

Plants in the Prevention and Management of Diabetic Nephropathy: Ethnobotany to Evidence-Based Therapeutics

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ABSTRACT

Diabetic nephropathy is characterized by sustained albuminuria exceeding 300 mg per 24-hour urine collection and represents a major microvascular complication of diabetes mellitus. Epidemiological data indicate that approximately one-third of patients with

diabetes in the Asia-Pacific region develop nephropathy, which has emerged as the leading cause of end-stage renal disease globally. Traditional medicine systems, particularly those utilizing botanical interventions, have demonstrated potential therapeutic value in managing diabetic nephropathy. There is growing scientific interest in phytotherapeutic approaches, especially within Asian populations, where various culinary and medicinal plants—including *Allium sativum* (garlic), *Curcuma longa* (turmeric), *Trigonella foenum-graecum* (fenugreek), *Zingiber officinale* (ginger), and *Ginkgo biloba*—have shown preliminary evidence for beneficial effects in diabetes mellitus and its associated nephropathic complications.

Keywords: Diabetic Nephropathy, Herbal Medicine

Introduction

Diabetes Nephropathy (DN) is characterized as kidney fractional loss. DN (diabetic nephropathy) caused by glomerular HTN, metabolic disorder, oxidative pressure and end product of glycation (Hemant VK and Subhash LB, 2013). One of the most significant causative components for diabetes nephropathy is hyperglycemia leads to oxidative stress (Kiran G et al., 2012). Diabetic nephropathy typically manifests initially through glycosuria accompanied by persistent hyperglycaemia. The excessive renal glucose excretion can precipitate osmotic diuresis, leading to volume depletion and subsequent dehydration (Giunta et al., 2024). Clinical manifestations of this fluid imbalance commonly include polydipsia and compensatory increased fluid intake as physiological responses to maintain homeostasis. The incapacity of insulin to achieve ordinarily influences on the pathway of carbohydrates, fat and protein metabolism. Insulin permits the ability to store of protein and lipids because it is a metabolic disorder. An absolute or relative lack of insulin eventually prompts weight reduction in spite of raise appetite (Dewangan H et al., 2017).

Diabetic nephropathy represents the predominant etiology of end-stage renal disease, accounting for approximately 40% of patients requiring haemodialysis (Yang WC et al., 2001). Longitudinal studies demonstrate that 25-40% of individuals with diabetes mellitus will develop nephropathy within 20-25 years of initial diagnosis, with approximately one-third of these patients progressing to end-stage renal disease (Ritz E and Orth SR, 1999). The substantial healthcare burden associated with diabetic nephropathy stems from its high prevalence and severe clinical consequences, resulting in

considerable socioeconomic impact on healthcare systems globally (Kuo HW et al., 2007; Yang WC and Hwang SJ, 2008).

Some Medicinal Plants used in Diabetic Nephropathy

Botanical therapeutics has maintained extensive clinical applications throughout human history (R. Teschke et al., 2015). Traditional Chinese Medicine (TCM) systems developed within Asia, particularly China, subsequently disseminating throughout neighbouring regions including Pakistan, Japan, India, South Korea, and Iran. The expanding global recognition of TCM has stimulated comprehensive scientific investigations into its therapeutic efficacy and mechanistic foundations across numerous pathological conditions. Traditional Chinese Medicine encompasses plant-based pharmaceuticals, moxibustion, acupuncture, therapeutic massage, nutritional interventions, and physical exercises including Qigong and Tai Chi, with herbal preparations representing the cornerstone of TCM practice in mainland China (G. Wang et al., 2007). Acupuncture has gained particular prominence within United States healthcare systems (R. Teschke et al., 2015).

Given the critical therapeutic demands for diabetic nephropathy management, this analysis focuses specifically on TCM botanical preparations avoiding its more serious implications like heart (Gao et al., 2025). Numerous investigators have conducted clinical and experimental trials examining individual TCM plants or isolated plant compounds for diabetic nephropathy treatment, identifying beneficial phytotherapeutic agents and establishing fundamental therapeutic frameworks for diabetic nephropathy intervention. The integration of traditional medicine formulations containing flavonoids, alkaloids, terpenoids, and saponins—whilst individually insufficient for complete disease arrest—with contemporary genetic technologies may enhance early diagnostic capabilities and facilitate timely therapeutic intervention or advanced treatment modalities (Amanat et al., 2025).

Garlic

Garlic is a traditional used plant, which is generally used as a food flavor. Garlic in its old form used as a pharmacological agent (Ali et al., 2000). Some ingredients of Garlic extract are medicinally valuable, such as, for the treatment hypertension, hyperglycemia and hyperlipidemia (Cicero et al., 2017; Ali et al., 2000; Sahebkar et al., 2016b; Thomson, Al-Qattan et al., 2006). Garlic extract has a useful role in function of kidneys and prevent

the complications of diabetic (Ahmad et al., 2006; Maldonado et al., 2003; Iqbal and Athar, 1998).

