TITLE

Usefulness of dietary components as sustainable nutraceuticals for chronic kidney disease

AUTHORS

Amaia Iriondo-DeHond¹, Jaime Uribarri², María Dolores del Castillo¹

¹Food Bioscience Group, Department of Bioactivity and Food Analysis, Instituto de Investigación en Ciencias de la Alimentación (CIAL) (CSIC-UAM), C/ Nicolás Cabrera, 9, Campus de la Universidad Autónoma de Madrid, 28049 Madrid, Spain.
amaia.iriondo@csic.es, mdolores.delcastillo@csic.es

²Department of Medicine, The Icahn School of Medicine at Mount Sinai, 1468 Madison Ave, New York, NY 10029, USA. jaime.uribarri@mountsinai.org

Keywords

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Synopsis

Chronic kidney disease (CKD) has become a global health concern because of its high incidence, prevalence and the healthcare burden cost associated with it. An extensive literature supports that phytochemicals and nutrients from edible plants, herbs, food and waste products generated during their processing represent a healthy, sustainable and safe strategy to produce functional foods and nutraceuticals. The addition of these functional foods and nutraceuticals to traditional medicine, a healthy diet enriched in fruits and vegetables with unprocessed foods and controlled levels of salts and sugars could be helpful strategies for people suffering CKD.

28 **Abstract**

29 Chronic kidney disease (CKD) is a worldwide public health problem with increasing
30 incidence and prevalence, poor outcomes, and high cost. The increasing incidence and
31 prevalence of obesity, poor nutrition and lack of exercise are associated with higher
32 incidence of diabetes mellitus and hypertension, main causes of CKD in the western
33 world. Therefore achieving a healthy lifestyle in order to prevent or reduce the risk of this
34 disease is of great importance. In this chapter we propose two different strategies to
35 prevent or reduce the risk of CKD beyond the effects of currently available
36 pharmaceutical drugs: a) innovative medicine based on dietary changes and consumption
37 of nutraceuticals obtained from foods, edible plants, food waste products or functional
38 foods and b) traditional medicine based on herbs and botanicals. The search for new
39 functional food ingredients from natural sources is one of the most important challenges
40 in order to achieve sustainable health.

41

Introduction

Chronic kidney disease (CKD) is a condition characterized by a gradual loss of kidney function over time. The loss of renal function may be due to previous episodes of acute renal failure with subsequent long term kidney damage or result from diseases which cause progressive deterioration of the kidney such as primary kidney diseases (glomerulonephritis) or secondary disorders such as diabetes, hypertension, or autoimmune disorders (International Society of Nephrology, 2013). The most common causes of CKD in the western world are diabetes and hypertension, both of which are mostly due to long-term unhealthy lifestyles. Some of the other diseases and conditions that lead to CKD are included in Table 1.

<Table 1 near here>

Cardiovascular disease (CVD) is the primary cause of morbidity and mortality in CKD patients and CKD is regarded as an independent risk factor for CVD events (Hill *et al.*, 2016). Chronic hyperglycemia in diabetes mellitus may be followed by kidney damage and diabetic nephropathy. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 (Wild Sarah *et al.*, 2004). Early nephropathy is characterized by the presence of microalbuminuria (30–300mg albumin/day), normal or increased glomerular filtration and eventually decreased GFR with proteinuria (Miranda-díaz *et al.*, 2016). Early detection of diabetic nephropathy might have an impact in the clinical course of the disease.

CKD is common, but usually asymptomatic and may go undiagnosed until the process is far advanced and renal failure is on the horizon. People with permanent kidney failure need dialysis or a transplanted kidney to do the work of their failed kidneys. Although the need for treatment of chronic kidney failure with dialysis and/or kidney transplantation

arises in only a small percent of people with CKD, this condition remains the most expensive of chronic diseases and reduces lifespan significantly. The costs of dialysis and transplantation consume disproportionate amounts of the health-care budgets of many countries (International Society of Nephrology, 2013).

