BLKS/J-db/m and C57BLKS/J-db/db mice, EMP treatment attenuated the DKD by inhibition of inflammation (TNF-α, IL-1β, and TGF-β1), lymphangiogenesis and lymphatic endothelial-to-mesenchymal transition via the VEGF-C [vascular endothelial growth factor-C]/VEGFR3 [vascular endothelial growth factor receptor 3] pathway (Huang et al., 2024).

Fang et al. (2024) reported that EMP treatment protect the DN in HFD and STZ-induced diabetic mice by improvement of renal function, and reduction of inflammatory marker (IL-1β) by targeting NF-κB and NLRP3 (NLR family pyrin domain containing 3) inflammasome.

In a study, EMP was found to protect against acetylcholine (ACh) and calcium chloride ($CaCl_2$)-induced atrial fibrillation (AF) and AKI in rats by targeting Nrf2 (nuclear factor erythroid 2-related factor 2)/HO-1 (hemoxygenase-1) and NF-κB/TNF-α signaling pathways showing antiinflammatory (TNF-α and IL-6) and antifibrotic effects (Badreldin et al., 2024).

Guo et al. (2020) observed that EMP attenuated the DN by inhibiting renal SGLT2 and activating the AMPK signaling pathway in db/db mice, suggesting antiinflammatory (IL-6 and MCP-1) and antifibrotic effect.

Yang et al. (2023) reported that EMP prevent the renal ischemia-reperfusion injury (IRI) via possessing antiinflammatory effect and modulation of AMPK (AMP-activated protein kinase)-OAP-1 (optic atrophy 1) pathway in C57BL/6 mice model of renal injury.

In non-diabetic rats, IRI led to a significant increase in BUN and serum creatinine and these elevated kidney injury markers were significantly decreased by EMP treatment. EMP treatment also decreased oxidative stress (i.e., MDA [malondialdehyde] levels) and the inflammatory markers (IL-1β and TNF-α). EMP treatment elevated the expression of Nrf2 and PPAR-γ (peroxisome proliferator-activated receptor gamma) coactivator 1-α (PGC-1α) providing defense against oxidative stress (Ala et al., 2022).

In a study by Duan et al. (2024), EMP treatment was associated with decrease of urinary levels of calcium oxalate and inhibited the inflammation (VEGF, IL-2, IL-1β, and MCP-1). The study showed promising results for managing hyperoxaluria in rats.

Chen et al. (2022) showed that EMP possess metabonomics-based nephroprotective mechanism in obese mice which could delay the progression of obesity-associated nephropathy. In this study EMP inhibited lipid deposition, glomerulus and tubules injury.

In hypertension-accelerated kidney disease in db/db mice, EMP inhibited the progression of nephropathy and showed nephroprotective effect in synergism with lisinopril (Østergaard et al., 2021).

Kim et al. (2019) found that in nondiabetic salt-sensitive male hypertensive rats, EMP treatment normalized the pressure natriuresis and increased kidney medullary expression of HIF-1α (hypoxia-inducible factor 1-alpha) and inhibited the inflammation in renal tissue.

In a gentamicin-induced rat model of AKI, EMP treatment showed the renoprotective effect via modulation of sirtuin 1 (SIRT1)/NF-κB pathways resulting in decreased renal inflammation, oxidative stress, and apoptosis (Botros et al., 2022).

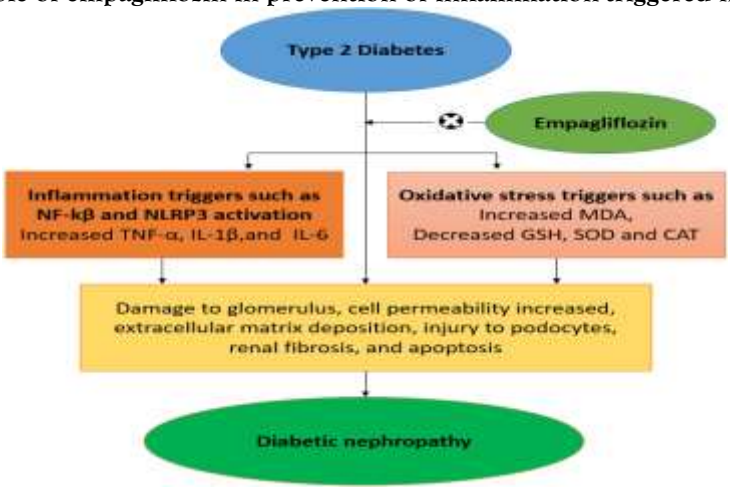
Similarly, in a paracetamol-induced mice model of AKI, EMP treatment was associated with renoprotective effect by modulation of AMPK/SIRT1/PGC-1α pathway. EMP treatment was associated with reduced oxidative stress

