Role of Antioxidant Herbal Drugs in Renal Disorders: An Overview

Rasikh Javaid[1], Mohd Aslam[1], Qudsia Nizami[1], Raheela Javaid[2]

[1]*Deptt.of Ilmul Advia (Pharmacology), Faculty of Medicine, Hamdard University, New Delhi 110062.*
[2]*Deptt. of Phytochemistry and Pharmacognosy, Faculty of Pharmacy, Hamdard University, New Delhi 110062.*

ABSTRACT

Renal disorders have always remained a major area of concern for physicians since a long time. It is the 9th leading cause of death in United States. Incidence of kidney diseases leading to kidney failure is increasing day by day. A large number of chemicals in common use are potential renal toxins. The use of herbal drugs for the prevention and treatment of various diseases is constantly developing throughout the world. Many studies have been carried out that strongly support the contribution of antioxidants to the prevention of cardiovascular diseases, cancer, osteoporosis, neurodegenerative diseases, and diabetes mellitus, and suggest a role in the prevention of peptic ulcer. Polyphenols display a number of pharmacological properties in the renal area, acting as diuretic, anti inflammatory, antispasmodic, and antioxidant agents. The antioxidant properties of phenolic compounds have been widely studied, but it has become clear that their mechanisms of action go beyond the modulation of oxidative stress. Various polyphenolic compounds have been reported for their nephroprotective activity with a good level of renal protection. Therefore, considering the important role of polyphenolic compounds in the prevention or reduction of renal disorders induced by various nephrotoxic chemical agents, in this review, we have summarized the literature on some potent nephroprotective plants, such as, Achyrocline satureioides, Zingiber officinalis, Teminalia chebula etc having antioxidant properties.

Key words- Nephroprotection, herbal drugs, nephrotoxicity, antioxidants

INTRODUCTION

Kidneys are the organs that have numerous biological roles. Their primary role is to maintain the homeostatic balance of body fluids by filtering and secreting metabolites (such as urea) and minerals from the blood and excreting the nitrogenous wastes along with water, as urine. Because the kidneys are poised to sense plasma concentrations of ions such as sodium, potassium, hydrogen, and compounds such as amino acids, creatinine, bicarbonate, and glucose, they are important regulators of blood pressure, glucose metabolism, and erythropoiesis. Kidney disease not only has a significant morbidity, but a high mortality as well. Besides, the high costs and complexity of the treatments, very few patients are able to obtain adequate treatment and kidney disorders place a heavy financial burden on society. Nephrotoxicity is an inherent adverse effect of certain antibiotics, anticancer drugs and other synthetic molecules. A number of extracts of natural products and dietary antioxidants have been reported to show protective effects against nephrotoxicity. Following herbal drugs have shown their potent nephroprotective effect due their antioxidant, diuretic, anti inflammatory, antispasmodic properties.

***Address for correspondence:**
Rasikh Javaid,
Deptt.of Ilmul Advia (Pharmacology),
Faculty of Medicine, Hamdard University, New Delhi 110062.
E-mail: drrasikh@gmail.com
Mobile No.: 91 9716602197

DOI: 10.5530/ax.2012.2.2

Desmodium canadense

The effect of the dry extract obtained from the aerial parts of *d. canadense* on the course of CCl4 induced acute renal insufficiency was studied in male white rats. A marked nephroprotective effect was obtained with a dose of 50 mg/kg, with regeneration of the functional activity of the kidneys early in the pathological process. The protective effect of the extract may be explained by its antioxidant activity which is due to the high content of phenolic compounds[1].

Salvia miltiorrhiza

In this study isolated magnesium lithospermate B isolated from *Salvia miltiorrhiza*, which proved to be protective in renal dysfunction[2].

Tribulus terrestris and Crataeva nurvala

Both are reported to be nephroprotective against gentamicin induced nephrotoxicity in albino rats[3].

