CHAPTER 28

Nephroprotective and Gastroprotective Benefits of Medicinal Plants: An Integrative Approach

RIMSHA BASHIR[1], TAYYEBA YASIN[2*], USWA SHAMAZ[2], ANAM ISHTIAQ[3], MUHAMMAD ADEEL RAZZAQ[4], ABUZAR MUJAHID[5], NIMRA ASLAM[6], LAIBA RANA[7]

[1]Department of Allied Health Professionals, Government College University, Faisalabad, Pakistan
[2]Institute of Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan
[3]Yusra Institute of Pharmaceutical Sciences, Rawalpindi, Pakistan
[4]Department of Biochemistry, University of Agriculture, Faisalabad, Pakistan
[5]Faculty of Veterinary Science, Bahauddin Zakariya University, Multan, Pakistan
[6]Department of Radiology and Medical Imaging, The University of Faisalabad, Faisalabad, Pakistan
[7]Ibn e Sena Research Institute of Health Sciences, Multan, Pakistan
[*]Corresponding author: tayyebjmal321@gmail.com

SUMMARY

Medicinal plants are used in home remedies and cultural health practices such as Ayurvedic medicine and Japanese Kampo medicine for the well-being of humans. In contrast, Occidental medicine confides in drug therapy with prospective adverse reactions and side effects like gastro-toxicity, nephrotoxicity, etc. Medicinal plant extracts have been preferred for fulfilling the nutritional requirements by the provision of therapeutic benefits like anti-inflammatories, anti-microbial, antioxidants, and anti-cancer properties. The merging of Western and Eastern medicine raises new probabilities in the medical field. Kidneys are essential organs liable for eliminating wastes from the body and thus are sensitive to nephrotoxic chemicals. Nephrotoxic disorders can increase the risk of chronic and acute renal failures, leading to the destruction of the main functional unit (nephrons) of kidneys. Various plants have been explored for their nephroprotective action, which is usually done by restoring serum creatinine levels and eliciting antioxidant effects. Gastric disorders such as Gastroesophageal reflux disease (GERD), stomach ulcer, or peptic carcinoma have been recognized as significant challenges in public health for several reasons of *Helicobacter (H.) pylori* infection, genetic predispositions, and lifestyle aspects. Medicinal plants such as *Aegle marmelos*, *Withania somnifera*, *Asparagus racemosus* and *Ficus religiosa* have been explored for their gastroprotective action in combating disorders like GERD, dysentery and peptic ulcers.

INTRODUCTION

Since ancient times, medicinal plants have been used for health procurement and protection in various traditional healthcare systems such as traditional Chinese Medicine, Japanese Kampo Medicine, or Ayurveda medicine (Mai et al., 2021). Conventional utilization of plants for treatment purposes depends on knowledge transferred over generations. On the contrary, western medicine is based on lifetime drug therapy, thus making people unable to survive (Kessler et al., 2019). Other than dependence, many other short-term and long-term adverse effects for instance hepatotoxicity, neurotoxicity, nephrotoxicity, and gastrointestinal (GI) upset, etc. have been reported for allopathic medicine in patients of all ages (Peterson et al., 2017). Furthermore, the drugs can cause rebound symptoms, and abstinence syndrome in patients (Rastogi, 2021).

In the past 2 decades, medicinal plant extracts have been used as healthy substitutes in the form of nutritional supplements, phytomedicines, or herbal medicines to promote the well-being of individuals (Yoo et al., 2018). It is a renowned fact that plants and their phytoconstituents exert a particular therapeutic impact on various health problems, such as anti-oxidants, anti-inflammatories, contraceptives, and anti-cancer drugs, etc (Pan et al., 2014). For instance, in the case of renal pathophysiology, a plant-based diet has been approved for its health benefits, specifically for diabetic nephropathy. Similarly, medicinal formulations help in lowering the incidence of GI toxicity, nephrotoxic events, etc. (Campagne et al., 2019). Therefore, the recent approach of considering plants as a complementary treatment can provide twofold benefits, they boost the immunity to fight and prevent ailments and act as the nephroprotective, and gastroprotective agents (Dwyer et al., 2018). The blended use of Western and traditional Eastern medicine raises many questions and opens new horizons for medical and pharmaceutical research (Pfister

