

REVIEW ON NEPHROPROTECTIVE ACTIVITY OF SOME MEDICINAL PLANTS

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Summary

Medicinal plants have curative properties due to the presence of various complex chemical compositions, which are found as secondary plant metabolites in one or more parts of these plants. In the present study it is dealt with the plants used in the treatment of nephrotoxicity. Now a days a lot of people are suffering from kidney disease and their numbers are increasing day by day. These days many of us are acquainted with words like – Kidney stone, renal failure, Kidney transplantation, Dialysis etc. Kidney disease has reached in an alarming situation now days. Our modern lifestyle is much more responsible for creating problems of kidneys. Persons having high blood pressure (hypertension), diabetes, having habits of eating junk food and taking excessive pain killer medicines have high risk. In the present review an attempt has been made to explore a literature survey on the various plants established for nephroprotective activity.

Key words: Medicinal plants, nephrotoxicity, renal failure, nephroprotective.

1. Introduction

It is greatly to the credit of people of India, that they were acquainted with a far large number of medicinal plants than the natives of any other country on the face of the earth.[1] Many Indians fruits, grains and vegetables employed as useful dietary articles forms a chief factor in the cure of diseases, as well as preservation of health and good nutrition.[2] Herbs have always been the principle form of medicine in India and they are becoming popular through out the world, as people strive to stay healthy in the face of chronic stress and pollution and to treat illness with medicine that works in concert with the body's own defences. Thus medicinal plants play an important role in the lives of rural people. A plant is said to be medicinal when "at least one part possesses therapeutic properties". Ancient literature has prescribed various herbs for cure of kidney disease. Some other plants mentioned in literature include *Vernonia cinerea*, *Prosthechea michuacana*, *Strychnos potatorum*, *Plectranthus amboinicus* etc.

Ayurveda and siddha system of medicine, the traditional heritage of India include many true medicinal plants/drugs for various diseases and to which there is no answer in modern medicines till today.

1.1 Introduction to Nephrology

Nephrology is indeed an ancient discipline with a noble and distinguished legacy that spans at least three previous millennia. A bronze artefact closely resembling the human kidney and dating to 1300 BC was excavated from the ruins of the temples of kition and at least thirteen references to the kidney can be found in the Old Testament. Before the time of the Christ, Greek physician prescribed botanical material to promote diuresis and employed blood letting and other means for removal of excess body fluids. Hippocrates (460-375BC) was skilled in microscopic detail of urine analysis. Artaeus of Cappadoicia(30-90AD) and Galan(130-200AD) recognized kidney as the organ responsible for urine formation.[3] By the middle of 1800, the structural complexity of mammalian kidney was revealed and unravelled through improved optics and microscopy. If a few names had to be chosen among the pioneers, we could mention Marcello Malpigi and Loreuzo Bellin in Italy and Antoine Ferrein in France for the birth of renal anatomy, Sir William Bowman in England and Karl Ludwig in Germany for renal physiology and Richard Bright in London and Pierra Rayer in Paris for the disease of Kidney. Kidney is an important excretory organ in the human body. The function of kidney is not only to excrete metabolic waste products, but also to maintain the acid base balance, endocrine function like erythropoietin production.[4]

1.1.1 Anatomy and physiology of kidney

Paired kidneys are reddish bean shaped organs about 10-12 cm wide, 3cm thick and has a mass of 150g.[6] The kidney lie on the posterior abdominal wall, one on each side of vertebral column, behind the peritoneum below diaphragm. They extend from the level of 12th thoracic vertebrae to 3rd human vertebrae.[7] Near the centre of concave border is a deep vertical fissure called the renal hilum, through which the ureter emerges from the kidney along with blood vessels, lymphatic vessels and nerves.

The kidney is composed of several layers and is covered with a fibrous capsule, the renal capsule. The outer layer of the kidney is the cortex. It contains the major (upper) portion of the nephron. The middle layer of the kidney is the medulla. It is composed of the triangular shaped pyramids and the renal columns. The functional unit of kidney is nephron and there are about 1 million nephron in each kidney. The pyramids contain the collecting tubules and loops of Henle, the lower portion of the nephron. These tubules run nearly parallel to one another and give the pyramids a grain which leads to their points or papillae. The renal columns are regions between the pyramids in which blood vessels run to and from the cortex. The papilla of each pyramid projects into a funnel-shaped area known as the calyx. The calyces (plural of calyx) collect the urine released from the papillae and allow it to drain into a large area known as the renal pelvis and then into the ureter.