Experimental evidence indicates that garlic supplementation ameliorates renal dysfunction in animal models of chemically induced kidney injury and provides protection against iron-mediated nephrotoxic effects (Iqbal and Athar, 1998). Mechanistic studies have demonstrated that garlic constituents enhance endogenous antioxidant capacity whilst reducing oxidative cellular damage, resulting in nephroprotective outcomes in toxin-induced models (Maldonado et al., 2003). Additional research has established that garlic administration attenuates oxidative injury within renal parenchyma during periods of ischemic insult and subsequent reperfusion (Kabasakal et al., 2005). Accumulating data support the therapeutic application of garlic-derived compounds in diabetic kidney disease management. Investigators have reported that garlic supplementation mitigates diabetes-associated renal pathology by reducing oxidative burden and promoting microvascular integrity through enhanced endothelial nitric oxide production within intrarenal vessels, thereby serving as an effective reactive oxygen species scavenger. Complementary studies utilizing diabetic rodent models have shown that garlic administration prevents structural kidney deterioration whilst significantly lowering circulating glucose concentrations. These findings suggest that aged garlic preparations possess glucose-lowering, lipid-modulating, and antioxidant activities that collectively provide kidney protection against diabetic complications (Shiju et al., 2013; Al-Qattan et al., 2008; Mariee et al., 2009).

Researchers have demonstrated that garlic supplementation reduces serum insulin concentrations while simultaneously decreasing urinary albumin and protein losses, accompanied by diminished oxidative stress markers, resulting in improved renal function in diabetic animal models (Thomson et al., 2013). These findings suggest that garlic-derived compounds confer renoprotective effects against hyperglycaemia-induced injury through enhanced insulin sensitivity and oxidative stress reduction, with additional therapeutic mechanisms potentially involving anti-inflammatory pathways (Atkin et al., 2016).

Curcuma Longa

Curcuma is an ancient plant, which is present in the *Zingiberaceae* family and is a rhizomatous herbaceous perennial plant (Chan E et al., 2009). Curcumin, the principal

bioactive polyphenolic compound [1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione] responsible for turmeric's characteristic pigmentation, possesses significant therapeutic potential. This naturally occurring dietary constituent represents a promising therapeutic candidate for diabetic nephropathy management, offering advantages over conventional pharmaceutical interventions due to its established safety profile and accessibility. Curcumin's therapeutic efficacy derives from its capacity to modulate multiple cellular signalling cascades and regulatory enzymes through its inherent antioxidant, anti-inflammatory, and antidiabetic mechanisms (Rashid K and Sil PC, 2015; Gupta SC et al., 2011; Zhou H et al., 2011). The antioxidant activity is attributed to the hydroxyl groups and the methylene moiety within the heptadiene-dione structure (Zhou H et al., 2011).

Numerous investigations have established curcumin's nephroprotective properties in diabetic kidney disease (Huang J et al., 2013). Treatment protocols demonstrate improved creatinine and urea clearance alongside normalisation of elevated blood urea nitrogen concentrations (Soetikno V et al., 2011; Tikoo K et al., 2008). Additionally, curcumin administration modulates enzymatic activity levels including N-acetyl- β -D-glucosaminidase, aspartate aminotransferase, alkaline phosphatase, alanine aminotransferase, and acid phosphatases.

Furthermore, curcumin supplementation normalises ATPase activity, catalase, aldose reductase, superoxide dismutase, glutathione levels, glucose-6-phosphate dehydrogenase, lactate dehydrogenase, and transaminase function whilst optimising membrane polyunsaturated-to-saturated fatty acid ratios, thereby restoring overall renal functional integrity through its multifaceted therapeutic mechanisms (Suresh Babu P and Srinivasan K, 1998). Study revealed that curcuma decreases the appearance of VEGF receptor and VEGF (Sawatpanich T et al., 2010) in that way preventing PKC- β 1 and PKC- α oxidative actions (Soetikno V et al., 2011) by the activation of adenosine monophosphate (AMP) (Soetikno V et al., 2013). This causes standardization of antioxidant defense systems due to the consequent renovation of structure and role of kidney tissue and inhibition of peroxidation of lipids (Soetikno V et al., 2011). Curcumin demonstrates inhibitory effects on p300 histone acetyltransferase and nuclear factor-KB activation, subsequently altering heat shock protein-27 expression and p38 mitogen-