Achyrocline satureioides

Hydroalchoholic abstract of *A. satureioides* might change renal ion transport based on observations that it affects gastro-intestinal reabsorption.[4]

Boerhaavia diffusa

Clinical, experimental and immunological studies on Punarnava (*Boerhaavia diffusa*), an Ayurvedic drug showed equivalent diuretic effect to Furosimide an established diuretic drug. B.diffusa increases the protein level and reduces urinary protein excretion in patients of nephritic syndrome. Increase was noted also in the level of immunoglobulins and lower immune complex after one month of medication in patients of Nephrotic syndrome. Clinically punarnava proved to be useful and safe drug in patients of Nephrotic syndrome.[5]

Clerodendron trichotomum

Intravenous administration of the extract to rats and dogs, elicits renal vasodilatation and increased urine flow and urinary sodium excretion.[6]

Tinospora cordifolia

In experimental rats, *T. cordifolia* (100 mg/kg/day for 5 weeks) was found to decrease the renal damage, improved the fibrinogen levels and reduced lead acetate induced endotoxaemia. *T. cordifolia* was also found to decrease renal ischaemia induced mortality to 36.36%.[7]

Desmodium canadense

The effect of the dry extract obtained from the aerial parts of *d. canadense* on the course of CCl4 induced acute renal insufficiency was studied in male white rats. A marked nephroprotective effect was obtained with a dose of 50 mg/kg, with regeneration of the functional activity of the kidneys early in the pathological process. The protective effect of the extract may be explained by its antioxidant activity which is due to the high content of phenolic compounds.[1]

Ephedra distachya

Administration of *E. distachya* extract caused to decrease the concentration of urea nitrogen, creatinine, methylguanidine and guanidinosuccinic in serum of rats significantly.[8]

Ginko biloba

G. biloba leaf extract exhibited good protection against gentamicin induced nephrotoxicity in rats. Significant reduction in lipid peroxidation, urea and creatinine has been reported.[9] (Niazi 1994), G. biloba extract was increased. Histopathological examinations of the kidney revealed that those kidneys were completely protected against carbon tetrachloride induced toxicity by extract[10].

Portulacca pilose

Hydroalcoholic extract of *P. pilose* cause an increase in K excretion without a con-comitant change in water diuresis or Na excretion[4].

Teminalia chebula

The extract of *T. chebula* has been reported to possess uraemic toxin decreasing action in rats. It lowers the serum concentration of urea nitrogen, creatinine, methyl guanidine and guandiniosuccenic acid significantly[8].

Moringa oleifera

Methanolic extract of *Moringa oleifera* root was found to contain some alkaloids (total alkaloids 0.2%). Effects of multiple weekly (35, 46, 70 mg/kg) and daily therapeutic (3, 5, 4, 6, 7.0 mg/kg) ip doses of the crude extract (CE) on liver and kidney functions and hematological parameters in mice were studied. No alteration in hematological and biochemical parameters at low and moderate dose level of daily and low dose of weekly treatment of the extract was observed. The result indicate that the weekly moderate and high dose (less than 46 mg/kg body wt.) and daily/therapeutic high dose (7 mg/kg) and low and moderate daily/therapeutic dose (3.5 and 4.6 mg/kg) did not produce adverse effect on liver and kidney functions[11].

Dolichos biflorus

The extract of *Dolichos biflorus* contains phytonutrients such as alkaloids, flavonoids & isoflavone. Administration of it significantly lowered the level of thiobarbituric acid reacting substances (TBARS) and enhanced the level of glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD), thus protecting the tissues from oxidative stress[12].

Crataeva nurvala

Lupeol isolated from stem bark extract of *Crataeva nurvala* Buch-Ham (Cappavaceae) offered significant activity against free radical induced nephrotoxicity in rats[13].

Didymocarpus pedicellata

Ethanolic extract of the aerial parts of *Didymocarpus pedicellata* demonstrated significant antioxidant and protective activity against ferric nitriloacetate induced renal oxidative stress, nephrotoxicity and tumor promotion response. Further the extract provided significant protection against. The extract also significantly and dose-dependently protected against ferric nitriloacetate mediated damage to lipids and DNA. The nephroprotective activity of the plant is attributed to polyphenolic compounds. The study further supported ancient use of plant in the treatment of kidney diseases[14].

Astragalus and Salvia miltiorrhiza bunge

The *Astragalus* and *Salvia miltiorrhiza bunge* alcohol extracts were used in preventive treatment of glycerol induced acute renal failure (ARF) in rabbits. The experimental rabbits were divided: astragalus group (AB), salvia miltiorrhia bunge group (SM), two extracts mixture group (ABSM), and normol saline control group (C). The extracts, mixtures and normol saline were administrated before and after the induced ARF. The counts of Na, K, creatinine in urine and blood and urinary AAP, NAG were determinated during 24-14 days periodically in all 4 groups, and the renal tissues were taken from same periods for pathomorphological studies by microscopy and transmission electromicroscopy. The damage of the glycerol induced ARF was not only in the convolute tubules but also in the glomerulus. The glomerulor filtration rate reduced abruptly, and oligouria or auria developed. The study of renal functions and renal morphogy showed that the AB and ABSM groups were damaged more lesser and promptely repaired than the SM and C groups in the early stage. No glomerular sclerosis was noted in the AB, ABSM groups in later stage, but it occurred sporadically or diffusely in the SM, C groups. Therefore, astragalus is an ideal protective drug of traditional chinese medicine for ARF[15].

