

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Nephro- Protective Effects Of Arabian Medicinal Plants.

Ali E Al-Snafi^{1*}, and Mahdi M Thuwaini².

¹Department of Pharmacology, College of Medicine, Thi qar University, Nasiriyah, Iraq.

²Department of Basic Sciences, College of Nursing, University of Thi qar, Iraq.

ABSTRACT

Kidneys play an important part in the maintenance of our endocrine, acid-base balance, blood pressure, erythropoiesis etc. Kidney harm is one of the most vital health issues. Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin. Many medicinal plants have been reported to exhibit protective effect of renal tissues against injuries. Nephroprotective effects were mediated via modulating the expression of inflammatory, oxidative stress and apoptotic mediators. The current review will highlight the medicinal plants possessed nephroprotective effects.

Keywords: Medicinal plants, Pharmacology, Nephroprotective, Toxicology.

**Corresponding author*

INTRODUCTION

Kidneys play an important part in the maintenance of our endocrine and acid-base balance, blood pressure, erythropoiesis etc. Kidney harm is one of the most vital health issues. Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin[1]. A number of potent therapeutic drugs like penicillins, cephalosporins, tetracycline, sulfonamides, amino glycosides, NSAID's, chemotherapeutic agents and chemical reagents like ethylene glycol, carbon tetrachloride, sodium oxalate and heavy metals such as lead, mercury, cadmium and arsenic can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome, rapid decline in renal function resulting in abnormal retention of serum creatinine and blood urea, which must be excreted[2]. Many medicinal plants have been reported to exhibit protective effect of renal tissues against injuries. Nephroprotective effects were mediated via modulating the expression of inflammatory, oxidative stress and apoptotic mediators[3-4]. The current review was designed to highlight the medicinal plants possessed nephroprotective effects.

Table 1: Medicinal plants with nephro-protective effects

Plant	Extract or compounds	Model	Animal	Results	Ref
<i>Bauhinia variegata</i>	ethanolic and aqueous extracts of root of <i>Bauhinia variegata</i> , 200 and 400 mg/kg bw.	gentamicin-induced nephro-toxicity	Rats	Both extracts produced significant nephro-protective activity in gentamicin induced nephrotoxicity model as evident by decrease in elevated serum creatinine, serum urea, urine creatinine and blood urea nitrogen (BUN) levels, which was further confirmed by histopathology.	[5-6]
	ethanolic and aqueous extracts of root of <i>Bauhinia variegata</i> , 400 mg/kg bw	gentamicin and cisplatin induced nephrotoxicity	Rats	Both extracts showed nephroprotective activity in both gentamicin and cisplatin induced nephrotoxicity models as evident by decrease in serum creatinine, serum urea, urine creatinine and BUN levels.	
<i>Benincasa hispida</i>	hydro-alcoholic extract of <i>Benincasa hispida</i> whole fruit extract, 200 and 400 mg/kg bw.	paracetamol induced nephrotoxicity	Rats	Hydro-alcoholic extract significantly increased the tissue <i>glutathione</i> (GSH) levels and reduced lipid peroxidation levels. Histopathologically observed degenerative changes caused by paracetamol were also restored by treatment with hydro-alcoholic extract.	[8]
	total amino acids and cncurbitacine	mercury poisoning	Rats	It showed significant nephroprotective activity	[9-10]
<i>Brassica nigra</i>	methanol extract of <i>Brassica nigra</i> leaves, 200 and 400 mg/kg bw.	Dgalactosamine (D-GalN)-induced hepatic and nephrotoxicity.	Rats	It showed significant (p < 0.001) reduction in the DGalN-induced toxicity as obvious from biochemical parameters, which further confirmed by histology.	[11-12]
<i>Brassica rapa</i>	ethanol extract of the	cisplatin-induced	Rats	Rats given EBR showed lower	[13]

