Austin Journal of Plant Biology

Open Access

Austin Publishing Group

Short Communication

Search for Promising Plant Extracts and Active Principles to Prevent and Treat Diabetic Nephropathy

Lysiuk RM* and Mboya JM

Department of Pharmacognosy and botany, Danylo Halytsky Lviv National Medical University, Ukraine

***Corresponding author:** Lysiuk Roman, Department of Pharmacognosy and botany, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Received: October 14, 2019; **Accepted:** November 20, 2019; **Published:** November 27, 2019

Abstract

Diabetes mellitus is a significant health challenge, which leads to development of various conditions, including diabetic nephropathy. There is a growing need to find a cure for the prevention and treatment of such conditions. Medicinal herbs and individual active ingredients found in plants have shown promising effects in the treatment, prevention and management of diabetic nephropathy. The review summarizes current scientific data concerning extracts and individual active principles of medicinal plants that have shown nephroprotective effects in *in vivo* experimental studies. The following herbal substances might be considered as promising agents for application in diabetic nephropathy: *Galega officinalis, Glycyrrhiza glabra, Glycine max, Crataegus oxyacantha* and *Oleae europae, Fagopyrum esculentum, Brassica oleracea, Allium cepa, Zea mays,* rosmarinic acid, berberine, rhein.

Keywords: Diabetic nephropathy; nephroprotective plant extracts; individual herbal compounds; *in vivo* experimental studies.

Introduction

In recent years, there has been an increasing interest in the use of natural substances, and some questions concerning the safety of synthetic compounds have encouraged more detailed studies of plant resources. In addition to small molecules from medicinal chemistry, natural products are still major sources of innovative therapeutic agents for various conditions, including metabolic disorders.

The kidneys are important organs for elimination of toxic waste products, and maintaining fluid, mineral and electrolytes at levels which are vital for life. High blood glucose can damage the cells and micro blood vessels of the kidney. Advanced stage of renal damage results in the need for artificial filtration of the blood by dialysis and ultimately the need for a kidney transplant [1].

The kidneys are among the organs that diabetes impairs their activity. One amongst the indicators of renal failure (glomerular filtration) is increased blood levels of Urea (U) and Creatinine (Cr) caused by oxidative stress [2], that has been known to contribute significantly into the development and progression of Diabetic Nephropathy (DN). The formation of ROS (Reactive Oxygen Species) is a direct consequence of hyperglycemia. The severity of kidney damage in diabetic patients correlates with the levels of blood U and serum Cr. Antioxidants can diminish the level of U and Cr [3].

Even though the precise mechanism of DN is still arguable, oxidative stress has been regarded as a significant mediator in the progression of DN in diabetic patients. Process of excessive generation of ROS induced by sustained hyperglycemia is a central contributor underlying the pathogenesis of diabetes associated with vascular complications including DN [4].

DN is a common complication of diabetes and the leading cause of chronic kidney disease in the developed world, accounting for about half of all end stage renal disease cases. Approximately 40% of people with diabetes develop DN, manifested as albuminuria and/or decreased glomerular filtration rate [5].

The objective of the current research is summarization of scientific data related to promising effects of herbal drugs for the treatment of diabetic nephropathy, which were demonstrated in *in vivo* experimental studies.

Application of *Galega officinalis* extract, known as a rich source of flavonoids and microelements [6], resulted in protection of kidney tissue of rats against diabetes-induced degenerative injury (streptozotocin, 50 mg/kg) [2]. The levels of Cr and U were significantly decreased in group, received hydroalcoholic extract of *Galega officinalis* (50 mg/kg) as compared with the diabetic control group. Reduction of the diameter of glomeruli, increase in the diameter of the urinary spaces and the number of glomeruli, a decrease of the thickness of the basement membrane, kidney weight and the level of Cr and U in diabetic rats may be as a result of the presence of antioxidant principles in the investigated extract [2].

Licorice (*Glycyrrhiza glabra*) extract was used for oral ingestion by rats for 60 days (1 g/kg Body Weight (BW) daily) after the onset of diabetes. It reversed the adverse effect of diabetes on rats due to its antioxidant and hypoglycemic effects. The extract restored renal function, reduced blood glucose level, weakened body-weight loss, regulated the adverse impact of diabetes on renal malondialdehyde, glutathione, superoxide dismutase, and catalase activity [7].

Soybeans (*Glycine max*) exhibit positive effect on reducing urinary albumin excretion and total cholesterol in non-diabetic patients with nephrotic syndrome. It has been demonstrated [8] that soybean consumption reduced urinary protein excretion in type 1 diabetic patients with DN, otherwise it elicit an increase in the excretion in type 2 diabetic patients. Improvement in glomerular and tubulointerstitial lesions, also as decrease of osteopontin and aquaporin expression in the kidney specimens were shown in the

Citation: Lysiuk RM and Mboya JM. Search for Promising Plant Extracts and Active Principles to Prevent and Treat Diabetic Nephropathy. Austin J Plant Biol. 2019; 5(1): 1022.

diabetic rat group given a soybean diet. Soybeans may avert the renal weight loss and morphological changes related to diabetes mellitus [8].