activated protein kinase signalling whilst inducing post-translational histone H3 modifications within diabetic renal parenchyma, ultimately attenuating oxidative stress-mediated nephropathy (Tikoo K et al., 2008; Chiu J et al., 2009). The compound reduces cellular oxidative burden through downregulation of NADPH oxidase 4 and p67phox subunit expression (Trujillo J et al., 2013). Clinical investigations have validated curcumin's beneficial impact on end-stage renal disease progression through significant reductions in interleukin-8, urinary protein excretion, and transforming growth factor- β levels (Khajehdehi P et al., 2011). Despite these diverse therapeutic effects, curcumin's clinical translation remains limited due to inherent physicochemical constraints including poor aqueous solubility, pronounced pigmentation characteristics, and suboptimal bioavailability profiles (Prasad S et al., 2014). Beyond its established antioxidant and antidiabetic properties, emerging evidence suggests curcumin may suppress T-lymphocyte-mediated pancreatic β -cell destruction in autoimmune diabetes models (Castro CN et al., 2014).

Fenugreek (*Trigonella Foenum-Graecum*)

Trigonella foenum-graecum (fenugreek) represents a widely consumed dietary constituent across multiple global populations. Experimental investigations have demonstrated that fenugreek extracts possess both antioxidant and hypoglycaemic properties. Additionally, these preparations exhibit beneficial effects on peripheral glucose utilisation and pancreatic insulin secretion mechanisms. (Jin Y et al., 2014). Moreover, another examination demonstrated that fenugreek improves SCr in diabetes-induced animals (Sayed AA et al., 2012). Cure the diabetic induced mice, with fenugreek for 03 months decreases the raised levels of glucose, SCr, IL-6 and BUN. Fenugreek seed administration significantly reduces interleukin-6 and malondialdehyde concentrations in renal tissue homogenates whilst concurrently elevating glutathione levels and enhancing both superoxide dismutase and catalase enzymatic activities. These findings suggest that fenugreek seeds possess therapeutic potential for diabetic nephropathy management through their anti-inflammatory and antioxidant mechanisms (Sayed AA et al., 2012).

In STZ-prompted diabetic nephropathy (DN) in mice, treatment fenugreek seed improved kidney capacities, expressively decreased BGL, stop accumulation of ECM, and it calmed OS with the controlled TGF- β 1 or CTGF flagging passageway (Koya D et al.,

1997). Introduce of cisplatin in rats activated apoptosis and anti-inflammatory action in kidneys and liver by raised of cytokine expression, apoptotic marker p38 mitogen-activated protein kinases, TNF- α , and consequences of increased ROS production. The cisplatin-incited biochemical significantly reduced by fenugreek seed and change in histopathological, apoptosis and inflammation in kidneys of mice. The outcomes of above experiment are that fenugreek has a dominant antioxidant activity (Hegazy MG and Emam MA, 2015).

Zingiber Officinale

Zingiber officinale rhizomes serve multiple functions as culinary seasoning, food preservation agent, and therapeutic compound within traditional medicine practices (Kemper, 1999). This botanical species demonstrates established antioxidant and anti-inflammatory bioactivities (Thomson et al., 2002; Ghasemzadeh et al., 2010).

Contemporary investigations indicate that ginger supplementation functions as a beneficial therapeutic intervention for diabetic patients by improving renal function and preventing nephropathy complications (Rafieian-Kopaei M and Nasri, H, 2014). Experimental studies have confirmed that ginger extract attenuates diabetic nephropathy progression through amelioration of histopathological alterations in renal microvascular and glomerular structures (Al-Qattan et al., 2008). Additional research has documented ginger's protective efficacy against gentamicin-induced tubular nephrotoxicity (Nasri et al., 2013b). Further investigations demonstrated that ethanolic ginger extracts prevented experimentally induced diabetic nephropathy via adenosine monophosphate-activated protein kinase-dependent mechanisms (Tzeng et al., 2013). Subsequent studies revealed that eight-week ginger treatment ameliorated oxidative stress parameters, reduced malondialdehyde concentrations, and enhanced antioxidant defence system capacity within diabetic renal tissue (Afshari et al., 2007). In additionally, ginger may be another feasible preventive herbal-based mediator towards diabetic nephropathy, performing as an antioxidant and with AMPK-dependent mechanism (Tzeng et al., 2013).