(with increase expression of Nrf2) and inhibition of NF-κB inflammatory mediators (IL-1β and TNF-α) (Mosalam et al., 2025).
Huang et al. (2021) reported that EMP can ameliorate the free fatty acid (FFA)-induced lipotoxicity in mice renal tubule cells. EMP's protective effects were reported to be mediated via PPARγ/CD36 pathway.
In wild-type or drug-inducible low-density lipoprotein receptor-related protein 2 (LRP2)/Megalin and Atg5 knockout mice, EMP treatment decreased albumin exposure and prevents autophagy stagnation in kidney proximal tubules, which showed EMP's potential in mediation of renoprotection by SLC5A2 (solute carrier family 5 member 2) inhibition (Matsui et al., 2025).
In LPS-induced sepsis model of mice, EMP treatment was associated with survival benefits likely to be mediated via reduced systemic and renal inflammation (Maayah et al., 2021).
Osman et al. (2021) reported that EMP possess renoprotective effect against methotrexate-triggered kidney injury. EMP's beneficial effects were mediated through reduced NF-κB, Keap1 (Kelch-like ECH-associated protein 1), HSP70 (heat shock protein 70), and caspase-3 expression and elevated in Nrf2, PPAR-γ and HO-1 expressions.

DISCUSSION AND CONCLUSION

Inflammation triggered by high glucose level is the major factor in the generation of DN (Dua et al., 2021). Activation of the inflammasome pathways lead to elevated levels of proinflammatory cytokine which subsequently stimulates the NF-κB transcription factor phosphorylation (Aboismaiel et al., 2024; Sahakyan et al., 2022). NF-κB after activation (phosphorylation) further triggers transcriptional up-regulation of NLRP3 and proinflammatory cytokines and stimulates the inflammatory cascade leading to renal injury in DM (Guo et al., 2024; Wieser et al., 2013; Samra et al., 2016; Bhol et al., 2024). Inflammatory signals including NLRP3 and NF-κB protein expressions are considerably elevated in DN, suggesting their potential role in causing the DKD (Aboismaiel et al., 2024; Dua et al., 2021; Ram et al., 2023).
Animal data have consistently shown that EMP has renoprotective effects in DKD, through its potent antiinflammatory and antioxidant effect in addition to improvement in glycemic status. The antiinflammatory effects of EMP are exerted by inhibition of cytokine release and inflammatory signals such as NF-κB and NLRP3 activation thereby preserving renal architecture (Figure 1). Therefore, targeting these inflammatory pathways could be an important strategy for the prevention of DKD.

Figure 1: Role of empagliflozin in prevention of inflammation-triggered nephropathy



CAT: Catalase; GSH: Reduced glutathione; IL-1β: Interleukin-1beta; IL-6: Interleukin-6; MDA: Malondialdehyde; NF-κB: Nuclear factor κB; NLRP3: NLR family pyrin domain containing 3; SOD: Superoxide dismutase; TNF-α: Tumor necrosis factor-alpha.
These findings support the potential of EMP for glycemic control as well as for protection of DKD and future studies can be planned with other potential emerging drugs for the prevention of DN by targeting the inflammatory pathways.

Data availability

Data sharing is not applicable to this article as the data generated has been presented in this review.

Disclosure Statement

The authors report no potential competing interest.