Sanguisorbae radix

The effect of *Sanguisorbae radix* extract, a traditional crude drug, was investigated in renal dysfunction induced by lipopolysaccharide (LPS) endotoxin. Injection of LPS in rats resulted in a sharp rise in the serum levels of urea nitrogen and creatinine (Cr), indicating impairment of renal function. Nitrite and nitrate levels and the activity of inducible nitric oxide synthase (iNOS), an enzyme which participates in NO synthesis, were also significantly increased in the serum of LPS-treated rats compared with normal rats. In rats pretreated with Sanguisorbae Radix extract, renal dysfunction was attenuated and the increases in serum urea nitrogen and Cr induced by LPS were significantly reduced. The administration of Sanguisorbae Radix extract also effectively lowered serum nitrite/nitrate level. A similar effect was observed on the iNOS activity. These results indicate that Sanguisorbae Radix extract contributes to the regulation of renal function under conditions where there is excessive generation of NO[16].

Hirsutella sinensis

Hirsutella sinensis can inhibit the production of TGF-beta1 and CTGF, factors that promote the extracellular matrix (ECM) synthesis and TIMP-1 and PAI-1, factors that antagonize ECM degradation in kidney tissues, thus alleviating renal interstitial fibrosis and improving renal function in CAAN (chronic aristolochic acid nephropathy)[17].

Glycyrrhizae radix

Study suggests that *Glycyrrhizae radix* extract could protect the kidneys against ONOO- through scavenging ONOO- and/or its precursor NO, inhibiting protein nitration and improving renal dysfunction caused by ONOO (Peroxinitrate).[18]

Coptidis rhizoma

This study suggested that *Coptidis rhizoma* could protect against ONOO (-)-induced oxidative damage and that this effect was mainly attributable to the constituent alkaloids, especially berberine. This study is the first to demonstrate an antioxidative effect of alkaloids, including berberine, against ONOO (-)-induced damage.[19]

Hemidescus indicus linn

The treatment with *H. indicus* helped in the management of renal impairment, which was induced by gentamicin in rats. This is evident from the results obtained for various kidney function tests for gentamicin, along with the results from the plant treated group, and is in comparison with the results found for the gentamicin recovery group. A histological examination of kidneys also supports the findings from haematological evaluations. The plant shows promise as an adjunct therapy along side aminoglycosides as it reduces nephrotoxicity caused by aminoglycosides.[20]

Zingiber officinale

Evidences suggested that ROM is involved in the nephrotoxicity of a widely used synthetic anticancer drug cisplatin. The nephroprotective effects of ethanol extract of *Zingiber officinale* alone and in combination with vitamin E (alpha/tocopherol) were evaluated using cisplatin (single dose of 10 mg/kg body wt, i.p) induced acute renal damage in mice. The results of the study indicated that *Z. officinale* significantly and dose dependently protected the nephrotoxicity induced by cisplatin[21].

CONCLUSION

In view of the above mentioned pharmacological studies, herbal drugs having antioxidant properties have proved their significant effects not only in preventing but also curing various kidney diseases. Plants have not only been the source of drug molecules but as well as the source of feedstock molecules that can be transformed in drugs.