	roots of <i>Brassica rapa</i> (EBR)	nephrotoxicity		blood levels of BUN and creatinine, and of urinary LDH. Moreover, EBR prevented the rise of MDA production and the induction of AO and XO activities. This extract also recovered the reduced activities of GPx, SOD and CAT.	
<i>Bryophyllum calycinum</i>	aqueous and hydroalcoholic extracts of the leaves	gentamycin-induced nephrotoxicity	Rats	Aqueous extract possessed potent nephroprotective activity, while, hydroalcoholic extract exerted significant diuretic and antiurolithitic activity.	[14-17]
<i>Carum carvi</i>	aqueous extract of <i>Carum carvi</i> seeds, 30 and 60 mg/kg bw and essential oil 10 mg/kg bw.	experimentally induced diabetic nephropathy	Rats	It significantly decreased the levels of the biochemical parameters. High dose of <i>Carum carvi</i> aqueous seeds extract (60 mg/kg) showed renoprotection against STZ induced diabetic nephropathy. The kidney of <i>Carum carvi</i> essential oil treated rats showed marked improvement with minor pathological changes.	[18-19]
<i>Cassia occidentalis</i>	70% hydroalcoholic extract, 200 and 400 mg/kg bw.	gentamicin induced nephrotoxicity	Rats	Hydroalcoholic extract markedly reduced gentamicin induced elevation of urinary sodium, potassium electrolytes, urinary glucose, blood urea and creatinine levels. It also increased the body weights. The histopathological study of kidney exhibited almost normal architecture.	[20-22]
<i>Casuarina equisetifolia</i>	methanolic extract of <i>Casuarina equisetifolia</i> leaves, 300 mg/kg bw.	gentamicin induced nephrotoxicity	Rats	Administration of extract restored normal renal functions and attenuated oxidative stress. It ameliorates gentamicin-induced nephrotoxicity and oxidative damage by scavenging oxygen free radicals, decreasing lipid peroxidation and improving intracellular antioxidant defense.	[23-24]
<i>Citrullus colocynthis</i>	The extract of <i>Citrullus colocynthis</i> fruit, 50mg/kg bw/day.	streptozotocin induced diabetic nephropathy	Rats	<i>Citrullus colocynthis</i> fruits extract caused significant decrease in blood glucose, urea, creatinine, microalbuminuria and uric acid, while, GSH, GPx and SOD were significantly increased in	[25-26]

				comparison with diabetic untreated group. The histopathological findings were coincided with biochemical findings.	
	extract of <i>Citrullus colocynthis</i> , 25 mg/kg bw /day	gentamicin induced nephrotoxicity	Rats	Co-therapy of <i>Citrullus colocynthis</i> with gentamicin inhibited changes in the body weight, blood urea nitrogen, creatinine clearance, proteins and lactate dehydrogenase excretions.	[27]
<i>Crocus sativus</i>	saffron extract and crocin, 30 mg/kg bw of each	chronic - stress induced oxidative stress damage of kidneys	Rats	Saffron and its active constituent crocin can prevent chronic stress-induced oxidative stress damage of kidneys.	[28-29]
	saffron 40 or 80 mg/kg bw/day	gentamicin induced nephrotoxicity	Rats	Saffron at 40 mg/kg/day significantly reduced gentamicin-induced increases in BUN and histological scores (p<0.05). Gentamicin-induced increases in BUN, SCr and MDA and histological injury were significantly reduced by treatment with saffron 80 mg/k/d (p<0.05, p<0.001, p<0.05, and p<0.001 respectively).	[30]
<i>Cuminum cyminum</i>	Cumin fruit extracts	Profenofos exposed kidney	Mice	Cumin was effective in normalizing the uric acid and creatinine level.	[31-32]
	6% <i>Cuminum cyminum</i> fruit	Paracetamol induced nephrotoxicity	Rats	It caused significant improvement of serum biochemical and hematological parameters.	[33-34]
<i>Cymbopogon schoenanthus</i>	<i>Cuminum cyminum</i> fruit extracts	experimental oxalate stone formation	Rats	It significantly corrected the incidence of nephrotoxicity (BUN, creatinine and calcium level differences). Moreover, a highly potent diuretic activity was recorded for <i>Cymbopogon schoenanthus</i> .	[35-36]
<i>Cynodon dactylon</i>	hydroalcoholic extract of <i>Cynodon dactylon</i>	ethylene glycol-induced nephrolithiasis	Rats	<i>Cynodon dactylon</i> extract reduced the levels of calcium oxalate deposition especially in medullary and papillary sections of kidney.	[37]
	different fractions of <i>Cynodon dactylon</i> , 12.8 mg/kg bw.	ethylene glycol-induced kidney calculi	Rats	<i>Cynodon dactylon</i> n-butanol fraction, significantly reduced the number of the kidney CaOx deposits compared to ethylene glycol group. In preventive protocol, treatment of rats with <i>Cynodon dactylon</i> ethyl	[38-40]