Since the incidence, prevalence, and cost of CKD are increasing, and currently there are limited pharmacological therapeutic approaches, research into new compounds is badly needed and should be accelerated. Some therapies can help control the signs and symptoms, reduce the risk of complications, and slow the progression of this disease.

Many of the causes and risk factors that lead to CKD (Table 1, in italics) originate from an unhealthy diet and inappropriate eating behavior. Dietary advice is routinely recommended in people with CKD, but mostly concentrated on limiting sodium, potassium, phosphorus and protein intakes. Moreover, there is some evidence that certain healthy eating patterns may prevent cardiovascular events, diabetes and therefore, lower mortality in the general population and in CKD patients (Rebholz *et al.*, 2016; Sc *et al.*, 2017). An extensive literature supports that phytochemicals and nutrients from edible plants, herbs, food and waste products generated during their processing represent a healthy, sustainable and safe strategy to produce functional foods and nutraceuticals. To increase the knowledge on phytochemicals, their bioactivity and impact in human health and disease, “Phytochemomics” was proposed as an advanced analytical approach. This multidisciplinary research field is essential for establishing a cause-effect relationship and authorizing or rejecting nutrition and health claims made on foods, herbs and botanicals enriched in phytochemicals (del Castillo *et al.*, 2013).

In this chapter we propose two different approaches to prevent or reduce the risk of CKD:

a) innovative medicine based on dietary changes, consumption of nutraceuticals,

functional foods or bioactive compounds present in food waste and b) traditional medicine based on herbs and botanicals.

Healthy and sustainable diet to prevent or reduce the risk of CKD

Food has a vital role in maintaining our health properly and helps in the prevention and cure of certain diseases. There is evidence that diet rich in fruits, vegetables, and some sorts of oil seeds and nuts may prevent chronic diseases (Manach *et al.*, 2004; Piscopo, 2009; Bahadoran, Mirmiran and Azizi, 2013). Since prehistoric times, humans have used natural products, such as plants, animals, microorganisms, and marine organisms in medicines to alleviate and treat diseases (Yuan *et al.*, 2016).

The Spanish Society for Community Nutrition (SENC) has proposed a new Healthy Eating Pyramid, which includes food recommendations and healthy lifestyle advice (Figure 1) (Aranceta Bartrina *et al.*, 2016). On the top of the pyramid, a new tip appears regarding nutritional supplements, nutraceuticals and functional foods. Moreover, the SENC recommends healthy culinary practices such as steaming, grilling and oven cooking, and a sustainable diet committed to the environment. Different cooking methods can substantially affect the content of advanced glycation end products (AGEs) in food without necessarily changing the nutrient composition. AGEs are important in clinical science because they are associated with oxidative stress and inflammation, processes that eventually cause most chronic diseases, including cardiovascular disease, diabetes, chronic kidney disease (CKD), and neurodegenerative diseases (Uribarri *et al.*, 2015).

<Figure 1 near here>

Management of the diet is important in the prevention of disease progression and symptom alleviation of CKD (Hasegawa, Jao and Inagi, 2017). The main nutrition-related

goals for people with CKD involve the slowing of kidney failure progression rate and minimizing uremic toxicity and metabolic disorders of kidney failure, diminishing proteinuria, maintaining good nutritional status, and lowering the risk of secondary complications including cardiovascular disease, bone disease, and disturbed blood pressure control (Gluba-Brzózka, Franczyk and Rysz, 2017). The following dietary recommendations are made in order to reduce the risk and treat CKD:

1. A plant-based diet, containing large amounts of whole-grains, nuts, fruits and vegetables, and rich in dietary fibers, n-6 fatty acids, folic acid, potassium, magnesium, vitamin E, vitamin C, carotenoids, as well as many phytochemicals, can delay the progression of CKD (Gluba-Brzózka, Franczyk and Rysz, 2017).

Careful assessment of the potassium content is important when dealing with very advanced stages of CKD since these patients may have problems eliminating potassium from the body.

