

COMPREHENSIVE REVIEW ON NEPHROPROTECTIVE MEDICINAL PLANTS

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ABSTRACT

This review investigated the alternative herbal remedy against nephroprotective effect. Kidney diseases are a worldwide proportions major problem of renal damage. In this review carried out essential plants and their active constituents which used in treatment of renal diseases. The most common cause of kidney diseases is known as Nephrotoxicity, Chronic kidney disease, High blood pressure, glomerulonephritis, Kidney stone, Tumour infiltration Nephrotoxicity occurs when body exposed toxins and drugs. Various medicinal plants are used for the treatment of nephrotoxicity. Kidney filter daily in every minute's half cup of blood, and remove waste materials transform in to urine and also its control the fluid balance of body. 125 to 170gram weight of male kidney and 115-to-155-gram weight of female kidney. Structural and functional unit of the kidney is nephron. 1 million nephron contain in adult human kidney. Various volume controlled by kidney such as electrolyte concentrations, body fluid, removal of toxin. Reabsorbed substance such as solute-free water, sodium, bicarbonate, glucose, and amino acid. If the damage is severe, it can lead to kidney failure which such as Loss of appetite, swelling of the hands, legs or other areas of the body, burning sensation, fatigue, High blood pressure, shortening of breath, Ammonia-smelling breath, itching in the skin, nausea, vomiting. Waste product and drugs remove from the body, Maintain the body's fluid balance and release hormones that regulates blood pressure promotes healthy and strong bone by active form of vitamin D, and kidney Control the red blood cells production.

KEY WORD: *Nephrotoxicity, Glomerulonephritis, Medicinal plants.*

1. Introduction

In human body kidney plays an important role such as maintenance of acid-base balance, endocrine, erythropoiesis and blood pressure etc. The most common cause of kidney is known as Nephrotoxicity, Chronic kidney disease, High blood pressure, glomerulonephritis, Kidney stone, Tumour infiltration. Nephrotoxicity occurs when body exposed toxins and drugs^{1,2}, for the treatment of Nephrotoxicity effect various medicinal plants are used^{3,4}. Structure of kidney is like a pair bean shaped on other side of spine and present below the ribs, behind the belly. Kidney filter daily in every minute's half cup of blood, and remove waste materials transform in to urine and also its control the fluid balance of body. 125 to 170gram weight of male kidney and 115-to-155-gram weight of female kidney. Structural and functional unit of the kidney is nephron. 1 million nephron contain in adult human kidney^{5,6}. About 12,500 nephrons contain in mouse kidney. Various volume controlled by kidney such as electrolyte concentrations, body fluid, removal of toxins^{7,8}. volume control by the kidney and filtration can occur in the Glomerulus filtration one fifth of blood volume filtered in the kidney. Reabsorbed substance such as solute-free water, sodium, bicarbonate, glucose, and amino acid^{9,10}. Their basic functions include: Waste product and drugs remove from the body, Maintain the body's fluid balance and release hormones that regulates blood pressure promotes healthy and strong bone by active form of vitamin D, and kidney Control the red blood cells production^{11,12}. There are two types of renal failure that is acute renal disease and chronic renal disease. If the damage is severe, it can lead to kidney failure which such as Loss of appetite, swelling of the hands, legs or other areas of the body, burning sensation, fatigue, High blood pressure, shortening of breath, Ammonia-smelling breath, itching in the skin, nausea, vomiting^{13,14}. The check-up of kidney must be done by your healthcare team before beginning the treatment for cancer. Kidney problems are usually diagnosed by Physical exam, including measuring blood pressure, Urinalysis + urine protein creatinine ratio, Complete blood counts, with electrolyte count, Serum Biochemical profile, with electrolytes and acid- base measurement, Ultrasound of the kidney.

Blood Urea Nitrogen (BUN): Blood urea nitrogen is a medical test for the measures the amount of urea nitrogen found in blood. It is used to determine if there are extra nitrogenous wastes in your blood stream, it should be filtered out of our kidneys. An excess of nitrogen compounds in the blood may lead to uraemia.

Uric acid: It is commonly in raised with chronic kidney disease. If high uric acid level in the body can cause crystals of uric acid to form leading to gout. When body is created breaks down chemical called as purines.

Creatinine: Creatinine is the parameter of renal disease. Creatinine is produced after the muscle metabolism. Kidneys are normally filter out in large amounts of creatinine on a daily basis. During the renal failure the level of creatinine will increased.