				acetate fraction significantly decreased the number of CaOx deposits compared to ethylene glycol group.	
<i>Daucus carota</i>	<i>Daucus carota</i> root extract, 250 & 500 mg/kg bw.	renal ischemia reperfusion injury	Rats	The biochemical changes were significantly less in the group treated with petroleum ether, fractional methanolic and direct methanolic extract of <i>Daucus carota</i> root compared with those in ischemia reperfusion group.	[41-42]
	ethanolic root extract of <i>Daucus carota</i> , 200 and 400 mg/kg bw	gentamicin-induced nephrotoxicity	Rats	Gentamicin intoxication induced elevated serum urea, BUN, uric acid, and creatinine levels which was found to be significantly ($P < 0.01$) decreased in a dose-dependent manner in groups received <i>Daucus carota</i> . The nephroprotective effects were further confirmed by histological observations.	[43]
<i>Foeniculum vulgare</i>	aqueous extract of <i>Foeniculum vulgare</i> seeds, 250 mg/kg bw.	gentamicin induced nephrotoxicity	Rabbits	The aqueous extract of <i>Foeniculum vulgare</i> seeds, <i>Solanum nigrum</i> fruit and their mixture significantly prevented renal damage by normalizing increased levels of renal markers. Mixture of both plants at high doses exhibited improved nephroprotective and antioxidant activities.	[44]
	aqueous extract of <i>Foeniculum vulgare</i> , 150 mg/kg bw.	experimental PCOS	Rats	The mean values of blood urea nitrogen in PCOS rats treated with low dose of extract of <i>Foeniculum vulgare</i> and estradiol valerate and non-treated, was significantly ($p < 0.05$) increased compared with non-PCOS and PCOS rats treated with high dose of extract of <i>Foeniculum vulgare</i> .	[45]
	fennel essential oil (250, 500, and 1000 mg/kg bw)	cisplatin -induced nephrotoxicity	Rats	Fennel essential oil did not reduce the levels of BUN and Cr, KTDS, and KW and body weight changes. Also, the serum and tissue levels of nitrite were not altered significantly by fennel essential oil.	[46]
<i>Glycyrrhiza glabra</i>	Glycyrrhizin, 200 mg/kg bw /day	gentamicin-induced acute renal failure	Rats	The changes in renal functional parameters (creatinine clearance, urinary osmolality, and solute-free	[47]

				reabsorption), accompanying acute renal failure were also partially restored after administration of glycyrrhizin. Histological changes in rats with gentamicin-induced acute renal failure were also abrogated by glycyrrhizin.	
	Glycyrrhizic acid	sepsis-induced acute kidney injury	Rats	It alleviated sepsis-induced acute kidney injury by improving the pathological changes, decreasing the levels of blood urea nitrogen, creatinine, and increasing the survival rate of rats significantly.	[48]
<i>Juglans regia</i>	walnut extracts	Cyclophosphamide - induced nephrotoxicity		It caused significant reduction in the content of CYP, significant increase in the level of GSH and in the activities of GP in the kidneys.	[49]

CONCLUSION

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin. Many medicinal plants have been reported to exhibit protective effect of renal tissues against injuries. The current review will highlight the medicinal plants possessed nephroprotective effects as possible future drugs because of effectiveness and safety.