To investigate the renoprotective role of 70% ethanolic alcohol extract of Hawthorn (*Crataegus oxyacantha*) and crude polyphenolic compounds of black olive fruits (*Oleae europae*), a study [9] was conducted on some physiological functions of the male rats kidney treated with 1% hydrogen peroxide. The extract ingestion resulted in significant reduction in the concentration of uric acid, Cr, glucose of treated groups G2 (Hawthorn 300 mg/ kg with 1% H_2O_2 in drinking water) and G3 (200mg /kg of crude extract of black olive with 1% H_2O_2), also significant decline in the concentration of U of treated group (G3) as compared with control one. The treatment with hawthorn and crude polyphenol manifested no clear pathological lesions.

The totality of flavonoids of buckwheat (*Fagopyrum esculentum*) flowers and leaves decreased blood glucose and blood lipid levels, impeded the formation of products from the glycation of proteins *in vitro* and *in vivo*. The flavonoid extract possessed a prominent protective effect on kidney injury in diabetes mellitus type 2 rats, declined 24 h urinary protein output, renal indexes and morphological changes of the renal tissue, enhanced glucose tolerance, reduced blood glucose dose-dependently [10].

Oral use (1 g/kg BW daily) of red cabbage (*Brassica oleracea*) extract for 60 days reversed the symptoms of diabetes in rats. The extract decreased blood glucose levels and restored renal function and body weight loss. It also vitiated the adverse effects of diabetes on malondialdehyde, glutathione and superoxide dismutase activity as well as catalase activity and total antioxidant power of diabetic renal tissue [11].

Anti-diabetic and hypoglycemic effects of *Allium cepa* juice were demonstrated by a study conducted using (2ml 100g BW/day), proposing its possible nephroprotective action in improving kidney injury in diabetic rats [12]. Plasma glucose level of Streptozotocin (STZ)-induced diabetic animals was lowered significantly after treatment with onion juice. Tubular damage, degenerative and atrophic manifestations in kidney glomeruli observed in untreated diabetics were less prominent and well – improved in the treated diabetic group. Another research [13], confirmed that *Allium cepa* possesses kidney protective action in diabetic rabbits (single intraperitoneal injection of alloxan) due to occurrence of anti oxidants which in diabetes mellitus could avert kidney injury caused by hyperglycemia.

The action of aqueous extract from the style of *Zea mays* on was tested against the DN model, development of which was confirmed by urinary albumin excretion and Cr clearance [1]. The extract reduced effectively the progression of diabetic glomerular sclerosis and averted glomerular hyper filtration in STZ-induced diabetic rats.

Rosmarinic acid, a plant phenolic substance, was applied as an antioxidant agent for inhibition of the experimental DN [14], caused in uni nephrectomized male rats by subcutaneous alloxan injection. After 8 weeks treatment, the level of glomerular number and serum malondialdehyde in the treated groups (100 mg/kg or 200mg/kg of rosmarinic acid) was maintained at the same level as compared to the control group. Rosmarinic acid significantly hindered glomerular hypertrophy, glomerular number loss, glomerulosclerosis, lipid peroxidation, serum U and Cr compared with the diabetic untreated group [14].

The study [15] revealed the anti-inflammatory effects of berberine, an isoqunoline alkaloid, in STZ-induced DN. Berberine boosts the kidney function in diabetic rats, evidenced by extenuation of diabetes induced in kidney index, albuminuria, U nitrogen and Cr clearance. The observations assumed that berberine -treated groups could ameliorate histological changes of DN.

Rare structure of rhein, a plant quinone compound, comprising of strong polar carboxyl and hydroxyls groups, adds to the benefits of antioxidant, exhibiting promising therapeutic potential in disrupting the progression of DN, considering its ability to decrease ROS production and NADPH oxidase p47(phox) activation. Rhein can terminate hyperglycemia, hyperlipidemia, inflammation and oxidative stress, improving the pathological changes occurring in the progress of DN [4].

Activities of resveratrol, a plant phytoalexin polyphenolic substance, have been extensively examined for its potent antioxidant and specific effects on proteins and/or signaling cascades, such as Sirt1, AMPK, PI3K/Akt, and JNK/ NF-κB in DN both i*n vivo* and *in vitro* [16]. Resveratrol reduced the activity of PI3K/Akt phosphorylation, resulting in a decline in BAX and an augmentation in BCL-2 and superoxide dismutase production in diabetic renal tissue of *db*/*db* mice [17]. Resveratrol averted renal mesangial cell proliferation and fibronectin expression due to suppression of high glucose-induced JNK and NF-κB activation, NADPH oxidase activity advancement and ROS production. Resveratrol prohibits diabetes-induced kidney inflammation and mesangial cell proliferation possibly through delay of Akt/NF-κB pathway [18].