REFERENCES

- Aboismaiel MG, Amin MN, Eissa LA. Renoprotective effect of a novel combination of 6-gingerol and metformin in high-fat diet/streptozotocin-induced diabetic nephropathy in rats via targeting miRNA-146a, miRNA-223, TLR4/TRAF6/NLRP3 inflammasome pathway and HIF-1α. Biol Res. 2024;57(1):47.
- Ala M, Khoshdel MR, Dehpour AR. Empagliflozin enhances autophagy, mitochondrial biogenesis, and antioxidant defense and ameliorates renal ischemia/reperfusion in nondiabetic rats. Oxid Med Cell Longev. 2022;2022(1):1197061.
- Al-Wakeel DE, El-Kashef DH, Nader MA. Renoprotective effect of empagliflozin in cafeteria diet-induced insulin resistance in rats: Modulation of HMGB-1/TLR-4/NF-κB axis. Life Sci. 2022;301:120633.
- Awad MMY, Younis AM. Empagliflozin alleviates diabetic nephropathy in albino rats through its antioxidative and anti-inflammatory action. JJOAS. 2024;17:33-7.
- Badreldin H, El-Karef A, Ibrahim T, Elshal M. Targeting Nrf2/HO-1 and NF-κB/TNF-α signaling pathways with empagliflozin protects against atrial fibrillation-induced acute kidney injury in rats. Toxicology. 2024;506:153879.
- Benetti E, Mastrocola R, Vitarelli G, Cutrin JC, Nigro D, Chiazza F, Mayoux E, Collino M, Fantozzi R. Empagliflozin protects against diet-induced NLRP-3 inflammasome activation and lipid accumulation. J Pharmacol Exp Ther. 2016;359:45-53.
- Bhattacharjee N, Barma S, Konwar N, Dewanjee S, Manna P. Mechanistic insight of diabetic nephropathy and its pharmacotherapeutic targets: an update. Eur J Pharmacol. 2016;791:8-24.
- Bhol NK, Bhanjadeo MM, Singh AK, Dash UC, Ojha RR, Majhi S, Duttaroy AK, Jena AB. The interplay between cytokines, inflammation, and antioxidants: mechanistic insights and therapeutic potentials of various antioxidants and anti-cytokine compounds. Biomed Pharmacother. 2024;178:117177.
- Botros SR, Matouk AI, Anter A, Khalifa MM, Heeba GH. Protective effect of empagliflozin on gentamicin-induced acute renal injury via regulation of SIRT1/NF-κB signaling pathway. Environmental Toxicology and Pharmacology. 2022;94:103907.
- Chen X, Chen S, Ren Q, Niu S, Yue L, Pan X, Li Z, Zhu R, Jia Z, Chen X, Zhen R. A metabonomics-based renoprotective mechanism analysis of empagliflozin in obese mice. Biochem Biophys Res Commun. 2022;621:122-9.
- Donate-Correa J, Ferri CM, Sánchez-Quintana F, Pérez-Castro A, González-Luis A, Martín-Núñez E, Mora-Fernández C, Navarro-González JF. Inflammatory cytokines in diabetic kidney disease: pathophysiologic and therapeutic implications. Front Med. 2021;7:628289.
- Dua TK, Joardar S, Chakraborty P, Bhowmick S, Saha A, De Feo V, Dewanjee S. Myricitrin, a glycosyloxyflavone in Myrica esculenta bark ameliorates diabetic nephropathy via improving glycemic status, reducing oxidative stress, and suppressing inflammation. Molecules. 2021;26(2):258.
- Duan Y, Wang Q, Chen X, Deng G, Huang K, Sun F, Zhu J, Jiang K. Empagliflozin reduces renal calcium oxalate deposition in hyperoxaluria rats induced with ethylene glycol-ammonium chloride. Biochem Biophys Res Commun. 2024;737:150912.