REFERENCES

- [1] Porter GA, Bennett WM. Nephrotoxic acute renal failure due to common drugs. *American Journal of Physiology* 1981; 241(7): 252-56.
- [2] Sundararajan R, Bharampuram A, Koduru R. A review on phytoconstituents for nephroprotective activity. *Pharmacophore* 2014;5(1):84-84.
- [3] Radwan RR, Abdel Fattah SM. Mechanisms involved in the possible nephroprotective effect of rutin and low dose γ irradiation against cisplatin-induced nephropathy in rats. *J Photochem Photobiol B* 2017;169:56-62.
- [4] Supriya R, Lalitha PR, Gaddam RR, Dyaga VC, Gaddam S. Evaluation of nephroprotective activity of the methanolic extract of *Phyllanthus Niruri* (Family-Euphorbiaceae). *International Journal of Pharmaceutical and Phytopharmacological Research* 2015;4: 276-80.
- [5] Sharma RK, Rajani GP, Sharma V, Komala N. Effect of ethanolic and aqueous extracts of *Bauhinia variegata* Linn. on gentamicin-induced nephrotoxicity in rats. *Ind J Pharm Edu Res* 2011; 45(2): 192-98.
- [6] Al-Snafi AE. The Pharmacological importance of *Bauhinia variegata*. A Review. *Journal of Pharma Sciences and Research* 2013; 4(12): 160-64.
- [7] Sharma RK. Pharmacological evaluation of *Bauhinia variegata* Linn. for wound healing and nephroprotective activity. MSc Thesis, Rajiv Gandhi University of Health Sciences: Karnataka; 2010.
- [8] Varghese HS, Kotagiri S, Vrushabendra SBM, Archana SP, Raj GG. Nephroprotective activity of *Benincasa hispida* (Thunb.) Cogn. fruit extract against paracetamol induced nephrotoxicity in rats. *Research Journal of Pharmaceutical Biological and Chemical Science* 2013; 4(1): 322-32.
- [9] Mingyu D, Mingzhang L, Quihong Y, Weiming U, Jianxing X, Weinming X. A study on *Benincasa hispida* contents effective for protection of kidney. *Jiangsu J Agri Sci* 1995; 11: 46-52.
- [10] Al-Snafi AE. The Pharmacological Importance of *Benincasa hispida*. A review. *Int Journal of Pharma Sciences and Research* 2013; 4(12): 165-170.
- [11] Rajamurugan R, Suyavaran A, Selvaganabathy N, Ramamurthy CH, Reddy GP, Sujatha V, Thirunavukkarasu C. *Brassica nigra* plays a remedy role in hepatic and renal damage. *Pharm Biol* 2012; 50(12): 1488-97.