2. Epidemiology and Incidence of Renal Diseases

In worldwide population acute kidney injury is affected the 2147 and 4085 per million populations per year. Current report of worldwide indicate dup to 3.2 to 9.6% of acute kidney injury of hospitalization and this may occur 20 % to 50% mortality in ICU patients^{15,16}. 5 to 6% renal replacement therapy demanding by acute renal injury with 60% mortality rate. Nearly 2 million people globally die by occurring of acute kidney injury per year. In case

those patients survive from acute kidney injury at a risk later occurrence of chronic kidney disease chronic kidney disease^{17,18,19}. Causes of acute kidney injury by pre and post renal ones. Commonest form of acute renal failure is by pre-renal failure, when decrease renal blood flow cause hypovolemia. If decreased renal blood flow reversibly can notify and rectified occurs before kidney damage^{20,21}. About 40 to 70% of acute kidney injury may causes by pre-renal. Acute kidney injury may affect the parenchyma by intrinsic renal causes which can be based on kidney compartment affected such as tubulointerstitial diseases, tubular injury, renal microcirculation, larger vessels and glomeruli^{22,23}. About 5 % of renal failure cause disease which are associated with urinary tract obstruction may cause by post renal. In nephroprotective activity different regions and varied plant species having effective constituent in area at interval the succeeding portion^{24,25}. The chemo profile totally different region of world for tend of eliminatory organ disease with considerable press on their active constituent^{26,27}.

Avera lanata: *A. lanata* consist of leaves and root and belonging from the family of Amaranthaceae. Plant lying down generally build herb 30-60 cm tall. It is issuing throughout tropical India. It is found in Africa, Sri Lanka, and Philippines. In traditional system of medicine are used in diuretic, expectorant, anthelmintic. Leaves extract of area lanata used as sap for eye-complaints, cure diarrhoea, kidney stone and in root part used for the treatment of snake bite. Active compound of the plant such as alkaloids, flavonoids, tannins, and phenolic compound. Plant work in haemorrhage during pregnancy, anti-inflammatory, skin disease, burn healing, gall bladder stone clearance of uterus after delivery and forestall lactation. In ethanolic extract of area lanata occur nephroprotective activity marked and toxicity become flavanol, glycoside like kaempferol-3-rhamnogalactoside and kaempferol-3-rhamnoside. It supplied a good role with the treatment of acute nephritic injury caused by nephrotoxins such as cisplatin and some antibiotics²⁷.

Andrographis paniculate: *A paniculate* is consisting of leaves and roots belonging from the family of Acanthaceae. It is also called as king of bitter and mostly cultivated in southern Asia. Leaves and root ae traditionally used all over the countries for various medicinal resolution in Europe, folklore, Asia. these remedy generally for wide spectrum of ailment or herbal supplement for the treatment of common cold. *Andrographis paniculate* has rich source of diterpenoid and 2-oxygenated flavonoids as well as stigmaterol, neo andrographolide and andrographolide. It has a wide range of pharmacological activities such as anti-tumour, anti-inflammatory, cardiovascular, hepatoprotective, anti-viral, anti-diarrhoea, anti-malarial, immunostimulatory activities. In chloroform extract of *Andrographis paniculate* against nephroprotective because of diterpenoid like and rographidoids²⁸.

Artemisia annua: *A annua* is consist of green herbs belonging from the of Asteraceae. it is native to China and used for over a period of 500 years to treat symptoms related to protozoal infection and fever. In traditional used for the treatment of fever and haemorrhoid. It is together employed in the preparing of aromatic arrangement as a flavouring for the spirit such as vermouth as well as essential oil for the fragrance business. Artemisinin is the main supply of sweet wormwood, a critical natural sesquiterpene lactone impact with antiprotozoal drug and against multi-drug resistant plasmodium species. Crude extract and sweet wormwood are wellbeing supply of antioxidant capability due to high content and mixture of leaf flavonoids. Recently reported c-glycosyl flavonoids are possible composition of the antiviral activity and

antioxidant. In ethanolic extract in nephroprotective effect is due to the terpenoids like artemisia ketone, 1,8-cineole of artemisia annua Linn²⁹.