1.1.2 Functional units of the kidney

The nephrons are the functional units of the kidney. They consist of a number of specific parts. Nephrons are microscopic, and there are up to a million in two kidneys.

Each nephron is served with blood by the afferent arteriole. This vessel brings blood into a capillary tuft called the glomerulus. Blood leaving the glomerulus flows into the efferent arteriole.

A capillary tuft differs from a capillary bed in that it does not perfuse a tissue like a capillary bed does. Instead this capillary tuft is a condensed mass of capillaries which allows substances to escape by filtration. The capillaries of this tuft are surrounded by specialized cells which form the inner (visceral) layer of Bowman's capsule. The parietal layer is composed of simple squamous cells with tight junctions that form an outer wall which contains the filtrate.

1.1.3 Structure of the Nephron

The Bowman's capsule opens into the proximal convoluted tubule which leads to the loop of Henle. The loop of Henle has a descending limb which passes into the medulla, recurves, and becomes the ascending limb which leads back up to the distal convoluted tubule in the cortex. Most human

nephrons are termed cortical nephrons because their corpuscles are located in the mid to outer cortex and their loops of Henle are very short and pass only into the outer medulla. But a small portion is called juxtamedullary nephrons and their loops travel deep into the inner medulla. These nephrons are important in concentrating the urine by increasing the amount of water reabsorbed. Distal convoluted tubules lead into collecting tubules and ducts which pass through the medullary pyramids to the papillae.

1.1.4 Vascular System of the Nephron

Usually an arteriole flows into a venule. But in this case the efferent arteriole flows into more capillaries, the peritubular capillaries, and, in juxtamedullary neurons, the vasa recta. The peritubular capillaries and vasa recta then lead to venules and the venous drainage of the kidney.

Cortical nephrons have short loops of Henle which barely enter the medulla. Longer loops which dip much further into the medulla belong to juxtamedullary nephrons. These nephrons are important for concentrating the urine by absorbing extra water.

1.2 Steps involved in urine formation

1.2.1 Step 1: Filtration

In urine formation, Filtration - Fluid pressure forces water and dissolved substances out of the blood into Bowman's capsule. Filtration averages 125 ml/min for your two kidneys. This amounts to about 180 liters per day. Since we urinate an average of 1500 ml per day, more than 99% must be returned to the blood. Filtration involves the small molecules: water, electrolytes, urea, glucose, amino acids. It does not involve the blood proteins or cells. The large amount of filtration is the result of the porous glomerular membrane and filtration slits in the visceral layer of Bowman's capsule.

Filtration – Hydrostatic pressure (blood pressure) forces water and dissolved substances out of the glomerular blood into Bowman's capsule.

H₂O, glucose, amino acids, electrolytes, wastes

Averages 125 ml/min for both kidneys 180 liters/day

The vast majority of the filtrate must be taken back!

Filtration is a product of the blood pressure and the nature of the fenestrated capillaries which make up the glomerulus.

The Glomerulus and Bowman's Capsule: The capillaries of the glomerulus are surrounded by specialized cells which form the inner (visceral) layer of Bowman's capsule. These specialized cells are called podocytes (foot cells) because they have processes called pedicels which interdigitate or

interlace producing openings called filtration slits. The capillaries are fenestrated in order to allow a large amount of filtration. The outer (parietal) layer of Bowman's capsule consists of epithelial cells with tight junctions and serves to contain the filtrate in the capsular space.

The filtration membrane is a double layered membrane composed of the endothelial cells of the capillary wall juxtaposed with the podocytes of the visceral layer of Bowman's capsule. Substances make their way through the capillary fenestrations, then through the combined basement membranes of capillary and podocyte cells, and through the filtration slits into the capsular space.

1.2.2 Step 2, Reabsorption - The return of substances from the filtrate to the blood and interstitial fluid. The major substances reabsorbed are water, NaCl, glucose, and amino acids. Some of the urea, together with other salts is also reabsorbed.

Locations of Reabsorption

Reabsorption occurs in each of these areas for various substances and to various degrees. Most reabsorption occurs in the PCT (Proximal Convoluted Tubule), but reabsorption of water also occurs from the descending limb of the Loop of Henle, reabsorption of salt from the ascending limb and the DCT (Distal Convoluted Tubule), and more water from the Collecting Duct.