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et al., 2017). Traditional Chinese and other herbal medicines are widely acknowledged for their greater therapeutic efficacy and low number of side effects (Kesari et al., 2006). Moreover, many plants in disease management are used as a cost-effective alternative to occidental medicine (Oketch-Rabah et al., 2020). The chapter is written to unveil the achievable nephroprotective and gastroprotective properties of particular medicinal plants as their mechanism is shown in Fig. 1. A probable alternative to standard therapies is the investigation of natural cures for common health issues such as renal dysfunction and peptic ulcers. The curative properties of these medicinal plants on the GI and renal systems will be analyzed in this chapter, combined with the biologically active elements, mechanisms of action, and scientific backing for such advantages. This chapter seeks to assist in the development of novel, secure, and productive methods for the procurement and prevalence of certain health conditions by acquiring knowledge of the curative abilities of these natural herbal assets.

NEPHROTOXICITY AND MEDICINAL PLANTS

Throughout history, human beings have mostly been exposed to various potentially toxic circumstances and face numerous agents in their domestic and professional environments. The Kidneys are among the essential organs of the human body that excrete the metabolic waste and toxic chemicals from the body (Negi & Mirza, 2020). Certain physiological characteristics of the kidneys like elevated metabolic activity, high endothelial surface-weight ratio, increased concentration of filtered biochemical in the renal tubules, and high blood flow (more than 20% of total cardiac output) to the organs also play a role in its high vulnerability towards toxins (Hoitsma et al., 1991). A large number of nephrotoxicity's can cause damage in specific parts of the nephron such as chronic or acute tubular injury, whereas the widely recognized syndromes of toxic renal damage are acute renal failure (ARF), chronic interstitial nephritis, chronic renal failure (CRF) and nephritis syndrome (Negi & Mirza, 2020).