Ginkgo Biloba

Ginkgo biloba has been associated with several benefits, including its ability to scavenge reactive oxygen species (ROS) (Akisu M et al., 1998). Additionally, *Ginkgo biloba* extract exhibits the capacity to inhibit the formation of advanced glycation end products (AGEs)

and normalize receptor for advanced glycation end products (RAGE) expression by reducing oxidative stress (OS) and enhancing kidney function and tissue structure in diabetic nephropathy (DN) mice (Li X et al., 2011). Furthermore, in DN, *Ginkgo biloba* extract demonstrates a protective role against glomerulosclerosis of mesangial cells (Tang D et al., 2009). In DN rats, the extract of *Ginkgo biloba* was found to reduce serum creatinine (SCr), blood urea nitrogen (BUN), proteinuria, and blood glucose levels (BGL). It also decreased laminin, collagen IV, transforming growth factor-beta 1 (TGF- β 1) mRNA, AGEs, connective tissue growth factor (CTGF), glomerular basement membrane (GBM) thickness, and mesangial hyperplasia (Lu Q et al., 2007). A comprehensive review of randomized controlled trials conducted in adults with early-stage diabetic nephropathy revealed that *Ginkgo biloba* supplementation significantly reduced BGL, BUN, SCr, and albuminuria (Li X et al., 2011)(Zhang L et al., 2013).

Olive Oil

Olea europaea represents a small arboreal species within the *Oleaceae* family, valued primarily for its nutritious fruit production (Beauchamp et al., 2005). Olive oil exhibits significant pharmacological properties, particularly antioxidant activity, and serves as an effective food preservation agent (Fitó, M et al., 2007). This oil demonstrates substantial nephroprotective characteristics across various pathological conditions, including diabetes mellitus (Hoile et al., 2014; Tripoli et al., 2005). The therapeutic efficacy of olive oil derives from its abundant polyphenolic constituents and polyunsaturated fatty acid content, conferring protection against oxidative stress-induced pathologies through potent antioxidant mechanisms (Fitó et al., 2007).

Epidemiological evidence from traditional Mediterranean populations, characterised by high olive oil consumption, demonstrates associations with reduced acute kidney injury risk and approximately 50% decreased incidence of chronic kidney disease. Mediterranean dietary patterns are recommended for diabetic patients to enhance renal function and prevent diabetic nephropathy development (Chauveau et al., 2017). International cohort studies have established correlations between Mediterranean dietary adherence and reduced risk of estimated glomerular filtration rate decline (Khatri et al., 2014). Randomised controlled trials indicate that Mediterranean dietary interventions reduce systemic and DNA oxidative damage whilst significantly improving glycaemic

control (Mitjavila et al., 2013). However, in type 2 diabetes, Mediterranean dietary patterns showed no protective effects against diabetic nephropathy progression, despite improving retinal outcomes and preventing diabetic retinopathy (Díaz-López et al., 2018). Current evidence strongly supports olive oil's therapeutic potential for enhancing renal function and delaying diabetic nephropathy onset, although direct mechanistic evidence for these nephroprotective effects remains limited (Chauveau et al., 2017; Khatri et al., 2014).

Silybum Marianum

Milk Thistle (*Silybum marianum*) belongs to the *Asteraceae* family. In streptozotocin-induced diabetic mice, diabetes nephropathy was treated by the extract of Milk thistle. This result was maybe by raising kidney catalase (CAT) and decreasing lipid peroxidation in renal tissue and glutathione peroxidase (GPx) activity (Vessal et al., 2010).

Linum Usitatissimum

Linum usitatissimum (flaxseed) is a member of the *Linaceae* botanical family. Dietary protein substitution with flaxseed meal has demonstrated efficacy in reducing glomerular damage, urinary urea excretion, and tubulointerstitial lesions in spontaneously hypertensive obese rodent models. Flaxseed meal exhibits superior therapeutic effects compared to soy protein preparations in attenuating renal histopathological alterations and urinary urea levels. These nephroprotective benefits appear to be independent of glycaemic regulation and dietary protein intake quantities (Velasquez et al., 2003).

Conclusion

This comprehensive review demonstrates that phytotherapeutic compounds possess significant therapeutic potential for diabetes mellitus and diabetic nephropathy management through their inherent anti-inflammatory and antioxidant mechanisms. These bioactive constituents modulate nuclear factor- κ B and Kelch-like ECH-associated protein 1/nuclear factor erythroid 2-related factor 2/antioxidant response element signalling pathways. Natural compounds enhance cellular antioxidant capacity whilst upregulating the Keap1/Nrf2/ARE pathway. Furthermore, these substances attenuate cytokine production and activity, reduce growth factor and chemokine expression, diminish adhesion molecule formation, and ameliorate inflammatory cascades.

Evidence suggests that isolated antioxidant interventions demonstrate limited therapeutic

efficacy, whereas complete natural preparations exhibit substantial beneficial outcomes in preclinical investigations. Currently, there is a paucity of randomised controlled trials evaluating whole plant extracts or combined antioxidant formulations for diabetic nephropathy management.

Consequently, future clinical research should prioritise investigating comprehensive plant-derived preparations or multi-component antioxidant therapies, which may demonstrate optimal therapeutic benefits in patients with diabetic nephropathy and diabetes mellitus.