Reabsorption from Proximal Convoluted Tubule:

A) H₂O – pulled by osmosis into hypertonic blood.

65% occurs in PCT

B) NaCl – active transport of either Na⁺ or Cl⁻, pulls water along Glucose.

C) 100% of glucose and amino acid transported - occurs in PCT by active co-transport.

Water is reabsorbed by osmosis. Entering the proximal convoluted tubule the filtrate is very dilute compared to the blood. 65% of water reabsorption occurs from the PCT as a result of this osmotic gradient.

Reabsorption from Loop of Henle: As the filtrate enters the descending limb of the loop of Henle, especially in juxtamedullary nephrons with long loops, it is exposed to increasingly hypertonic medulla. This pulls at least another 20% of absorbable water out of the filtrate. Reabsorption in this area is termed obligatory because it must occur due to the osmolarity of the surrounding interstitial fluid.

1.2.3 Step 3: Secretion

Secretion is the active release of substances into the nephron tubule by the tubular lining cells. Secretion is the release by active transport of substances into the filtrate. It is accomplished by the tubular lining cells. The substances released are usually derived from the blood in the peritubular capillaries. Actually secretion has already been going on but it is the third process we consider. It begins in the proximal convoluted tubule and continues in the distal convoluted tubule and the collecting tube. It is done for three purposes:

- 1) To release any residues from toxins and drugs which haven't been filtered.
- 2) To establish electrolyte balance. Since positive ions, namely sodium, are reabsorbed, positive ions must be secreted in exchange. The first choice is potassium, K^+ . In addition negative ions will be managed. This usually means chloride, Cl^- , will either be secreted or will diffuse down its electrochemical gradient. Other anions may be available for release such as sulphate, but certain ions will never be secreted. For example, bicarbonate will always be retained to help manage the buffering capacity of blood.
- 3) Acid - base balance - Usually this means getting rid of acid. The first choice for this is H^+ . Hydrogen ions are derived from the reaction of carbon dioxide and water, just as they are in the RBC and in stomach lining cells. The reaction yields carbonic acid which dissociates into H^+ and HCO_3^- - as you've already learned. The bicarbonate produced is retained for the buffer (as mentioned above) and exchanged for chloride, called the chloride shift.

Normal Constituents of Urine:

Water (sp. Gravity 1.001 to 1.035),

Urea - Nitrogenous waste from deamination.

Uric acid - Waste product from purine metabolism.

Creatinine – Released during anaerobic muscle activity.

Na^+ , K^+ , PO_4^{3-} , SO_4^{2-} , Ca^{+2} , Mg^{+2}

Urine has a specific gravity slightly higher than pure water due to the solutes. Urea and uric acid are nitrogenous wastes which have been put into the blood by the liver. Creatinine is a combination of two creatine molecules, released from skeletal muscle during exercise. The other electrolytes are normal and vary in amount.

1.3 Abnormal Constituents of Urine

Glucose - Recent intake of sugary foods, diabetes mellitus.

Protein - Physical exertion.

High protein- Hypertension, glomerulonephritis.

Ketone bodies - Starvation, untreated diabetes mellitus.

Haemoglobin - Haemolytic anaemia, severe burns.

Bile pigments - Hepatitis, cirrhosis, bile obstruction.

Erythrocytes - Bleeding due to trauma, kidney stones, infection, cancer.

Leucocytes - Urinary tract infection.

Plasma filtrate (white arrows) enters nephron through glomerulus. NaCl is actively transported (thick black arrows) from ascending loop of Henle and urea passively diffuses (thin black arrows) from collecting duct to renal medulla to generate a solute concentration gradient that is progressively higher in inner medulla than in outer medulla and cortex. Inner medulla corresponds to medullary tips seen at CT.

1.4 Function of kidneys

Main function of kidney is to bring out waste products of body metabolism and extra water from blood in the form of urine.

Other functions of kidneys are:-

- 1) Kidneys control the volume of body fluid
- 2) Kidneys control mineral contents of our body.
- 3) Kidneys produce active form of vitamin-D which is beneficial for the health of bones.
- 4) Kidneys help to regulate blood pressure.
- 5) Kidneys control the acidity and alkalinity of blood.
- 6) Kidneys produce erythropoietin that increases the rate of production of red blood cells.