- [12] Al-Snafi AE. The pharmacological importance of *Brassica nigra* and *Brassica rapa* grown in Iraq. J of Pharm Biology 2015; 5(4): 240-53.
- [13] Kim YH, Kim YW, Oh YJ, Back NI, Chung SA, Chung HG, Jeong TS, Choi MS, Lee KT. Protective effect of the ethanol extract of the roots of *Brassica rapa* on cisplatin-induced nephrotoxicity in LLC-PK1 cells and rats. Biol Pharm Bull 2006; 29(12): 2436-41.
- [14] Majaz QA, Tatiya AU, Khurshid M, Nazim S. The miracle plant (*Kalanchoe pinnata*): A photochemical and pharmacological review. International Journal of Research in Ayurveda and Pharmacy 2011; 2(5): 1478-82.
- [15] Harlalka GV, Patil CR. Protective effect of *Kalanchoe pinnata* pers.(Crassulaceae) on Gentamicine induced nephrotoxicity in rats. *Indian Journal of Pharmacology*, 39(4), 2007, 201-05.
- [16] Patil R, Bhargava K, Ptel P, Singh K, Surana J. Diurtic and anti urolthiatic activity of hydroalcoholic extracts of leaves of *Kalanchoe pinnata* pers. *Journal of Pharmaceutical Research* 2008; 7(2): 87-91.
- [17] Al-Snafi AE. The Chemical constituents and pharmacological effects of *Bryophyllum calycinum*-A review. *Journal of Pharma Sciences and Research* 2013; 4(12): 171-76.
- [18] Abou El-Soud N H, El-Lithy N A, El-Saeed G, Wahby M S, Khalil M Y, Morsy F, Shaffie N. Renoprotective effects of caraway (*Carum carvi* L.) essential oil in streptozotocin induced diabetic rats. *Journal of Applied Pharmaceutical Science* 2014; 4(02): 27-33.
- [19] Al-Snafi AE. The chemical constituents and pharmacological effects of *Carum carvi* - A review. *Indian Journal of Pharmaceutical Science and Research* 2015; 5(2): 72-82.
- [20] Kumar AR, Abbulu K. Antioxidant activity of ethanolic extract of *Cassia occidentalis* against carbon tetrachloride induced oxidative stress in Wistar rats. *Int J Chem Sci* 2011; 9(1): 378-86.
- [21] Gowrisri M, Kotagiri S, Vrushabendra SBM, Archana SP, Vishwanath KM. Anti-oxidant and nephroprotective activities of *Cassia occidentalis* leaf extract against gentamicin induced nephrotoxicity in rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences* 2012; 3(3): 684-94.
- [22] Al-Snafi AE. The therapeutic importance of *Cassia occidentalis* - An overview. *Indian Journal of Pharmaceutical Science & Research* 2015; 5 (3): 158-71.
- [23] El-Tantawy WH, Mohamed SA, Abd Al Haleem EN. Evaluation of biochemical effects of *Casuarina equisetifolia* extract on gentamicin-induced nephrotoxicity and oxidative stress in rats. *Phytochemical analysis. J Clin Biochem Nutr* 2013; 53(3):158-65.
- [24] Al-Snafi AE. The pharmacological importance of *Casuarina equisetifolia* - An overview. *International Journal of Pharmacological Screening Methods* 2015; 5(1): 4-9.
- [25] Abd El-baky AE, Amin HK. Effect of *Citrullus colocynthis* in ameliorating the oxidative stress and nephropathy in diabetic experimental rats. *International Journal of Pharmaceutical Studies and Research* 2011; 2: 1-10.
- [26] Al-Snafi AE. Chemical constituents and pharmacological effects of *Citrullus colocynthis* - A review. *IOSR Journal of Pharmacy* 2016; 6(3): 57-67.
- [27] Ullah N, Khan MA, Asif AH, Khan T, Ahmad W. *Citrullus colocynthis* failed to combat against renal derangements, in spite of its strong antioxidant properties. *Acta Pol Pharm* 2013;70(3):533-38.
- [28] Bandegi AR, Rashidy-Pour A, Vafaei AA, Ghadrdoost B. Protective effects of *Crocus sativus* L extract and crocin against chronic-stress induced oxidative damage of brain, liver and kidneys in rats. *Adv Pharm Bull* 2014; 4(Suppl 2): 493-99.
- [29] Al-Snafi AE. The pharmacology of *Crocus sativus*- A review. *IOSR Journal of Pharmacy* 2016; 6(6): 8-38.
- [30] Ajami M, Eghtesadi S, Pazoki-Toroudi H, Habibey R, Ebrahimi SA. Effect of *Crocus sativus* on gentamicin induced Nephrotoxicity. *Biol Res* 2010; 43: 83-90.
- [31] Kumar A, Singh JK, Ali M, Kumar R, Kumar A, Nath A, Roy AK, Roy SP, Singh JK. Evaluation of *Cuminum cyminum* and *Coriandrum sativum* on profenofos induced nephrotoxicity in Swiss albino mice. *Elixir Appl Botany* 2011; 39 : 4771-73.
- [32] Al-Snafi AE. The pharmacological activities of *Cuminum cyminum* - A review. *IOSR Journal of Pharmacy* 2016; 6(6): 46-65.
- [33] Elhabib EM, Homeida MMA, Adam SEI. Effect of combined paracetamol and *Cuminum cyminum* or *Nigella sativa* used in Wistar Rats. *Journal of Pharmacology and Toxicology* 2007; 2: 653-59.
- [34] Al-Snafi AE. The pharmacological activities of *Cuminum cyminum* - A review. *IOSR Journal of Pharmacy* 2016; 6(6): 46-65.
- [35] Al Haznawi AM, Attar AS, Abdulshakoor AA, Ramadan MA. Inhibition of calcium oxalate nephrotoxicity with *Cymbopogon schoenanthus* (Al-Ethkher). MSc thesis. Faculty of Applied Medical Sciences: Saudi Arabia; 2007.