Berberis vulgaris: *B. vulgaris* consist of wood plant in Fruits, bark belonging from the family of Berberidaceae. It is the native to central and southern Europe, western Asia, northwest continent. Medicative plant have been used large scale in ancient drugs. It is observed that *Berberis vulgaris* contain Phenol compounds and contain organic acids and also contain antioxidant and anthocyanin as well as glycosidase enzymes, phenolase, and polyphenolase enzyme. An iso-kinolin alkaloid occur by berbamin and exits in bark of given its root, that is a Strong antioxidant. T is help in the treatment of fibrosis caused by anti-cancer medicine like bleomycin. In berberis vulgaris have a pharmacological action such as antimicrobial, antipruritic, cholagogue actions, antiemetic, antipyretic and in some cases like dysentery, cholelithiasis, leishmaniasis, malaria and gall stones³⁰.

Ceratonia siliqua: *C. siliqua* is consisting of green shrub belonging from the family of Leguminosae. Tree up to 10 m height, bark is brown rough, trunk is thick, and broad are semi- spherical. It has well grown in worm temperature and semi tropical area; drug tolerates hot and humidity coastal areas.it is resistant evergreen and high temperate tree grow vigorously in habitats with delicate mare nostrum climates. It contains embrace carob polyphenols, tannins etc. Tannins are extracted from the pulp of antidiarrhoeic properties. Endosperm and pulp seed are occurred in the preparation of pharmaceutical products. the application of carob bean gum includes cosmetics. film emulsions, pharmaceutical product, paint, polishes, adhesive and ceramics. In phytoconstituent carob polyphenols are the important in *Ceratonia siliqua*, it shows the defensive effect of nephrotoxicity³¹.

Curcuma longa: *C. longa* is consisted of dried rhizomes belonging from the family of Zingiberaceae, it grows the height of 3 to 5 feet and that are cultivated into in large scale in Asia, India, China and many other countries with a tropical climate. The main principal of curcumin is the curcuminoid in the very Indian spice turmeric, are ginger family member. In curcuminoids other two components are desmethoxycurcumin and bisdemethoxycurcumin. The yellow colour produced in turmeric by present of polyphenols in curcuminoid. Dried turmeric is used for the spices. Turmeric aue used in food for flavour and colour and also used in treatment of ayurvedic purpose. In medication ayurvedic system are treated for jaundice, expelling difficulties, flatulence, anti-inflammatory, haematuria, haemorrhage, anti-oxidant, antiviral, antifungal, action. Curcumin showed that exhibit Nephroprotective action³².

Nigella sativa: *N. sativa* is consisted of herb belonging from the family of Ranunculaceae. It is found and cultivated in southern Europe, Syrian Arab republic, Israel. Seed and oil are employed for many diseases. It contains Di thymoquinone, p-cymene, carvacrol, 4-terpinol, Thymoquinone, Thymohydroquinone, sesquiterpene longifolene and phenol. Seed are considered carminative, purgative, thermogenic, diuretic, Deodat, expectorant and oil considered local anaesthetic¹⁹.

Panax ginseng: *P. ginseng* consisted of leaves belonging from the family of Araliaceae. It is found in East Asia and Russia, and harvested in different area of Asia. *Panax ginseng* is cultivated in Japan, China, Korea used as a medical herb. Morphology of panax ginseng plant with five -finger leave, tiny white flowers and yellowish-brown root. It contains triterpene glycosides, saponins also called as ginsenosides. It has been employed by Asian culture

thousand year used for condition like fatigue, mental stress, blood sugar regulation, improving libido, and supporting longevity, in modern clinical studies have ben use of ginseng in cancer presentation, fatigue, blood sugar regulation, immunomodulation in human health care and disease³²⁻³³.

Romulus mori: *R. mori* consisted tree belonging from the Moraceae is a fast-growing plant that grown under entirely different climate likes subtropical, semitropic, and temperature. *Romulus mori* have constituent are important feed for silkworm. In Chinese medicine used for the treatment of joint pain³³⁻³⁴. It contains the stilbenes, morin, flavonoids, cis-mulberrosideA, resveratrol like rutin, quercetin. The pharmacological actions of *Romulus mori* plant are found to be anti-rheumatoid activity, anti-inflammatory, potential analgesic activity. Caffeic acid phenylethyl ester are organic compound is a strong part of propolis from bee hives. It is better-known to own medicine, anti-carcinogenic, anti-mitogenic and immunomodulatory properties. It is an effective and specific inhibitor of nuclear transcription factor activation. Recent studies disclose the effect that it also exhibits nephroprotective activity³⁵. The principal of lupeol has active constituent found in good vegetables and fruits such as white cabbage, date palm, soya beam, black tea, tomato, pea, bitter root, mulberries, carrot. Lupeol have been found to possess a large vary of medicative properties that embrace conditions like inflammation, microbial infection, cancer, kidney disease, arthritis, diabetes, cardiovascular ailments, hepatic toxicity. Scientific studies disclosed the effect that lupeol plant is a possessor of nephroprotective activity³⁶.