Renal or kidney failure occurs when the excretory function of the kidney fails. The kidneys are unable to filter out metabolic waste products (creatinine and blood urea nitrogen) and to concentrate urine, and this is accompanied to a variable degree by a failure of the regulation of the composition of body fluids, the control of red blood cell production (through the hormone erythropoietin), blood pressure (through the hormone renin), Vitamin D metabolism, and salt balance.

Acute Renal Failure:

Acute renal failure may or may not be accompanied by oliguria (reduced urine production) or anuria (ceasing of urine production) and should be treated as a medical emergency. Acute renal

failure successfully treated, usually lasts several days to several weeks at the most, and therefore would not fulfil the qualifying criteria for DLA.

Chronic Renal Failure:

Chronic renal failure results from any progressive, destructive condition affecting both kidneys. The loss of kidney (renal) function progresses slowly over a period of months or years, and is not reversible.

1.5 Kidney diseases

There are various types of kidney disease -

- 1) Kidney failure- (a) Acute kidney failure (b) Chronic kidney failure
- 2) Polycystic kidney disease
- 3) Kidney stone
- 4) Renal tubular acidosis
- 5) Lupus nephritis
- 6) Kidney infection
- 7) Kidney cancer etc.

1.6 Symptoms of kidney disease

- 1) Swelling of legs, ankles etc.
- 2) Scanty and painful urination.
- 3) Sometimes coming of blood with urination.
- 4) Anaemia.
- 5) High blood pressure.
- 6) Sometimes burning sensation during urination.
- 7) Vomiting, nausea.
- 8) Loss of appetite, headache etc.

1.7 Precautions

- 1) In case of painful and scanty urination consult a doctor immediately.
- 2) Don't take pain killer medicines without the advice of a doctor.

3) If anybody in your family has got polycystic kidney disease then you should also consult a doctor.

4) Try to control your blood pressure. If necessary take medicines to control your blood pressure but don't discontinue.

5) If your body water is lost due to heat or any reason then drink sufficient water.

6) Try to control your blood sugar. If necessary take insulin.

Sometimes it so happens that a person's kidney damage is noticed after performing blood and urine tests but the person was not aware of the fact.

So from time to time blood test, urine test are required. Particularly for the following categories of persons regular check-up

Blood test and urine tests are essential:-

- 1) Persons having high blood pressure and diabetes.
- 2) Persons who suffered from disease like nephritis in childhood.
- 3) Persons whose family member is suffering from polycystic kidney disease.
- 4) Persons having anaemia.
- 5) Persons having swelling in legs, ankles.
- 6) Persons who often suffer from urinal infection.

1.8 Nephrotoxic agents

Drugs, diagnostic agents and chemical are well known to be nephrotoxic. The following are some of the important nephrotoxic agents.[11]

- a) Heavy metal – Mercury, arsenic, lead, bismuth
- b) Antineoplastic agents – Alkylating agents (eg: Cisplatin, Cyclophosphamide), Nitrosoureas (eg: Streptozotoin, Carmustin, Lomustine and Semustine), Antimetabolites (eg: High dose Methotrexate, Cytosine, Arabinose, High dose 6- thioguanine, 5-fluorouracil), Antitumor antibiotics (eg: Mitomycin, Mithramycin, Doxorubicin), Biological agents (eg: Recombinant leukocyte and interferon)

- c) Antimicrobial agents – Tetracycline, Acyclovir, Pentamidine, Sulphadiazine, Trimethoprin, Rifampicin, Amphotericin B.
- d) Aminoglycosides – Gentamicin, Amikacin, Kanamycin, Streptomycin.
- e) Miscellaneous – Radiocontrast agents, Non-steroidal anti-inflammatory agents.