2. A protein-restricted diet can slow down progression and loss of residual renal function in patients with advanced CKD (Fouque *et al.*, 2001).
3. Phosphate reduction. Epidemiological data strongly suggest that serum phosphorus concentrations higher than the normal range are associated with increased (cardiovascular) morbidity and mortality (Gansevoort *et al.*, 2013).
4. Salt-restricted diets have been associated with less proteinuria and glomerulosclerosis. High dietary sodium is an important factor influencing blood pressure, predisposing patients with established CKD to salt-sensitive hypertension and fluid retention. It may also directly cause renal damage (Rysz *et al.*, 2017).

5. A diet rich in dietary fiber is recommended in patients with early CKD to reduce inflammation and mortality (Ash *et al.*, 2014).
6. Calorie restriction and weight loss. Obese (BMI > 30.0 kg/m²) and overweight (BMI 25.0–29.9 kg/m²) people should be encouraged to reduce their BMI to lower their risk of chronic kidney disease and end-stage renal disease (Ash *et al.*, 2014).
7. Dietary restriction of AGEs may be a reasonable method to reduce the excessive amount of AGEs in vital tissues and potentially the many complications associated with CKD due to their accumulation (Uribarri *et al.*, 2003). Healthy cooking techniques may allow achieving this goal (Figure 1).
8. Vitamin D nutritional supplementation in cases of deficiency and insufficiency of this micronutrient is recommended (Ash *et al.*, 2014). Dietary supplementation with vitamins is advised to achieve a healthy nutrition (Figure 1).

Innovative medicine

The nutraceutical industry is growing very fast exceeding the expansion in the food and pharmaceutical industries. Consumption of nutraceuticals and functional foods is considered an important approach to maintain health of the population and to prevent and treat nutritionally induced chronic diseases, therefore promoting optimal health, longevity and quality of life. Although nutraceuticals have significant promise in the promotion of human health and disease prevention, health professionals, nutritionists and regulatory toxicologists should strategically work together to plan appropriate regulations to assure ultimate health and therapeutic benefit to mankind (Kumar and Kumar, 2016).

Nutraceuticals

Nutraceuticals have received considerable interest in recent times because of their safety and potential positive physiological effects on the human body. The term Nutraceutical was first defined by Dr. Stephen L. De Felice, founder and chairman of the Foundation for Innovation in Medicine, as “any non-toxic food extract supplement that has scientifically proven health benefits for both disease prevention and treatment” (Singh and Geetanjali, 2013).

The prevention of renal dysfunction by nutraceuticals is one of the strategies followed by some researchers in order to reduce the risk of CKD. Studies carried out by Al-Okbi *et al.* (2014) investigated the protective effect of extracts prepared from avocado, walnut, flaxseed and *Eruca sativa* seeds in a rat model of kidney dysfunction induced by intraperitoneal administration of cisplatin. Cisplatin treatment induced a significant increase in plasma urea, creatinine and malondialdehyde along with a significant reduction of plasma albumin, total protein, catalase and total antioxidant activity as well as a reduction in creatinine clearance. Administration of extracts improved biochemical, histopathological and cytogenetic parameters showing a protective role against cisplatin-induced nephrotoxicity in this animal model (Al-Okbi *et al.*, 2014).

Almomen *et al.*, (2017) investigated the beneficial effect of whole grape powder (WGP) on CKD associated with metabolic syndrome. Obese diabetic ZSF1 rats, a kidney disease model with metabolic syndrome, were fed with a WGP (5%, w/w) diet for six months. Kidney disease was determined using blood and urine chemical analyses, and histology. When compared to controls, WGP intake improved renal function as urination and proteinuria decreased, and it prevented kidney tissue damage in these diabetic rats. The renal protection of WGP was associated with up-regulation of antioxidants (Dhcr24, Gstk1, Prdx2, Sod2, Gpx1 and Gpx4) and downregulation of Txnip (for ROS production)

186 in the kidneys. Furthermore, addition of grape extract reduced H₂O₂-induced cell death
187 of cultured podocytes. This study concluded that daily intake of WGP reduces the
188 progression of kidney disease in obese diabetic rats, suggesting a protective function of
189 antioxidant-rich grape diet against CKD in the setting of the metabolic syndrome
190 (Almomen *et al.*, 2017).