References

- Afshari, A. T., Shirpoor, A., Farshid, A., Saadatian, R., Rasmi, Y., Saboory, E. Allameh, A. (2007). The effect of ginger on diabetic nephropathy, plasma antioxidant capacity and lipid peroxidation in rats. *Food Chemistry*, 101(1), 148–153.
- Ahmad, M. S., & Ahmed, N. (2006). Antiglycation properties of aged garlic extract: Possible role in prevention of diabetic complications. *The Journal of Nutrition*, 136(3), 796S–799S.
- Akisu M, Kultursay N, Coker I, et al. Platelet-activating factor is an important mediator in hypoxic ischemic brain injury in the newborn rat. Flunarizine and Ginkgo biloba extract reduce PAF concentration in the brain. *Biol Neonate*. 1998;74:439–444.
- Ali, M., Al-Qattan, K., Al-Enezi, F., Khanafer, R., & Mustafa, T. (2000). Effect of allicin from garlic powder on serum lipids and blood pressure in rats fed with a high cholesterol diet. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 62(4), 253–259.
- Al-Qattan, K., Thomson, M., & Ali, M. (2008). Garlic (*Allium sativum*) and ginger (*Zingiber officinale*) attenuate structural nephropathy progression in streptozotocin-induced diabetic rats. *e-SPEN, the European e- Journal of Clinical Nutrition and Metabolism*, 3(2), e62–e71.
- Amanat, M., Lal, K., Singh, T.G. *et al.* Molecular insights of diabetic nephropathy and chemical constituents-based treatment approach. *Phytochem Rev* (2025). <https://doi.org/10.1007/s11101-025-10068-y>
- Atkin, M., Laight, D., & Cummings, M. H. (2016). The effects of garlic extract upon endothelial function, vascular inflammation, oxidative stress and insulin resistance in

- adults with type 2 diabetes at high cardiovascular risk. A pilot double blind randomized placebo controlled trial. *Journal of Diabetes and its Complications*, 30(4), 723–727.
- Beauchamp, G. K., Keast, R. S. J., Morel, D., Lin, J., Pika, J., Han, Q. Breslin, P. A. S. (2005). Phytochemistry: Ibuprofen-like activity in extra-virgin olive oil. *Nature*, 437(7055), 45–46.
- Castro CN, Barcala Tabarrozzi AE, Winnewisser J, Gimeno ML, Antunica Noguerol M, et al. (2014) Curcumin ameliorates autoimmune diabetes. Evidence in accelerated murine models of type 1 diabetes. *Clin Exp Immunol* 177: 149-160.
- Chan E, Lim YY, Wong SK, Lim K, Tan S, et al. (2009) Effects of different drying methods on the antioxidant properties of leaves and tea of ginger species. *Food chemistry* 113: 166-172.
- Chauveau, P., Aparicio, M., Bellizzi, V., Campbell, K., Hong, X., Johansson, L., ... Carrero, J. J. (2017). Mediterranean diet as the diet of choice for patients with chronic kidney disease. *Nephrology Dialysis Transplantation*, 33(5), 725–735
- Chiu J, Khan ZA, Farhangkhoei H, Chakrabarti S (2009) Curcumin prevents diabetes-associated abnormalities in the kidneys by inhibiting p300 and nuclear factor-kappaB. *Nutrition* 25: 964-972.
- Cicero, A. F. G., Colletti, A., Bajraktari, G., Descamps, O., Djuric, D. M., Ezhov, M., Banach, M. (2017). Lipid-lowering nutraceuticals in clinical practice: Position paper from an International Lipid Expert Panel. *Archives of Medical Science*, 13(5), 965–1005.
- Dewangan H, Tiwari RK, Sharma V, Shukla SS, Satapathy T, Pandey R. Past and Future of in-vitro and in-vivo Animal Models for Diabetes: A Review. *Indian Journal of Pharmaceutical Education and Research* 2017; 51(4S):S522-S30
- Díaz-López, A., Babio, N., Martínez-González, M. A., Corella, D., Amor, A. J., Fitó, M., ... Salas-Salvadó, J. (2018). Erratum. Mediterranean diet, retinopathy, nephropathy, and microvascular diabetes complications: A post hoc analysis of a randomized trial. *Diabetes Care* 2015; 38: 2134–2141. *Diabetes Care*, 41(10), 2260–2261
- Fitó, M., de la Torre, R., & Covas, M. I. (2007). Olive oil and oxidative stress. *Molecular*

Nutrition & Food Research, 51(10), 1215–1224.

Gao, P., Cao, M., Wang, X., Zhang, H., Chen, X., Song, Z., ... & Zou, Y. (2025). G Protein–Coupled Receptor Kinase 3 Exacerbates Diabetic Heart Injuries Through Direct Phosphorylation of Cannabinoid Receptor 2 in Humans and Mice. *Circulation*.