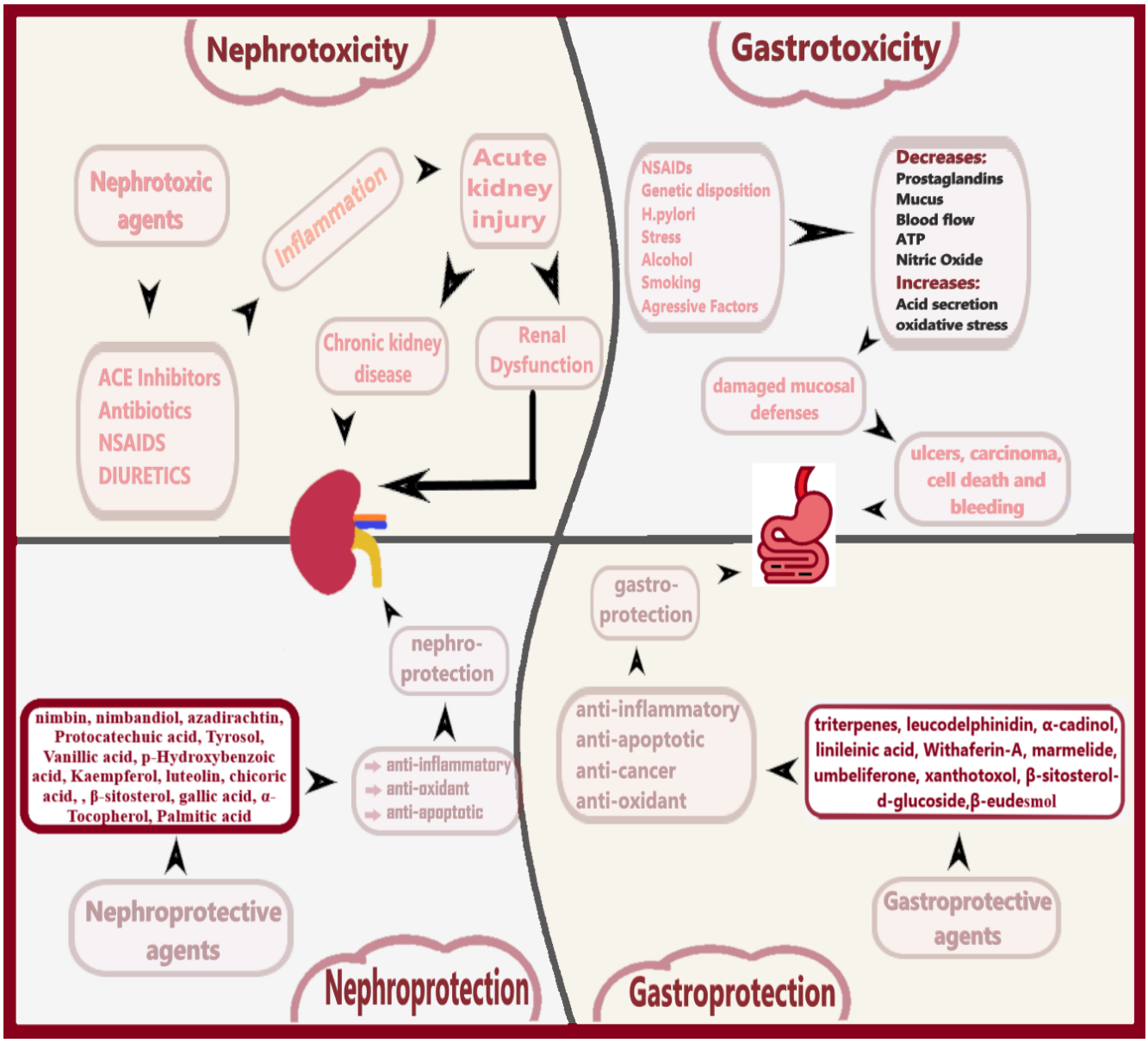

Fig 1. General mechanism for gastro-toxicity and nephrotoxicity and their management by phytoconstituents

Sudden and drastic reduction in glomerular filtration rate (GFR) is a major symptom of (ARF), which can be restored to treat the damage. CRF is referred to as one of the major causes of death in India. It develops gradually over many years, leading to continuous loss of metabolic and endocrine functions (Arany et al., 2008).

Renal cell death is the key indication of nephrotoxicity, that causes major changes in nephron. A typical kidney comprises millions of nephrons (its functional unit) which are responsible for its functioning in the body (Misurac et al., 2013). Damage or complete deterioration of the nephron occurs due to changes in either glomeruli, tubules, interstitial, or intra-renal blood vessels, thereby affecting kidney function. The Nephrotoxin-induced mechanism for nephrotic cell death may be due to loss of brush border membrane, oxidative stress, proximal tubular necrosis, oxidative stress, and renal blood flow (Barnett & Cummings, 2018). Various medicinal plants having nephroprotective potential have been reported in the literature (Table 1).

***Cucurbita pepo* L.**

Cucurbita plants such as watermelon, cucumber squash, and pumpkin possess numerous active phytoconstituents such as sterols, fatty acids, microelements, and vitamins responsible for their medicinal properties like anti-cancer, anti-diabetic, and nephroprotective effects (Malviya & Sharma, 2021). For instance, the methanolic or ethanolic extract of the seeds has been recognized for its characteristic amelioration of benign prostatic hyperplasia (BPH), attributed to its ability to decrease frequent urination e.g. in urinary incontinence, nocturnal enuresis, overactive bladder syndrome and prevent prostate enlargement by inhibition of 5-α-reductase (Tienda-Vázquez et al., 2022). Furthermore, it is also involved in boosting the endocrine system and promoting muscle relaxation (Ameen et al., 2023).