3. Conclusion

In this review discussed about the nephroprotective effects of various medicinal plants such as *Ceratonia siliqua*, *Artemisia annua*, *Berberis vulgaris*, *Curcuma longa*, *Nigella sativa*, *Panax ginseng*, *Romulus mori*, *Avera lanata*, *Juglans regia*, *Andrographis paniculate*, *Bauhinia variegata*, *Emblica officinalis*, *Hygrophilia spinosa*, *Kalanchoe pinnata*, *Morinda centifolia* L., *Crataeva nurvala*, *Rhazya stricta*, *Solanum nigrum*, *Strychnos potatorum*, *Orthosiphon stamineus* and *Withania somnifera*. These plants consist of various constituent's act on various diseases of renal disorder like nephritic syndrome, acute renal failure, and chronic interstitial nephritis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests that could have appeared to influence the work reported in this paper.

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Table 1: Nephroprotective Plants and their Phytoconstituent(s) with their therapeutic uses

S. No.	Name of Medicinal Plant	Family	Plant part used as Renal protective	Bioactive Phytoconstituent(s)	Therapeutic Use
1.	<i>Ceratonia siliqua</i>	Fabaceae	Green shrub, tree	carob polyphenols, tannins	Cosmetics, pharmaceuticals, film emulsions, paints, polishes, ceramics and antidiarrheal.
2.	<i>Artemisia annua</i>	Asteraceae	Green herb	Terpenoids like artemisia ketone, α -pinene, 1,8-cineole, artemin, arborescin, sesamin chrysoberyl, dehydroabietic, apigenin, deoxy artemisinin, artemisinin.	Antioxidant, antiviral activity, antibacterial, anticancer, anti-inflammatory and cytotoxic.
3	<i>Berberis vulgaris</i>	Burseraceae	Fruits, bark	Berberamine, oxyacanthine, berberine, vitamin C.	Cholecystitis, cholelithiasis, jaundice, dysentery, leishmaniasis, malaria gall stone, antimicrobial, antiemetic, antipyretic, antipruritic and cholagogue actions
4	<i>Curcuma longa</i>	Zingiberaceae	Dried rhizomes	Curcumin, curcuminoid, cymene, turmerone, bisdemethoxycurcumin, desmethoxycurcumin, diaryl heptanoids	Antioxidant, cardiovascular protection, cancer treatment, headache, lung infection,
5.	<i>Nigella sativa</i>	Ranunculaceae	herb,	protein, carbohydrate, fibers, vitamins, thymoquinone, Di thymoquinone, thymohydroquinone, thymol	Antioxidant, anti-inflammatory, immune-potentiating, anti-cancer, analgesic, anti-histaminic, anti-microbial
6.	<i>Panax ginseng</i>	Araliaceae	Root	Triterpene saponin, polysaccharides, fatty acid protopanaxadiol, carbohydrates, protopanaxatriol, nitrogen compound, phenolic compound, peptidoglycans	Antistress, anticancer, immune system, modulator, cardiovascular, central nervous system, hormonal effect, athletic performance, anti-inflammatory
7.	<i>Romulus mori</i>	Moraceae	Leaves	stilbenes, cis-mulberrosideA, resveratrol and flavonoids.	Joint pain, anti-inflammatory, potential analgesic activity and anti-rheumatoid activity
8.	<i>Avera lanata</i>	Amaranthaceae	Root, leaves	flavanol glycoside like kaempferol-3-rhamnoside & kaempferol-3-rhamnolactoside, alkaloids, flavonoids, tannins and phenolic compounds	diuretic and anthelmintic, expectorant, diarrhea and kidney stone; hemorrhage during pregnancy, burn healing, as an anti-inflammatory, headache, skin diseases, to dissolve kidney and gall bladder stones, for uterus
9	<i>Juglans regia</i>	Juglandaceae	Leaves, peel, green fruit& wood	tocopherols, epicatechin, syringe tin-o-hexaside, myricetin-3-o-glucoside, aesculetin, taxifolin	Antioxidant, antidiabetic, antihypertensive, antimicrobial, antifungal, liver and kidney, flavonoids, anticancer, inflammatory bowel disease.
10.	<i>Andrograp his paniculate</i>	Acanthaceae,	leaves and roots	diterpenoids, andrographolide, neo andrographolide and stigmasterol.	anti-tumor, anti-inflammatory, anti-viral, anti-diarrheal, anti-malarial, hepatoprotective, cardiovascular and immunostimulatory activities
11.	<i>Bauhinia variegata</i>	Caesalpiaceae	Stem	Stigmasterol, kaempferol-3-glucoside, β setoster	Antibacterial, antidiabetic, analgesic, anti-inflammatory, anti-diarrheal, anticancer, nephroprotective and thyroid hormone regulation activity.