Ghasemzadeh, A., Jaafar, H. Z. E., & Rahmat, A. (2010). Antioxidant activities, total phenolics and flavonoids content in two varieties of Malaysia young ginger (*Zingiber officinale* Roscoe). *Molecules*, 15(6), 4324–4333.

Giunta, R., Gervasi, L., Torrisi, I., Aliotta, R., & Marcantoni, C. (2024). Lesson for the clinical nephrologist: diagnostic approach to polyuria-polydipsia syndrome in the adult. *Journal of Nephrology*, 37(8), 2371–2374.

Gupta SC, Prasad S, Kim JH, Patchva S, Webb LJ, et al. (2011) Multitargeting by curcumin as revealed by molecular interaction studies. *Nat Prod Rep* 28: 1937–1955

Haeri MR, Limaki HK, White CJ, White KN (2012) Non-insulin dependent anti-diabetic activity of (2S, 3R, 4S) 4-hydroxyisoleucine of fenugreek (*Trigonella foenum graecum*) in streptozotocin-induced type I diabetic rats. *Phytomedicine* 19: 571–574.

Hamden K, Masmoudi H, Carreau S, Elfeki A (2010) Immunomodulatory, beta-cell, and neuroprotective actions of fenugreek oil from alloxan-induced diabetes. *Immunopharmacol Immunotoxicol* 32: 437–445.

Hegazy MG, Emam MA. Ethanolic extract of *Trigonella foenum graecum* attenuates cisplatin-induced nephro- and hepatotoxicities in rats. *Cell Mol Biol (Noisy-le-grand)*. 2015;61(7):81–87.

Hemant VK, Subhash LB. Trigonelline and sitagliptin attenuates nicotinamide streptozotocin induced diabetic nephropathy in wistar rats. *Int J Pharm Pharm Sci* 2013; 5(4): 583–589.

Hoile, S. P., Clarke-Harris, R., Huang, R.-C., Calder, P. C., Mori, T. A., Beilin, L. J., ... Burdge, G. C. (2014). Supplementation with N-3 long-chain polyunsaturated fatty acids or olive oil in men and women with renal disease induces differential changes in the DNA methylation of *FADS2* and *ELOVL5* in peripheral blood mononuclear cells. *PLoS One*, 9(10), e109896.

Huang J, Huang K, Lan T, Xie X, Shen X, et al. (2013) Curcumin ameliorates diabetic nephropathy by inhibiting the activation of the SphK1-S1P signaling pathway. *Mol*

Cell Endocrinol 365: 231-240.

Iqbal, M., & Athar, M. (1998). Attenuation of iron-nitrilotriacetate (Fe-NTA)-mediated renal oxidative stress, toxicity and hyperproliferative response by the prophylactic treatment of rats with garlic oil. *Food and Chemical Toxicology*, 36(6), 485–495.

Jin Y, Shi Y, Zou Y, et al. Fenugreek prevents the development of STZ-induced diabetic nephropathy in a rat model of diabetes. *Evid Based Complement Altern Med*. 2014;2014.

Kabasakal, L., Şehirli, Ö., Çetinel, Ş., Cikler, E., Gedik, N., & Şener, G. (2005). Protective effect of aqueous garlic extract against renal ischemia/reperfusion injury in rats. *Journal of Medicinal Food*, 8(3), 319–326.

Kemper, KJ. 1999. Ginger (*Zingiber officinale*). Longwood Herbal Task Force, Available at: <http://www.mcp.edu/herbal/default.htm>: 1–18.

Khajehdehi P, Pakfetrat M, Javidnia K, Azad F, Malekmakan L, et al. (2011) Oral supplementation of turmeric attenuates proteinuria, transforming growth factor- β and interleukin-8 levels in patients with overt type 2 diabetic nephropathy: a randomized, double-blind and placebo-controlled study. *Scand J Urol Nephrol* 45: 365-370.

Khatri, M., Moon, Y. P., Scarmeas, N., Gu, Y., Gardener, H., Cheung, K. Elkind, M. S. V. (2014). The association between a Mediterranean style diet and kidney function in the Northern Manhattan Study cohort. *Clinical Journal of the American Society of Nephrology*, 9, 01080114–01081875.

Kiran G, Nandani CD, Ramesh HP, Salimath PV. Progression of early phase of diabetic nephropathy in streptozocin induces: Evaluation of various kidney related parameter. *Int J Ex Bio* 2012; (50): 133-140.

Koya D, Jirousek MR, Lin YW. Characterization of protein kinase C beta isoform activation on the gene expression of transforming growth factor-beta, extracellular matrix components, and prostanooids in the glomeruli of diabetic rats. *J Clin Invest*. 1997;100:115–126.