191 Park *et al.* (2014) examined whether oligonol, a low-molecular-weight polyphenol
192 derived from lychee fruit, has an ameliorative effect on diabetes-induced alterations, such
193 as AGE formation or apoptosis in the kidneys of db/db mice with type 2 diabetes. The
194 administration of oligonol for 8 weeks decreased elevated renal glucose concentration
195 and reactive oxygen species in db/db mice. The increased serum urea nitrogen and
196 creatinine concentrations, which reflect renal dysfunction in db/db mice, were
197 substantially lowered by oligonol. Oligonol also reduced renal protein expression of
198 NAD(P)H oxidase subunits, AGEs, and c-Jun N-terminal kinase B-targeting
199 proinflammatory tumor necrosis factor- α ($P < 0.05$). Oligonol improved the expressions
200 of antiapoptotic (Bcl-2 and survivin) and proapoptotic (Bcl-2-associated X protein,
201 cytochrome c and caspase-3) proteins in the kidneys of db/db mice ($P < 0.05$). These
202 results provide important evidence that oligonol exhibits renoprotective effects against
203 the development of diabetic complications in db/db mice with type 2 diabetes (Park,
204 Yokozawa and Noh, 2014).

205 The effects of oral supplementation with pomegranate extract on cardiovascular risk,
206 physical function, oxidative stress, and inflammation were studied in a group of
207 hemodialysis patients (Wu *et al.*, 2015). Patients ingested a 1000 mg capsule of a purified
208 pomegranate polyphenol extract or a placebo 7 days/week for 6 months. Pomegranate
209 extract supplementation reduced blood pressure and increased the antioxidant activity,
210 but it did not affect other markers of cardiovascular risk in these patients.

211

212 *Functional foods*

213 The European Food Safety Authority (EFSA) defines functional foods as: “A food, which
214 beneficially affects one or more target functions in the body, beyond adequate nutritional
215 effects, in a way that is relevant to either an improved state of health and well-being and/or
216 reduction of risk of disease. A functional food can be a natural food or a food to which a
217 component has been added or removed by technological or biotechnological means, and
218 it must demonstrate their effects in amounts that can normally be expected to be
219 consumed in the diet” (The European Parliament and The Council of the European Union,
220 2006).

221 It is well known that oxidative stress plays a major role in the genesis and progression of
222 CKD. Oxidative stress-induced activation of inflammatory and apoptotic signals are two
223 major problems in the pathogenesis of diabetic CKD (Bhattacharjee *et al.*, 2016). “Super
224 foods” that contain antioxidants can help neutralize free radicals and protect the body.

225 Increased dietary fiber intake in CKD patients may reduce serum creatinine levels and
226 improve GFR (Salmean *et al.*, 2013), and lower cholesterol levels and improve human
227 gut microbiota metabolism (Cosola *et al.*, 2017; Lyu *et al.*, 2017). Resistant starch, a form
228 of starch that resists digestion in the small intestine, classified as a type of dietary fiber,
229 has shown the potential as an ingredient in the treatment of CKD (Lockyer and Nugent,
230 2017). Foods containing phytochemicals with antioxidant properties and dietary fiber are
231 usually included in the kidney diet and make excellent choices for dialysis patients or
232 people with CKD (NHS Foundation Trust, 2015; Hall *et al.*, 2016; Colman, 2018). The
233 top foods recommended for achieving this goal and food ingredients responsible for their
234 CKD therapeutic properties are as follows:

<Figure 2 near here>

1. Red bell peppers are low in potassium and are also an excellent source of vitamin C and vitamin A, as well as vitamin B6, folic acid and fiber. They also contain lycopene, an antioxidant that protects against certain cancers.
2. Cabbage possesses high amounts of phytochemicals, vitamin K, vitamin C, vitamin B6, folic acid and fiber.
3. Cauliflower is high in vitamin C and a good source of folate and fiber. It also has high amounts of indoles, glucosinolates and thiocyanates, compounds that help the liver neutralize toxic substances that could damage cell membranes and DNA.
4. Garlic helps preventing plaque formation on teeth, lowers cholesterol and reduces inflammation.
5. Onions are rich in flavonoids, especially quercetin, a powerful antioxidant that reduces heart disease and protects against many cancers. Onions are low in potassium and a good source of chromium, a mineral that helps with carbohydrate, fat and protein metabolism.
6. Apples have high amounts of dietary fiber and anti-inflammatory compounds, and are known to reduce cholesterol, prevent constipation, protect against heart disease and reduce the risk of cancer.
7. Cranberries protect against bladder infections and also protect the stomach and the gastrointestinal tract from ulcer-causing bacteria. Cranberries have also been shown to protect against cancer and heart disease.
8. Blueberries are high in anthocyanidins and other natural compounds that reduce inflammation. They are a good source of vitamin C, manganese and fiber.

- 258 9. Raspberries contain ellagic acid which helps neutralize free radicals in the body
259 preventing cell damage. They also contain anthocyanins, manganese, vitamin C,
260 fiber and folate.
- 261 10. Strawberries are rich in two types of phenols: anthocyanins and ellagitannins.
262 They are also an excellent source of vitamin C and manganese and a very good
263 source of fiber. They are known to provide heart protection, as well as anti-cancer
264 and anti-inflammatory components.
- 265 11. Cherries have been shown to reduce inflammation when eaten daily. They possess
266 high amounts of antioxidants and phytochemicals that protect the heart.
- 267 12. Red grapes contain several flavonoids that help protect against heart disease by
268 preventing oxidation and reducing the formation of blood clots. Resveratrol may
269 also stimulate production of nitric oxide which helps relax muscle cells in the
270 blood vessels to increase blood flow. These flavonoids also provide protection
271 against cancer and prevent inflammation.
- 272 13. Egg whites provide protein with less phosphorus than other protein sources such
273 as egg yolk or meats.
- 274 14. Fish provides high-quality protein and contains anti-inflammatory ω -3 fatty acids.
275 The healthy fats in fish can help fight diseases such as heart disease by lowering
276 LDL and raising HDL.
- 277 15. Olive oil is a great source of oleic acid, an anti-inflammatory fatty acid. The
278 monounsaturated fat in olive oil protects against oxidation. Olive oil is rich in
279 polyphenols and antioxidant compounds that prevent inflammation and oxidation.
280 Studies show that populations that use large amounts of olive oil instead of other
281 oils have lower rates of heart disease and cancer.

Food wastes are produced throughout all the food life cycle. Food wastes derive, in a decreasing order, from the following sectors: vegetables and fruits; milk; meat; fish, and wine (Baiano, 2014). In order to increase the eco-sustainability of the food processing industry, it is necessary to exploit co-products before they become wastes. Until a few decades ago, food wastes were considered neither a cost nor a benefit, they were used as animal feed or brought to landfills or sent for composting (Kumar *et al.*, 2017). Food waste reduction and valorization can be achieved through the extraction of high-value components such as proteins, polysaccharides, fibers, flavor compounds and phytochemicals, which can be re-used as nutraceuticals and functional ingredients (Baiano, 2014). Since natural bioactive compounds are being searched for the treatment and prevention of human diseases, recovered compounds from food by-products could be used for medicinal and pharmaceutical purposes. Various studies have indicated that different kind of food wastes obtained from fruits, vegetables, cereal and other food processing industries can be used as potential source of bioactive food components “also called functional food ingredients” and nutraceuticals (Kumar *et al.*, 2017).

The by-products of viticulture, grape skin and seeds, have been found to contain higher amounts of polyphenols than the edible portions. The use of these residues as valuable raw materials may lead to significant economic gain and decrease in the environmental problems associated to the accumulation of grape by-products (Rockenbach *et al.*, 2011). Charradi *et al.* (2013) analyzed the protective effect of grape seed and skin extract on obesity-induced oxidative stress, renal steatosis and kidney dysfunction. Rats were fed a high-fat diet for 6 weeks and were treated with grape seed and skin extract. Fat-induced oxidative stress was evaluated in the kidney with a special emphasis on transition metals. High-fat diet induced triglyceride deposition and disturbances in kidney function

parameters, which are linked to oxidative stress and depletion of copper from the kidney. Grape seed and skin extract eliminated almost all fat-induced kidney disturbances. Grape seed and skin extract exerted potential protection against fat-induced kidney lipotoxicity; therefore, it has the potential of its application in other kidney-related diseases (Charradi *et al.*, 2013).