12.	<i>Emblica officinalis</i>	Euphorbiaceae	Fruits	Carotene, Riboflavin, Myoinositol, Darabinosyl, D-xylosyl, Lrhamnosyl, G-glycosyl, Dmanosyl, D-galactosyl, Phyllambic Leucodelphinidin, Procyanidin, 3-O-gallated Prodelphinidin	Antioxidant, immune modulatory, antipyretic, analgesic, cytoprotective, antiulcer, anti-inflammatory, diuretic, antitussive, gastroprotective.
13.	<i>Hygrophilla spinosa</i>	Acanthaceae	Whole plants	B-sitosterol, Lupeol, Minerals like Anders6 Plant Na, K, Ca, P and Poluphenols.	Urinogenital tract, hyperdipsia, diarrhea, asthma, anasarca, vesical calculi, gonorrhoea.
14.	<i>Kalanchoe pinnata</i>	Crassulaceae	Leaves	Leaf Alkanes, Triacontane, Alpha & Beta Amyrin, Beta-Sitosterol, Fumaric acid, Quercetin, Kaempferol,	Kidney stone, gastric ulcer, pulmonary infection, rheumatoid arthritis.
15.	<i>Morinda centifolia L.</i>	Rubiaceae	Fruit	Americanol A, 3, 31-bis dimethyl pinoselinol, anthraquinones, Americanoic acid A, Morindolin and Isoprincepin, triterpenoids.	High blood pressure, arthritis, ulcer, depression, sprains, menstrual cramps, pain reilf, inflammatory, burns, fever, food poisoning, intestinal worms, joint problem
16.	<i>Crataeva nurvala</i>	Capparidaceae	Fruits	Kaemferol-3-O-a-D-glucoside, Quercitin-3-O-a-D-Glucosinolates,	Increase appetite, stimulates digestion, treatment for flatulence and abdominal disorders.
17.	<i>Rhazya stricta</i>	Apocynaceae	Leaves	1-carbomethoxy-β-carboline, Condyloacarpine and Vincanicine,	Diabetics, inflammatory, sore throat, arthritis, infectious disease, cancer antioxidant, hepatoprotective
18.	<i>Solanum nigrum</i>	Solanaceae	Whole plant	Glycosides, Leutein, Caffeicolasodine, Tamatidenol, Solamargine, Solasomine, Trigogenine,	Ulcer, skin disease, tonic, laxative, appetite, asthma, whooping cough, pneumonia, stomach, wring worm.
19.	<i>Strychnos potatorum</i>	Loganiaceae	Seeds	Diaboline beta-sitosterol, brucine, loganin, isomotioli, strychnine.	Gonorrhoea, leukorrhoea, gastropathy, bronchitis, chronic diarrhea, dysentery, renal and vesicle calculi, diabetes, conjunctivitis, ulcer eye disease.
20.	<i>Orthosiphon stamineus</i>	Lamiaceae	Whole plant	Sinensetin, rosmarinic acid, eupatorine, betulinic acid	Rheumatoid, diabetes, hypertension, epilepsy, renal calculus, edema, gallstone, hepatitis, jaundice.
21.	<i>Withania somnifera</i>	Solanaceae	Roots	Alkaloids (Somniferon), Withaminon, Wasamin, Withaniol, Hexatriacontane, Phyto sterol and oils.	Asthma, diabetes, stress, arthritis, cancer, hypertension