- Fang KL, Qi XY, Han QT, Chen LZ, Wang XN, Xu ZP, Shang LQ, Shen T. Protective effect of lycorine hydrochloride against diabetic nephropathy in high-fat diet and streptozotocin-induced diabetic mice. Pharmaceutical Science Advances. 2024;2:100035.
- Gao K, Zheng P, Yang T, Zhang X, Zhao Z. Tangshenping granule inhibits pyroptosis in a rat model of streptozotocin-induced diabetic nephropathy via the NLRP3/caspase-1/GSDMD pathway. Journal of Traditional Chinese Medical Sciences. 2021;8(4):317-26.
- Gembardt F, Bartaun C, Jarzebska N, Mayoux E, Todorov VT, Hohenstein B, Hugo C. The SGLT2 inhibitor empagliflozin ameliorates early features of diabetic nephropathy in BTBR ob/ob type 2 diabetic mice with and without hypertension. Am J Physiol Renal Physiol. 2014;307(3):F317-25.
- Guo Q, Jin Y, Chen X, Ye X, Shen X, Lin M, Zeng C, Zhou T, Zhang J. NF-κB in biology and targeted therapy: new insights and translational implications. Signal Transduct Target Ther. 2024;9(1):53.
- Guo Y, Ran Z, Zhang Y, Song Z, Wang L, Yao L, Zhang M, Xin J, Mao X. Maren ameliorates diabetic nephropathy by inhibiting renal sodium glucose transporter 2 and activating the AMPK signaling pathway in db/db mice and high glucose–treated HK-2 cells. Biomed Pharmacother. 2020;131:110684.
- Habli MM. Comprehensive insights into diabetic nephropathy: pathophysiology, clinical features, and emerging treatments. Journal of The Egyptian Society of Nephrology and Transplantation. 2024;24(4):163-8.
- Hoogeveen EK. The epidemiol diabetic kidney disease. Kidney Dial. 2022;2:433-42.
- Hsia DS, Grove O, Cefalu WT. An update on sodium-glucose co-transporter-2 inhibitors for the treatment of diabetes mellitus. Curr Opin Endocrinol Diabetes Obes. 2017;24:73-9.
- Huang CC, Chou CA, Chen WY, Yang JL, Lee WC, Chen JB, Lee CT, Li LC. Empagliflozin ameliorates free fatty acid induced-lipotoxicity in renal proximal tubular cells via the PPARγ/CD36 pathway in obese mice. Int J Mole Sci. 2021;22(22):12408.
- Huang J, Liu Y, Shi M, Zhang X, Zhong Y, Guo S, Ma Y, Pan L, Yang F, Wang Y. Empagliflozin attenuating renal interstitial fibrosis in diabetic kidney disease by inhibiting lymphangiogenesis and lymphatic endothelial-to-mesenchymal transition via the VEGF-C/VEGFR3 pathway. Biomed Pharmacother. 2024:180:117589.
- IDF Diabetes Atlas. Diabetes around the world. 2025. Available from: https://diabetesatlas.org/.
- Khanra R, Bhattacharjee N, Dua TK, Nandy A, Saha A, Kalita J, Manna P, Dewanjee S. Taraxerol, a pentacyclic triterpenoid, from Abroma augusta leaf attenuates diabetic nephropathy in type 2 diabetic rats. Biomed Pharmacother. 2017;94:726-41.
- Kim S, Jo CH, Kim GH. Effects of empagliflozin on nondiabetic salt-sensitive hypertension in uninephrectomized rats. Hypertens Res. 2019;42(12):1905-15.
- Maayah ZH, Ferdaoussi M, Takahara S, Soni S, Dyck JR. Empagliflozin suppresses inflammation and protects against acute septic renal injury. Inflammopharmacology. 2021;29(1):269-79.
- Madhag Z, Al-Isawi Z. Empagliflozin alone and in combination with metformin mitigates diabetes-associated renal complications. J Med Life. 2024;17(5):530-5.