Kuo HW, Tsai SS, Tiao MM, Yang CY. Epidemiological features of CKD in Taiwan. *Am J Kidney Dis*. 2007; 49(1):46–55.

Li X, Yan H, Wang J. Extract of Ginkgo biloba and alpha-lipoic acid attenuate advanced

- glycation end products accumulation and RAGE expression in diabetic nephropathy rats. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2011;31(4):525–531.
- Liu Y, Kakani R, Nair MG (2012) Compounds in functional food fenugreek spice exhibit anti-inflammatory and antioxidant activities. *Food Chemistry* 131: 1187-1192.
- Lu Q, Yin XX, Wang JY, et al. Effects of Ginkgo biloba on prevention of development of experimental diabetic nephropathy in rats. *Acta Pharmacol Sin*. 2007;28(6):818–828
- Maldonado, P. D., Barrera, D., Medina-Campos, O. N., Hernández-Pando, R., Ibarra-Rubio, E., & Pedraza-Chaverri, J. (2003). Aged garlic extract attenuates gentamicin induced renal damage and oxidative stress in rats. *Life Sciences*, 73(20), 2543--22556
- Mariee, A. D., Abd-Allah, G. M., & El-Yamany, M. F. (2009). Renal oxidative stress and nitric oxide production in streptozotocin-induced diabetic nephropathy in rats: The possible modulatory effects of garlic (*Allium sativum* L.). *Biotechnology and Applied Biochemistry*, 52(3), 227–232.
- Morcos M, Schlotterer A, Sayed A, Kukudov G, Oikomonou D, et al. (2008) Rosiglitazone reduces angiotensin II and advanced glycation end product-dependent sustained nuclear factor- κ B activation in cultured human proximal tubular epithelial cells. *Hormone and metabolic research* 40: 752-759
- Nasri, H., Nematbakhsh, M., Ghobadi, S., Ansari, R., Shahinfard, N., & Rafieian-kopaei, M. (2013b). Preventive and curative effects of ginger extract against histopathologic changes of gentamicin-induced tubular toxicity in rats. *International Journal of Preventive Medicine*, 4(3), 316
- Prasad S, Tyagi AK, Aggarwal BB (2014) Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. *Cancer research and treatment: official journal of Korean Cancer Association* 46: 2.
- Rafieian-Kopaei, M., & Nasri, H. (2014). The ameliorative effect of *Zingiber officinale* in diabetic nephropathy. *Iranian Red Crescent Medical Journal*, 16(5).
- Rashid K, Sil PC (2015) Curcumin ameliorates testicular damage in diabetic rats by suppressing cellular stress-mediated mitochondria and endoplasmic reticulum-dependent apoptotic death. *Biochim Biophys Acta -Molecular Basis of Disease* 1852:

70-82.

Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. *N Engl J Med.* 1999; 341 (15):1127–33.

Sahebkar, A., Serban, M. C., Gluba-Brzózka, A., Mikhailidis, D. P., Cicero, A. F., Rysz, J., & Banach, M. (2016). Lipid-modifying effects of nutraceuticals: an evidence-based approach. *Nutrition*, 32(11-12), 1179-1192.

Sawatpanich T, Petpiboolthai H, Punyarachun B, Anupunpisit V (2010) Effect of curcumin on vascular endothelial growth factor expression in diabetic mice kidney induced by streptozotocin. *Journal of the Medical Association of Thailand, Chotmaihet Thangphaet* 93: S1-8.

Sayed AA, Khalifa M, Abd el-Latif FF. Fenugreek attenuation of diabetic nephropathy in alloxan-diabetic rats: attenuation of diabetic nephropathy in rats. *J Physiol Biochem.* 2012;68(2):263–269

Shiju, T., Rajesh, N., & Viswanathan, P. (2013). Renoprotective effect of aged garlic extract in streptozotocin-induced diabetic rats. *Indian Journal of Pharmacology*, 45(1), 18.

Soetikno V, Sari FR, Sukumaran V, Lakshmanan AP, Harima M, et al. (2013) Curcumin decreases renal triglyceride accumulation through AMPK–SREBP signaling pathway in streptozotocin-induced type 1 diabetic rats. *J Nutr Biochem* 24: 796-802

Soetikno V, Sari FR, Veeraveedu PT, Thandavarayan RA, Harima M, et al. (2011) Curcumin ameliorates macrophage infiltration by inhibiting NF- κ B activation and proinflammatory cytokines in streptozotocin induced-diabetic nephropathy. *Nutr Metab (Lond)* 8: 35

Soetikno V, Watanabe K, Sari FR, Harima M, Thandavarayan RA, et al. (2011) Curcumin attenuates diabetic nephropathy by inhibiting PKC- δ and PKC- ϵ activity in streptozotocin-induced type I diabetic rats. *Mol Nutr Food Res* 55: 1655-1665.