2. Plants possessing Nephroprotective activity

Gutierrez et al., have evaluated nephroprotective activity of *Prosthechea michuacana* against cisplatin-induced acute renal failure in rats. Methanol, hexane, and chloroform extracts of bulbs of *P. michuacana* were studied in the cisplatin-induced renal injury model in rats. Results showed that treatment with cisplatin induced significant elevations in concentrations of blood urea and serum creatinine and in lipid peroxidation. Treatments with methanolic extract (200, 400 and 500 mg/kg) increased levels of biochemical markers of renal injury like reduced glutathione, glutathione S-transferase, and superoxide dismutase and inhibited the increases in blood urea and serum creatinine concentrations and lipid peroxidation induced by cisplatin.[7]

Olagunjua et al., evaluated nephroprotective activities of the aqueous seed extract of *Carica papaya* Linn. in carbon tetrachloride induced renal injured Wistar rats: a dose- and time-dependent study. Study showed that CPE (*Carica papaya* Extract) has nephroprotective effect on Carbon tetra chloride renal injured rats, an effect which could be mediated by any of the phytochemicals present in it via either antioxidant and/or free radical scavenging mechanism(s).[8]

Saumya et al., evaluated nephroprotective effect of *Bauhinia variegata* (Linn.) whole stem extract against cisplatin-induced nephropathy in rats. The nephroprotective activity of the ethanolic extract of *Bauhinia variegata* (Linn.) whole stem against cisplatin-induced nephropathy was investigated by an in vivo method in rats. Acute nephrotoxicity was induced by i.p. injection of cisplatin (7 mg/kg of body weight (b.w.)). Administration of ethanol extract at dose levels of 400 and 200 mg/kg (b.w.) to cisplatin-intoxicated rats for 14 days attenuated the biochemical and histological signs of nephrotoxicity of cisplatin in a dose-dependent fashion.[9]

Sreedevi et al., examined the effect of petroleum ether, ethyl acetate and alcoholic extracts of aerial parts of *Vernonia cinerea* (500 mg/kg, p.o.) on cisplatin-induced nephrotoxicity (6mg/kg, i.p.) in albino rats. alcoholic extract showed pronounced curative activity, ethyl acetate extract exhibited good prophylactic activity and petroleum ether extract showed moderate protection in both curative and prophylactic models against cisplatin-induced toxicity. [10]

Ghaisas et al., evaluated Antidiabetic and Nephroprotective effect of *Tectona grandis* linn. in Alloxan induced Diabetes. Ethanolic extract of bark of *Tectona grandis* Linn. (TG) was evaluated using alloxan induced diabetes and associated renal complication. The diabetes was induced by administration of alloxan to the rats at the dose of 140 mg/kg, i.p. TG was administered to diabetic animals for six weeks and various biochemical parameters in blood and urine (plasma glucose, serum albumin, total protein, and creatinine, urine total protein, urine albumin), tissue parameters (cholesterol and triglyceride in kidney homogenate) and % change in body weight were evaluated along with histopathological study. In present study diabetic animals treated with TG showed significant reduction in the elevated level of plasma glucose ($p < 0.01$) when compared with diabetic control.[11]

Ruby et al., evaluated nephroprotective effect of ethanolic extract of *Strychnos potatorum* seeds in Rat Models. Study concluded that the seeds of *Strychnos potatorum* possess marked nephroprotective activity and could have a promising role in the treatment of acute renal injury induced by nephrotoxins, especially gentamicin.[12]

Vadivukkarasi et al., evaluated antioxidant activity and nephroprotective effects of aqueous extract of *pleurotus eous* (berk.) sacc.: (apk1) pink edible oyster mushroom. *Pleurotus eous* is an edible oyster mushroom currently available in Southern part of India. Study reveals the medicinal beneficial effects of this mushroom which have not been explored so far.[13]

Shelke et al., evaluated nephroprotective activity of ethanolic extract of dried fruits of *Pedalium murex* Linn. Nephrotoxicity was induced in Wistar rats by intraperitoneal administration of Cisplatin 5mg/kg. Effect of concurrent administration of *Pedalium murex* ethanolic extract at a dose of 250 mg/kg given by oral route was determined using serum creatinine and blood urea and change in body weight as indicators of kidney damage. Cystone was used as standard drug. The extract significantly decreased the cisplatin induced nephrotoxicity. The study shows that the ethanolic extract of dried fruits of *Pedalium murex* is an excellent nephroprotective as compared to cystone.[14]

Kannappan et al., evaluated nephroprotective activity of orthosiphon stamineus benth extract using rat model. Gentamycin is an extensively used aminoglycoside antibiotic. It has been reported to produce nephrotoxicity even at normal therapeutic dose level. The drug was administered intra peritonially at a dose of 80mg/kg weight for 9 days. Histopathological sections showed marked glomerular, peritubular and blood vessel congestion. These increased levels of serum creatinine,

blood urea, urinary protein and extent of renal damage were decreased by the methanolic extract of *Orthosiphon stamineus* at both dose levels that is 100 and 200 mg/kg body weight in rats.[15]