- [36] Al-Snafi AE. The chemical constituents and pharmacological activities of *Cymbopogon schoenanthus*: A review. Chemistry Research Journal 2016; 1(5):53-61.
- [37] Mousa-Al-Reza H, Rad AK, Rajaei Z, Sadeghian MH, Hashemi N, Keshavarzi Z. Preventive effect of *Cynodon dactylon* against ethylene glycol-induced nephrolithiasis in male rats. Avicenna J Phytomed 2011; 1(1): 14-23.
- [38] Khajavi Rad A, Hadjzadeh MA, Rajaei Z, Mohammadian N, Valiollahi S, Sonei M. The beneficial effect of *Cynodon dactylon* fractions on ethylene glycol-induced kidney calculi in rats. Urol J 2011; 8(3): 179-84.
- [39] Al-Snafi AE. Chemical constituents and pharmacological effects of *Cynodon dactylon*- A review. IOSR Journal Of Pharmacy 2016; 6(7): 17-31.
- [40] Al-Snafi AE. Encyclopedia of the constituents and pharmacological effects of Iraqi medicinal plants. Rigi Publication: India; 2017.
- [41] Mital PR, Laxman PJ, Ramesshvar PK. Protective effect of *Daucus carota* root extract against ischemia reperfusion injury in rats. Pharmacology 2011;1: 32-439.
- [42] Al-Snafi AE. Nutritional and therapeutic importance of *Daucus carota*- A review. IOSR Journal of Pharmacy 2017; 7(2): 72-88.
- [43] Sodimbaku V, Pujari L, Mullangi R, Marri S. Carrot (*Daucus carota* L.): Nephroprotective against gentamicin-induced nephrotoxicity in rats. Indian J Pharmacol 2016;48(2):122-27.
- [44] Shaheen U, Manzoor Z, Khaliq T, Kanwal A, Muhammad F, Hassan JI, Munawar SH, ul-Haq M. Evaluation of nephroprotective effects of *Foeniculum vulgare* Mill, *Solanum nigrum* Linn and their Mixture against gentamicin-induced nephrotoxicity in Albino rabbits. Int J Pharm Sci Rev Res 2014; 25(1): 1-9.
- [45] Sadrefozalayi S, Farokhi F. Effect of the aqueous extract of *Foeniculum vulgare* (fennel) on the kidney in experimental PCOS female rats. J Phytomedicine 2014; 4(2): 110-17.
- [46] Mazaheri S, Nematbakhsh M, Bahadorani M, Pezeshki Z, Talebi A, Ghannadi R, Ashrafi F. Effects of fennel essential oil on cisplatin-induced nephrotoxicity in ovariectomized rats. Toxicol Int 2013; 20(2): 138-45.
- [47] Sohn EJ, Kang DG, Lee HS. Protective effects of glycyrrhizin on gentamicin-induced acute renal failure in rats. Pharmacol Toxicol 2003;93(3):116-22.
- [48] Zhao H, Zhao M, Wang Y, Li F, Zhang Z. Glycyrrhizic acid attenuates sepsis-induced acute kidney injury by inhibiting NF- κ B signaling pathway. Evidence-Based Complementary and Alternative Medicine 2016, <http://dx.doi.org/10.1155/2016/8219287>
- [49] Haque R, Bin-Hafeez B, Parvez S, Pandey S, Sayeed I, Ali M, Raisuddin S. Aqueous extract of walnut (*Juglans regia* L.) protects mice against cyclophosphamide - induced biochemical toxicity. Hum Exp Toxicol 2003;22(9):473-80.