Grape seed extract has also been studied *in vitro* as a candidate therapeutic agent against diabetes mellitus. The protective effects of grape seed extract were studied on high glucose-induced cytotoxicity in LLC-PK1 cells, a porcine proximal tubule cell line. A high concentration of glucose (30mM) induced cytotoxicity and oxidative stress (ROS and nitric oxide) in cells, but treatment with grape seed extract had potent protective effects against high glucose-induced oxidative stress reducing levels of ROS and nitric oxide (FUJII *et al.*, 2006).

Corn silk (*Maydis Stigma*) is a by-product from corn cultivation, which is available in abundance. This by-product has been frequently used in traditional Chinese herbal medicines (Suzuki, Okada and Okuyama, 2005). Pan *et al.* (2017) studied the physicochemical properties and antidiabetic effects of a polysaccharide obtained from corn silk (PCS2). The hypoglycemic effects were determined using the high-fat diet and streptozocin induced type 2 diabetic mellitus (T2DM) insulin resistance mice. PCS2 treatment significantly reduced body weight loss, decreased blood glucose and serum insulin levels, and improved glucose intolerance. The levels of serum lipid profile were regulated and the levels of glycated serum protein, non-esterified fatty acid were decreased significantly ($P < 0.01$). The activities of superoxide dismutase, glutathione peroxidase and catalase were notably improved ($P < 0.05$). PCS2 also exerted cytoprotective action as shown by histopathological observation. These results suggested

that PCS2 could be a good candidate for functional food or medicine for T2DM treatment (Pan *et al.*, 2017).

Traditional medicine

Traditional medicine refers to health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain well-being (Fokunang *et al.*, 2011). The study of traditional medicine is a much neglected aspect of global health care and it faces the following challenges (Cordell and Colvard, 2012):

1. Nations typically have no policies or regulations relating to all of the aspects of traditional medicine as an integral part of their overall health care system. This results in a minimal commitment to research and development funding.
2. The breadth and depth of the issues related to the quality control of traditional medicine products and practices may not be known to regulators, producers, and scientists.
3. Global attention (fiscal and human resources) is insufficient to enhance the basic, applied, and clinical sciences behind traditional medicine. This results in major deficiencies in the scientific evidence regarding the quality, safety, effectiveness, and/or health benefits of traditional medicine. Costs of traditional medicines may increase as investment is made to enhance product validity.
4. The literature and knowledge regarding traditional medicine are highly scattered, or are in library collections and databases that are not easily accessible.

5. Scientific and clinical research on traditional medicines does not always fit the Western model for medical research, which may make publication of results difficult. Health insurance coverage is very difficult to justify if traditional medicine products and practices are not evidence based.

Medicinal plants represent one of the most important fields of traditional medicine all over the world and are a natural source of nutraceuticals (Singh and Geetanjali, 2013). A crucial factor in medicinal plant research and in clinical practice is sustainability. The term “sustainable medicines” describes the importance of considering the long-term use of both traditional medicines and synthetic drugs from a perspective of reliable and non-destructive sourcing for the future (Cordell, 2009). This is of great importance since the population and the use of traditional medicines are growing fast, globalization of products is in increasing demand, and climate change may affect the growing of traditional medicines (Cordell and Colvard, 2012). In this sense, “ecopharmacognosy” becomes a research priority since it is the study of sustainable biologically active natural products, from sustainable plant materials (Cordell, 2014).