Yogesh et al., evaluated nephropharmacological activity of ethanolic extract *lepidium sativum* seeds in albino rats using cisplatin induced acute renal failure. Study was designed to investigate to possible potential nephrocurative & nephroprotective activity of 200mg/kg ethanolic extract of *Lepidium sativum* L. seed was used to against cisplatin (5mg/kg, i.p.) induced nephrotoxicity. present study data confirmed nephrotoxicity induced by cisplatin due oxidative stress and ethanolic extract of *Lepidium sativum* L. seeds may have nephroprotective and curative activity.[16]

Onyemaechi et al., evaluated the protective effect of methanol extract of *Kigelia africana* fruit extract (KAFE) against cisplatin-induced renal toxicity in male rats. results suggest that KAFE may protect against cisplatin-induced renal toxicity hence might serve as a novel combination agent with cisplatin to limit renal injury.[17]

Palani et al., evaluated effect of the ethanolic extract of *Indigofera barberi* (L) in acute Acetaminophen - Induced nephrotoxic rats. Nephrotoxicity was induced in rat by administering single dose of paracetamol (750 mg/kg). The degree of nephroprotective activity was measured by renal functional parameters such as serum urea (UR), uric acid (UA) and creatinine (CR).and hematological profile was concluded that the ethanol extract of *I-barberi* is an effective nephroprotective agent.[18]

Adeneye et al., evaluated nephroprotective effects of the aqueous root extract of *Harungana madagascariensis* (L.) In acute and repeated dose acetaminophen renal injured rats. Effects of the extract pretreatments on the hematological and renal histological profile in acetaminophen nephrotoxic rats were also evaluated. Results showed that treatment with intraperitoneal acetaminophen for 24 hours and 14 days induced significant ($p < 0.05$, $p < 0.01$, $p < 0.001$) elevations in the serum concentrations of UR(Serum urea), UA(Uric acid) and CR(Creatinine), varying degrees of tubular necrosis on histology and varying degrees of alterations in the hematological parameters in acute and repeated dose acetaminophen nephrotoxic rats, respectively. However, pretreatments with graded oral doses of the extract significantly ($p < 0.05$, $p < 0.01$, $p < 0.001$) attenuated elevations in the serum concentrations of UR, UA and CR, and improved diffuse tubular necrosis in both models of acetaminophen nephrotoxicity.[19]

Yogesh et al., evaluated preventive and curative effect of *Ficus religiosa* (L) latex for against cisplatin induced nephrotoxicity in wistar rats. The level of brush border enzymes like Na^+ / K^+

ATPase, *Ca⁺⁺ ATPase* and *Mg⁺⁺ATPase* were found significantly reduced after single dose cisplatin injection. It was overcome by treatment of same extract in curative and protective groups. Finally it is concluded that the present study data conformed nephrotoxicity induced by cisplatin due oxidative stress and methanolic extract of *Ficus religiosa* L. latex may have nephroprotective and curative activity.[20]

Sarumathy et al., evaluated biochemical studies show that there is an increase in the levels of serum urea and creatinine along with an increase in the body weight and reduction in the levels of uric acid in acetaminophen induced groups. These values are retrieved significantly by treatment with *Clitoria ternatea* extracts at two different doses. The antioxidant studies reveal that the levels of renal SOD(Superoxide dismutase), CAT(Catalase), GSH(Glutathione) and GPx(Glutathione peroxidase) in the APAP(acetaminophen) treated animals are increased significantly along with a reduced MDA content in ethanol extract of *Clitoria ternatea* treated groups. The study suggest that the ethanol extract of *Clitoria ternatea* can prevent renal damage from APAP induced nephrotoxicity in rats and it is likely to be mediated through active phytoconstituents and its antioxidant activities.[21]