Suresh Babu P, Srinivasan K (1998) Amelioration of renal lesions associated with diabetes by dietary curcumin in streptozotocin diabetic rats. *Mol Cell Biochem* 181: 87-96.

Tang D, Zhang Z, Gao Y, et al. Protective effects of serum containing Ginkgo biloba extract on glomerulosclerosis in rat mesangial cells. *J Ethnopharmacol.* 2009 6;124(1):26–33

- Teschke R. , A. Wolff, C. Frenzel, A. Eickhoff, and J. Schulze, “Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders,” *World Journal of Gastroenterology*, vol. 21, no. 15, pp. 4466–4490, 2015.
- Thomson, M., Al-Qattan, K. K., Al-Sawan, S. M., Alnaqeeb, M. A., Khan, I., & Ali, M. (2002). The use of ginger (*Zingiber officinale* Rosc.) as a potential anti-inflammatory and antithrombotic agent. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 67(6), 475–478.
- Thomson, M., Al-Qattan, K. K., Bordia, T., & Ali, M. (2006). Including garlic in the diet may help lower blood glucose, cholesterol, and triglycerides. *The Journal of Nutrition*, 136(3), 800S–802S.
- Thomson, M., Al-Qattan, K., Mansour, M. H., & Ali, M. (2013). Effects of Garlic (*Allium sativum*) on indicators of diabetic nephropathy. *Federation of American Societies for Experimental Biology*
- Tikoo K, Meena RL, Kabra DG, Gaikwad AB (2008) Change in posttranslational modifications of histone H3, heat-shock protein-27 and MAP kinase p38 expression by curcumin in streptozotocin-induced type I diabetic nephropathy. *Br J Pharmacol* 153: 1225–1231.
- Tripoli, E., Giammanco, M., Tabacchi, G., Di Majo, D., Giammanco, S., & La Guardia, M. (2005). The phenolic compounds of olive oil: Structure, biological activity and beneficial effects on human health. *Nutrition Research Reviews*, 18(1), 98–112.
- Trujillo J, Chirino Y, Molina-Jijón E, Andérica-Romero AC, Tapia E, et al. (2013) Renoprotective effect of the antioxidant curcumin: Recent findings. *Redox Biol* 1: 448–456.
- Tzeng, T.-F., Liou, S.-S., Chang, C. J., & Liu, I.-M. (2013). The ethanol extract of *Zingiber zerumbet* attenuates streptozotocin-induced diabetic nephropathy in rats. *Evidence-Based Complementary and Alternative Medicine*, 2013.
- Velasquez MT, Bhathena SJ, Ranich T, Schwartz AM, Kardon DE, Ali AA, et al. Dietary flaxseed meal reduces proteinuria and ameliorates nephropathy in an animal model of type II diabetes mellitus. *Kidney Int*, 64(6) 2003, 2100–7.
- Vessal G, Akmal M, Najafi P, Moein MR, Sagheb MM. Silymarin and milk thistle extract

may prevent the progression of diabetic nephropathy in streptozotocin-induced diabetic rats. *Ren Fail*, 32(6), 2010, 733-9

Wang G., Mao B., Z.-Y. Xiong et al., "The quality of reporting of randomized controlled trials of traditional Chinesemedicine: a survey of 13 randomly selected journals from mainland China," *Clinical Therapeutics*, vol. 29, no. 7, pp. 1456–1467, 2007.

Xue W, Lei J, Li X, Zhang R (2011) *Trigonella foenum graecum* seed extract protects kidney function and morphology in diabetic rats via its antioxidant activity. *Nutr Res* 31: 555-562.

Yang WC, Hwang SJ, Chiang SS, Chen HF, Tsai ST. The impact of diabetes on economic costs in dialysis patients: experiences in Taiwan. *Diabetes Res Clin Pract.* 2001; 54(Suppl 1):S47–54.

Yang WC, Hwang SJ. Taiwan Society of N: incidence, prevalence and mortality trends of dialysis end-stage renal disease in Taiwan from 1990 to 2001: the impact of national health insurance. *Nephrol Dial Transplant.* 2008; 23(12):3977–82.

Zhang L, Wei W, Guo X, et al. Ginkgo biloba extract for patients with early diabetic nephropathy: a systematic review. *Evid Based Complement Altern Med.* 2013;2013, article id 689142, 17 p., DOI:10.1155/2013/689142.

Zhou H, Beevers CS, Huang S (2011) The targets of curcumin. *Curr Drug Targets* 12: 332-347.