This plant is also explored for its potential in treating nephron-related disorders and kidney diseases and many clinical trials have been conducted on rats and rabbits in the past 2 decades (Caili et al., 2006). The nephroprotective activity of *Cucurbita (C.) pepo L.* was tested in the male Wistar rats which showed a remarkable reduction in the levels of serum creatinine and urea as well as normalized the elevated Mg levels, whereas reduced sodium and potassium levels also increased compared to toxic group (Coulson et al., 2013). Histopathological examination suggested that *C. pepo* extracts can exhibit bioactive phenolic compounds, namely flavonoids, iridoids, phenylethanoids, and phenolic acid compounds (Wang et al., 2008). These phytoconstituents are responsible for relieving the damage caused by the nephron's oxidative stress, leading to reduced pressure on the liver (Eneh et al., 2018).

Azadirachta indica

It is widely recognized as neem, a renowned member of the Meliaceae family, is famous across the globe for its superfluous medicinal characteristics and has been used in herbal medicinal remedies since old times (Talele et al., 2012). It would be right to say that all parts of this plant from flowers to seeds have extensive and unique complexes of the active constituents responsible for its therapeutic effects (Haque, 2013). For instance, the Neem extract is famous for its anti-hypertensive, anti-diabetic, anti-hyperlipidemic, and hepatoprotective effects (Rahmani et al., 2018). The plant also assists in the suppression of tumor cell growth by boosting the

Table 1. Nephroprotective effects of various medicinal plants

Botanical name	Part used	Active constituents	Pharmacological effects	References
Combretum micranthum G. Don	Hydroalcoholic extract of plant roots	Gallic acid, Combretine (Turicine), Combretine (Turicine), Betulin Alkaloids Betonicine, Stachydrin, 4-Hydroxyproline betaine, Betaine, α-Tocopherol, Homoorientin (isoorientin), Palmitic acid, oleic acid	Exhibits nephroprotective activity due to its lipid peroxidation, anti-oxidative, metal chelating, and free-radical scavenging activity	Kpemissi et al., 2019
Sonchus oleraceus	Ethanol extract of aerial part	Villosol, sesquiterpene lactones, luteolin, apigenin, caftaric acid , chicoric acid, ferulic acid, β-sitosterol, rutin, β-daucosterin, taraxasterol, ursolic acid, chlorogenic acid.	Normalizes the levels of serum creatinine, BUN, MDA, SOD, IL-1β, TNF-α and IL-6	Sujana et al., 2021
Cichorium intybus L.	Aqueous or methanolic extract of seeds, ethanolic extract of roots, ethanolic extract of aerial parts	Kaempferol, luteolin, phytosterols, sescviterpene lactones (lactucin and lactucopicrin), quercetin-3 galactoside, insulin, bioflavonoids.	Reduced triglyceride, serum uric acid, and abdominal fat deposition in clinical trials on French quails induced with hyperuricemia by varying the acetyl-CoA carboxylase protein expression, xanthine oxidase, and fatty acid synthase activities, anti-cancer effects	Lin et al., 2014
Azadirachta indica A. Juss.	Methanolic extracts from leaves	Quercetin, azadirachtin, numerous liminoids, nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosano and nimbosterol	Reduces nephrotoxicity by its free radical scavenging action, anti-oxidant and anti-inflammatory effects	Seriana et al., 2021
Cucurbita pepo L.	Pumpkin seeds, Cucurbita pepo L. cortex extract	Protocatechuic acid, Kaempferol, p-Hydroxybenzoic acid, Luteolin, trans-p-coumaric acid, Ferulic acid, Syringic acid, Caffeic acid, Tyrosol, Vanillic acid	Effective treatment of bacterial urinary tract infections, Bladder function disorders,	Tienda-Vázquez et al., 2022

pro-apoptotic gene transcription and modulating mechanisms of several cell-signaling pathways (Seriana et al., 2021). Likewise, nimbolide extracts including Azadirachtin are capable of inducing cytotoxicity in the cancerous cells by modulation of cellular proteins, cell cycle arrest and p53-dependent pathway (Shabbir et al., 2023). Moreover, it's anti-microbial potential has been discovered in previous research (Edwin et al., 2023). Whereas, the nephroprotective action of plants are accredited to its anti-cancerous and anti-oxidant properties which assist in the therapeutic management of nephrotic injuries, nephrotic tumors and nephrotoxicity (Devi & Sharma, 2023).