REFERENCES

1. Nikolayev SM, Glyzin VI, Shantanov LN, Mondodoyev AG. Pharmacological activity of the dry extract from the above ground part of Desmodium canadense (L.) DC. During toxic kidney disease. Rastitel nye-Resursy.1996; 32(3):113-118.
2. Yokozawa T, Dong E, Chun HY, Oura H, Nishika I. A protective action of magnesium lithospermate B on renal function of rats and cultured proximal tubular cells. Natural Medicines.1997; 51 (4):289-292.
3. Meher BK, Chaudhry SB, Marjit B, Mukherjee PK, Ram AK, Munshi S, Das N, Kundu KK, Islam CN, Das AK. Indian journal of pharmacology.2001; 33(2):128
4. Rocha MJA, Fuigenico SF, Rabetti AC, Nicolau M, Poli A, Simones CMO, Riberirodo-Valle RM. Effect of hydroalcoholic extracts of Portulaca pilosa and Achyroline satureiodes on urinary sodium and potassium excretion. Journal of Ethnopharmacology.1994; 43(3):179-183.
5. Singh RP, Shukla KP, Panday BL, Singh RG, Usha Singh RH. Recent approach in clinical experimental evaluation of diuretic action of punarnava (Boerhaavia diffusa) with special reference to nephritic syndrome. Journal of Research and Education in Indian medicines. 1992; 11(1):29-36.
6. Lu GW, Miura K, Yukimura T, Yamamoto K. Effect of extract from Clerodendron tichotomum on blood pressure and renal function in rats and dogs. Journal of Ethnopharmacology. 1994; 42(2):77-82.
7. Koti RS, Rege NN, Javla HS, Desai NK, Bapat RD, Dahanukar SA. Tinospora cordifolia: A boon in therapy of multi organ dysfunction in obstructive jaundice. Update Ayurveda – 94 Bombay, 1994; India p-40, 24-26th Feb.
8. Yokozawa T, Fujioka K, Oura H, Tanaka T, Nonaka G, Nishioka I. Confirmation that tannin containing crude drugs have a ureamic toxin decreasing action. Phytotherapy Reasearch. 1995; 9 (1):1-5.
9. Niazi FR (1994) Influence of PAF antagonist (Ginko biloba) and ACE inhibitors (Captopril and Lisinopril) on gentamicin- induced nephrotoxicity in rats. M. Pharm thesis, F/O Pharmacy Jamia Hamdard.
10. Asuzu IU, Abubaker II. The emetic, antihepatotoxic, and antinephrotoxic effect of an extract from Icania tricantha. Journal of herbs, spices & medicinal plants.1995; 3 (4):9-20.
11. Mazumdar UK, Gupta M, Chakrabarti S, Pal D. Evaluation of methanolic extract of Moringa oleifera Lam. Root treated mice. Indian Journal of Experimental Biology.1999; 37(6):612-614.
12. Muthu AK, Sethupathy S, Manavalan R, Karar PK. Anti-oxidant potential of methanolic extract of Dolichos biflorus linn. in high fat diet fed rabbits. Ind. J. Pharmacol.2006; 38(2):131-132
13. Anand R, Patnaik GK, Kulshreshtha DK, Dhawan BN. Anti-urolithiatic activity of Lupeol, the active constituent from Crateva nurvala. Phytoth. Res. 1994; 8:417.
14. Kaur G. Protective effect of Didymocarpus pedicellata on ferric nitriloacetate induced renal oxidative stress and hyperproliferative response. Chem Biol Interact.2007; 165(1):33-34
15. Hu L, Yu T, Jia Z. Experimental study of the protective effects of Astragalus and Salvia miltiorrhiza bunge on glycerol induced acute renal failure in rabbits. Zhonghua Wai Ke Za Zhi. 1996; 34(5):311-4.
16. Chen CP, Yokoazwa T, Kitani K. Beneficial effects of Sanguisorbae radix in renal dysfunction caused by endotoxin in vivo. Bio. Pharm. Bull. 1999; 22(12):1327-30.
17. Zhu YF, Chen YP, Rui HL, Dong HR, Hu Z. Protective effects of Hirsutella sinensis on renal interstitial fibrosis: experiment with rat model of chronic aristolochic acid nephropathy. Zhonghua Yi Xue Za Zhi. 2007; 16(38):2667-71.
18. Yokozava T, Cho EJ, Rhyu DY, Shibahara N, Aoyagi K. Glycyrrhizae radix attenuates peroxynitrite-induced renal oxidative damage through inhibition of protein nitration. Free Radic.Res. 2005; 39(2):203-11
19. Yokozava T, Ishida A, Kashiwada Y, Cho EJ, Kim HY, Ikshiro Y. Coptidis rhizoma: protective effects against peroxynitrite-induced oxidative damage and elucidation of its active components. J.Pharm. Pharmacol. 2004; 56(4):547-56
20. Mangala S, Patel P, Menon NS, Sane TR. Renoprotective effect of Hemidesmus indicus, a herbal drug used in gentamicin-induced renaltoxicity. Nephrology. 2004; 9 (3):142-152.
21. Ajith TA, Nivitha V, Usha S. Zingiber officinale Roscoe alone and in combination with alpha/tocopherol protect the kidney against cisplatin/ induced acute renal failure. Food Chem Toxicol. 2006; 29.