Mahgoub M. Ahmed performed biochemical studies on nephroprotective effect of Carob (*Ceratonia siliqua* L.) Growing in Egypt. The nephroprotective effect of carob pods and leaves (100 and 200 mg/kg, p.o.) was investigated using cisplatin (10 mg/kg body weight, i.p.) to induce oxidative renal damage in mice. Treatment of carob pods and leaves (100 and 200 mg/kg, p.o.) significantly attenuated the cisplatin-induced nephrotoxicity. Both pods and leaves of carob at 100 and 200 mg/kg increased the concentration of reduced glutathione (GSH) and protected against the increase of cisplatin induced lipid peroxidation.[22]

Sarumathy et al., evaluated protective effect of *Caesalpinia sappan* (CS) on acetaminophen induced nephrotoxicity and oxidative stress in male *albino* rats. The aim of this study was to examine the nephroprotective and antioxidant activities of ethanol extract of CS at two dose levels of 100 and 200 mg/kg B/W on acetaminophen (APAP) induced toxicity in male *albino* rats. APAP significantly reduced levels of uric acid and increased levels of serum urea, creatinine. Ethanolic extract CS significantly increased activities of renal superoxide dismutase, catalase, and glutathione peroxidase and decreased. Malondialdehyde content of APAP treated rats.[23]

Kaliwal et al., evaluated hepatoprotective and nephroprotective activity of bark extract of *Bridelia retusa* spreng in CCl₄ (Carbon tetra chloride) treated female Mice. Hepatoprotective and nephroprotective activity of ethanolic and aqueous extracts of the stem bark of *Bridelia retusa* in

carbon tetrachloride treated female mice. The protective activity of the extracts was justified by the significant decrease in the weights of adrenal glands when compared to CCl₄ treated group and the weights of ovary was increased to that of the normal control group. In general, both the extracts possessed protective activity though ethanolic extract was found to exhibit greater protection.[24]

Sharma et al., evaluated invitro antioxidant and protective effect of *Bauhinia variegata* linn on gentamicin induced nephrotoxicity in rats. The study was aimed at evaluating the ethanolic and aqueous extracts of the roots of *Bauhinia variegata* Linn. For antioxidant and nephroprotective effect in gentamicin induced nephrotoxicity in rats. Both the extracts produced significant nephroprotective activity as evident by decrease in serum creatinine, serum urea, urine creatinine and Blood urea nitrogen levels in extract treated groups which was elevated by gentamicin.[25]

Dheeraj et al., evaluated nephroprotective and antioxidant activity of *Anthoxanthum odoratum* on acetaminophen induced toxicity in rat. The experimental data suggest that the ethanol extract of *Anthoxanthum odoratum* can prevent renal damage from apap-induced nephro toxicity in rats and this is likely mediated through its antioxidant activities.[26]

Pratibha et al., evaluated nephroprotective activities of root extracts of *Andrographis paniculata* (*Burm f.*) *Nees* in gentamicin induced renal failure in rats: A time-dependent study. The extent of nephroprotection offered by various extracts under study increased with the increasing time of treatment and polarity of the solvents. The signs of Gentamycin nephrotoxicity in rats are significantly mitigated by petroleum ether and Chloroform extracts whereas the maximal alleviation of Acute renal failure was caused by Methanolic root extract; hence, the methanolic root extract of AP can be advocated as a nephroprotective agent.[27]

Shanmugam et al., evaluated nephroprotective effects of a ginger extract on Cytosolic and Mitochondrial Enzymes against Streptozotocin -Induced Diabetic Complications in Rats. The experimental results suggest that ginger extracts could be used as a nephro-protective supplement particularly to reverse diabetic-induced complications.[28]

Afzal et al., evaluated diuretic and nephroprotective effect of Jawarish Zarooni Sada(JZS)--a polyherbal unani formulation. Nephroprotective activity of JZS against gentamicin-induced nephrotoxicity was investigated by administering JZS along with high dose of gentamicin (40 mg/kg) and elevation of serum urea and serum creatinine was taken as the index of nephrotoxicity. JZS showed significant diuretic and nephroprotective effect.[29]

3. Conclusion

It can be concluded that herbal plants play a unique role in medicine. There is no synthetic drug which relieve overall insufficiency of kidney. But indigenous plants possess tissue rejuvenator property which is anyway un avoidable. To Indian, who are brought upon Indian food, soul and climate with Indian habits of life and environment, Indian drugs naturally suit better and safer than European constitution built upon the peculiar food, climate and manner of life. This may perhaps be the reason why in numerous cases where synthetic medicines fails, Indiginous system of medication succeed.

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