Conclusions

A variety of herb extracts and individual substances have been identified that show nephroprotective effect and help control the progression of DN and related disorders.

The presented investigation outcomes might be used as a useful tool for development of drugs of plant origin, as well herbal collection, of renoprotective (antidiabetic) activity.

The carried out investigation may provide an optimization pathway for application of safe and effective extracts of medicinal plant materials and their individual active substances for treatment of DN.

References

1. Suzuki R, Okada Y, Okuyama T. The favorable effect of style of Zea mays L. on streptozotocin induced diabetic nephropathy. Biological and Pharmaceutical Bulletin. 2005; 28: 919-920.

2. Abtahi-Evari SH, Shokoohi M, Abbasi A, Rajabzade A, Shoorei H, Kalarestaghi H. Protective Effect of Galega officinalis Extract on Streptozotocin-Induced Kidney Damage and Biochemical Factor in Diabetic Rats. Crescent Journal of Medical and Biological Sciences. 2017; 4: 108-114.

3. Sharma S, Kulkarni SK, Chopra K. Curcumin, the active principle of turmeric (Curcuma longa), ameliorates diabetic nephropathy in rats. Clin Exp Pharmacol Physiol. 2006; 33: 940-945.

4. Zeng CC, Liu X, Chen GR, Wu QJ, Liu WW, Luo HY, et al. The molecular

mechanism of rhein in diabetic nephropathy. Evid Based Complement Alternat Med. 2014; 2014: 487097.

5. Jing Chen. Diabetic Nephropathy: Scope of the Problem. In: E.V. Lerma, V. Batuman (eds.), Diabetes and Kidney Disease, Springer Science+Business Media, New York. 2014; 256.

6. Barchuk OZ, Lysiuk RM, Denys AI, Zaliska OM, Smalyuh OG, Nester MI. Experimental study of goat's rue (Galega Officinalis L.) herb and its liquid extracts. The Pharma Innovation Journal. 2017; 6: 393-397.

7. Kataya HH, Hamza AA, Ramadan GA, Khasawneh MA. Effect of licorice extract on the complications of diabetes nephropathy in rats. Drug Chem Toxicol. 2011; 34: 101-108.

8. Young EC, Soo KA, Won TL, Jong EL, Seung HP, Bang BY, et al. Soybeans Ameliolate Diabetic Nephropathy in Rats. 2010; 7: 433-440.

9. Anwar I.O, Al-Abdali. Study effect of crude alcoholic extract of Hawthorn (Crataegus Oxyacantha) and crude polyphenolic compounds from black olive (Olea Europae) fruits on some physiological parameters of kidney of male rats treated with hydrogen peroxide. Iraqi Journal of Cancer and Medical Genetics. 2014; 7: 113-120.

10. Chu JX, Wang ZL, Han SY. The Effects of Total Flavonoids from Buckwheat Flowers and Leaves on Renal Damage and PTP1B Expression in Type 2 Diabetic Rats. Iranian Journal of Pharmaceutical Research. 2011; 10: 511-517.

11. Kataya HA, Hamza AA. Red Cabbage (Brassica oleracea) Ameliorates Diabetic Nephropathy in Rats. 2008; 5: 281-287.

12. Ayelagbe OG, Adele AS. Effect of Allium Cepa Supplemented Diets on Plasma Glucose, Electrolytes and Renal Histology of Streptozotocin-Induced Diabetic Rats. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS). 2015: 25-32.

13. Yusuf UA, Olusola A, Salawu EO, Enaibe BU, Omotoso OD. Allium cepa Protects Renal Functions in Diabetic Rabbit. World J Life Sci. and Medical Research. 2012; 2: 86-90.

14. Tavafi M, Ahmadvand H, Khalatbari A. Rosmarinic Acid Ameliorates Diabetic Nephropathy in Uninephrectomized Diabetic Rats. Iranian Journal of Basic Medical Sciences. 2011; 14: 275-283.

15. Wu Z, Xie Z, Liu J, Wu Q, Xiaokang W. Renoprotective Effect of Berberine on Streptozotocin-induced Diabetic Nephropathy Rats. International Journal of Pharmacology. 2017; 13: 247-256.

16. Lastra de la CA, Villegas I. Resveratrol as an antioxidant and pro-oxidant agent: mechanisms and clinical implications. Biochem Soc Trans. 2007; 35: 1156-1160.

17. Jang IA, Kim EN, Lim JH, Kim MY, Ban TH, Yoon HE, et al. Effects of Resveratrol on the Renin-Angiotensin System in the Aging Kidney. Nutrients. 2018; 10.

18. Xu F, Wang Y, Cui W, Yuan H, Sun J, Wu M. Resveratrol Prevention of Diabetic Nephropathy Is Associated with the Suppression of Renal Inflammation and Mesangial Cell Proliferation: Possible Roles of Akt/NF-κB Pathway. Int J Endocrinol. 2014; 2014: 289327.