Traditional medicine, sustainable medicines and ecopharmacognosy contribute to achieve a sustainable health. Del Castillo et al. (2018) have defined “sustainable health” as: “a healthy and active ageing avoiding the risk of diseases”. Sustainable health may be accomplished by delivering high quality care and improved public health without exhausting natural resources or causing severe ecological damage (del Castillo, Iriundo-DeHond and Martirosyan, 2018). This can also be achieved by protecting and improving health now and for future generations using different strategies such as a healthy nutrition based on functional foods and the use of traditional sustainable medicines.

Herbs and botanicals

Numerous drugs are originated from herbs or natural substances. Herbal and natural therapies have been employed for their diuretic and renal protective actions for centuries and the use of these substances may prevent the risk of CKD or complement current treatments (Wojcikowski, Johnson and Gobe, 2006).

Some plant extracts can be effective in the protection against CKD. *Ecklonia cava* has shown anti-inflammatory and antioxidative effects, and its effect on renal damage of high fat diet induced obese mice has been investigated (Eo *et al.*, 2017). Natural agents that possess antioxidant and anti-inflammatory effects are expected to possess a renal protective effect. Treatment of obese mice with different doses of *E. cava* extract for 12 weeks lowered protein levels related to lipid accumulation (SREBP1c, ACC & FAS), inflammation (NLRP3 inflammasome, NF κ B, MCP-1, TNF- α & CRP), and oxidative stress (Nrf2, HO-1, MnSOD, NQO1, GPx, 4-HNE and protein carbonyls). Moreover, this extract also significantly up-regulated renal SIRT1, PGC-1 α , and AMPK, which are associated with renal energy metabolism (Eo *et al.*, 2017). These results provide novel insights into the anti-inflammatory roles of *E. cava* in obesity-induced renal inflammation.

Grover *et al.* (2001) investigated the effects of daily oral feeding of traditional Indian herbs (*Momordica charantia* (MC), *Eugenia jambolana* (EJ), *Mucuna pruriens* (MP) and *Tinospora cordifolia* (TC)) for 40 days on blood glucose concentrations and kidney functions in streptozotocin (STZ)-diabetic rats. Plasma glucose concentrations in STZ-diabetic mice were reduced by the administration of extracts of MC, EJ, TC and MP by 24.4, 20.84, 7.45 and 9.07%, respectively. Urine volume was significantly higher in diabetic controls and Indian herb extracts prevented polyuria. After 10 days of STZ administration urinary albumin levels (UAE) were over 6 fold higher in diabetic controls

as compared to normal controls. Treatment with MC, EJ, MP and TC significantly prevented the rise in UAE levels from day 0 to 40 when compared to diabetic controls. Renal hypertrophy was significantly higher in diabetic controls as compared to non-diabetic controls. Among the studied extracts, only MC and EJ prevented renal hypertrophy as compared to diabetic controls (Grover *et al.*, 2001). Results indicate that plant extracts have the potential in the prevention of renal damage associated with diabetes.

Aster koraiensis, a vegetable and medicinal plant in traditional Korean medicine, has also been studied on the damage of renal podocytes in streptozotocin (STZ)-induced diabetic rats for 13 weeks (Sohn *et al.*, 2010). Blood glucose, glycated haemoglobin (HbA1c), proteinuria and albuminuria were examined. Kidney histopathology, AGEs accumulation, apoptosis, and expression of Bax and Bcl-2 also were examined. In STZ-induced diabetic rats, severe hyperglycemia developed, and proteinuria and albuminuria were markedly increased. *Aster koraiensis* extract reduced proteinuria and albuminuria in diabetic rats, and AKE prevented AGE deposition and podocyte apoptosis. Expression of Bax and Bcl-2 protein in the renal cortex were restored by treatment with the extract (Sohn *et al.*, 2010). Since this extract showed an inhibitory effect of AGE accumulation and an anti-apoptotic effect in the glomeruli of diabetic rats, it could be beneficial in preventing the progression of diabetic nephropathy.

Conclusion

Prevention programs may be the best strategy for reducing the risk of CKD. Dietary interventions based on the use of bioactive compounds from food, edible plants and their

wastes can be considered a useful approach to reduce the risk and progression of this chronic pathology; as well as, to achieve a sustainable health.

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