- Matsui S, Yamamoto T, Takabatake Y, Takahashi A, Namba-Hamano T, Matsuda J, Minami S, Sakai S, Yonishi H, Nakamura J, Maeda S. Empagliflozin protects the kidney by reducing toxic ALB (albumin) exposure and preventing autophagic stagnation in proximal tubules. Autophagy. 2025;21(3):583-97.
- Mosalam EM, AboShabaan HS, Mahfouz MM, Sallam AS, Elhosary E, Allam A, Metwally EM, Shaldam MA, Ghoneim ME. Protective effect of empagliflozin against paracetamol-induced acute kidney injury through modulation of AMPK/SIRT1/PGC-1α pathway in experimental mice. Toxicol Appl Pharmacol. 2025;500:117382.
- Mujalli A, Farrash WF, Obaid AA, Khan AA, Almaimani RA, Idris S, Elzubier ME, Khidir EB, Aslam A, Minshawi F, Alobaidy MA. Improved glycaemic control and nephroprotective effects of empagliflozin and paricalcitol co-therapy in mice with type 2 diabetes mellitus. Int J Mol Sci. 2023;24(24):17380.
- Ojima A, Matsui T, Nishino Y, Nakamura N, Yamagishi S. Empagliflozin, an inhibitor of sodium-glucose cotransporter 2 exerts anti-inflammatory and antifibrotic effects on experimental diabetic nephropathy partly by suppressing AGEs-receptor axis. Horm Metab Res. 2015;47(9):686-92.
- Osman AT, Sharkawi SM, Hassan MI, Abo-Youssef AM, Hemeida RA. Empagliflozin and neohesperidin protect against methotrexate-induced renal toxicity via suppression of oxidative stress and inflammation in male rats. Food Chem Toxicol. 2021;155:112406.
- Østergaard MV, Secher T, Christensen M, Salinas CG, Roostalu U, Skytte JL, Rune I, Hansen HH, Jelsing J, Vrang N, Fink LN. Therapeutic effects of lisinopril and empagliflozin in a mouse model of hypertension-accelerated diabetic kidney disease. Am J Physiol Renal Physiol. 2021;321(2):F149-61.
- Ram C, Gairola S, Verma S, Mugale MN, Bonam SR, Murty US, Sahu BD. Biochanin A ameliorates nephropathy in high-fat diet/streptozotocin-induced diabetic rats: Effects on NF-kB/NLRP3 axis, pyroptosis, and fibrosis. Antioxidants. 2023;12(5):1052.
- Ramadan O, Taha R, Awad M, Abdelhay O, Ereba R, Younes A, Abd-Allah F, Darwish A, Moustafa A, Elgndy A, Omar N. Combination of empagliflozin and curcumin ameliorates the induced diabetic nephropathy in male albino rats, through their synergistic anti-diabetic and antioxidative effects. Bioactive Compounds in Health and Disease. 2025;8(3):90-103.
- Sahakyan G, Vejux A, Sahakyan N. The role of oxidative stress-mediated inflammation in the development of T2DM-induced diabetic nephropathy: possible preventive action of tannins and other oligomeric polyphenols. Molecules. 2022;27(24):9035.
- Said MA, Abdallah HA. Potential mechanisms underlying the renoprotective effect of empagliflozin, a novel selective sodium glucose co-transporter (SGLT) 2 inhibitor, against diabetic nephropathy in streptozotocin induced diabetic rats. Bull of Egyp Soc Physiol Sci. 2021;41(3):344-57.
- Samra YA, Said HS, Elsherbiny NM, Liou GI, El-Shishtawy MM, Eissa LA. Cepharanthine and Piperine ameliorate diabetic nephropathy in rats: role of NF-κB and NLRP3 inflammasome. Life Sci. 2016;157:187-99.
- Shelke V, Kale A, Dagar N, Habshi T, Gaikwad AB. Concomitant inhibition of TLR-4 and SGLT2 by phloretin and empagliflozin prevents diabetes-associated ischemic acute kidney injury. Food & Function. 2023;14(11):5391-403.
- Vallon V, Gerasimova M, Rose MA, Masuda T, Satriano J, Mayoux E, Koepsell H, Thomson SC, Rieg T. SGLT2 inhibitor empagliflozin reduces renal growth and albuminuria in proportion to hyperglycemia and prevents glomerular hyperfiltration in diabetic Akita mice. Am J Physiol Renal Physiol. 2014;306(2):F194-204.
- Wieser V, Moschen AR, Tilg H. Inflammation, cytokines and insulin resistance: a clinical perspective. Arch Immunol Ther Exp (Warsz). 2013;61(2):119-25.
- Wu X, Li H, Wan Z, Wang R, Liu J, Liu Q, Zhao H, Wang Z, Zhang H, Guo H, Qi C. The combination of ursolic acid and empagliflozin relieves diabetic nephropathy by reducing inflammation, oxidative stress and renal fibrosis. Biomed Pharmacother. 2021;144:112267.
- Yang CC, Chen YL, Sung PH, Chiang JY, Chen CH, Li YC, Yip HK. Repeated administration of adipose-derived mesenchymal stem cells added on beneficial effects of empagliflozin on protecting renal function in diabetic kidney disease rat. Biomed J. 2024;47(2):100613.
- Yang SC, Hsu CY, Chou WL, Fang JY, Chuang SY. Bioactive agent discovery from the natural compounds for the treatment of type 2 diabetes rat model. Molecules. 2020;25(23):5713.
- Yang W, Li X, He L, Zhu S, Lai S, Zhang X, Huang Z, Yu B, Cui C, Wang Q. Empagliflozin improves renal ischemia–reperfusion injury by reducing inflammation and enhancing mitochondrial fusion through AMPK–OPA1 pathway promotion. Cell Mol Biol Lett. 2023;28(1):42.