In a pharmacological trial supervised by (Alzohairy, 2016), the methanolic extract of plant was prepared and administered to rats to investigate its nephroprotective properties in rats. The findings were convincing since the extract's activity to ameliorate the nephrotic injuries occurred due to oxidative stress via its radical scavenging action (Moneim et al., 2014). Furthermore, the regaining of cellular activity of nephrons was observed by conducting polymerase chain reaction (PCR) which elicited the down-regulation of Caspase-9 and Caspase-3. The leaf extracts also improved the levels of important biomarkers such as malondialdehyde (MDA), nitric oxide (NO), etc. (Alzohairy, 2016).

***Cichorium intybus* L.**

The plant *Cichorium (C.) intybus* widely known as Chicory, has excessive phytochemicals like terpenoids, saponins, polyphenols, flavonoids, volatile compounds, phenolic acids, minerals, vitamins, insulin, minerals and alkaloids (Janda et al., 2021). Among these, seeds and aerial parts are storehouses for polyphenols whilst roots contain deposits of sesquiterpene lactones (Lin et al., 2014). Former studies suggest that Chicory plant extracts have profound health benefits including anti-microbial, hepato-protective, sedative, neuroprotective, anti-inflammatory, and diuretic effects (Javed et al., 2020). The effects are exhibited due to its unique mechanism of action and effects on the biomarkers for instance, it inhibits TNF-α, terminates prostaglandins E2 production, and possesses anti-inflammatory and anti-oxidative activity against many allergies (gingival inflammation) and disorders of kidney and liver (Kanj et al., 2019). The nephroprotective effects of *C. intybus* (aqueous and methanolic extract) were evaluated by (Zaman et al., 2017) by administrating the aqueous and ethanolic extracts of the plant and effective improvement was observed in the biomarker evaluation of the serum urea and serum creatinine were decreased remarkably with the administration of plant extract.

Histopathological examination illustrates tubular histology and normal glomerular physiology with reduced tissue necrosis and delicate blood vessel congestion (Tahir et al., 2018). The effect of aqueous extracts of plant showed better results regarding amelioration of the nephrotoxicity due to the presence of phytoconstituents such as quercetin-3 galactoside, Kaempferol, and bioflavonoids, etc (Khaliq et al., 2015). These biochemicals possess the anti-oxidant property, the most probable mechanism of nephroprotection from oxidative stress (Zaman et al., 2017).

***Combretum micranthum* G. Don**

It is quite popular in traditional medicinal systems for its massive therapeutic and nutritional benefits such as anti-oxidant, anti-diabetic, and anti-inflammatory properties. Ethno-medical studies exhibit promising information regarding the therapeutic benefits of these plants related to cisplatin-induced nephrotic injuries (Kpemissi et al., 2019). Several other in vivo and invitro clinical trials were also arranged during the past two decades to explore the therapeutic properties of *Combretum* (*Co.) micranthum* regarding renal damage (Tine et al., 2024). In one such study, the rats having cisplatin-induced toxicity were administered with hydro-alcoholic extract of *Co. micranthum* and convincing results regarding ameliorated nephrotoxicity were found in the HEK-293 cells of rats (Kpemissi et al., 2019). The Nephroprotective potential of this plant extract was observed against the acute toxicity induced in diabetic animals (Tine et al., 2024). Acute toxicity was induced in renal cells by exposing them to elevated Glucose levels for 72 hours which was indicated by abnormal cell dimensions, vacuolation and cell depreciation in the cellular cytoplasm (Kpemissi et al., 2019). After administration of *C.micranthum* extract, more than 20% betterment was observed in cell viability contrary to elevated gucose-exposed cells (Tine et al., 2024). The amelioration includes vigorous anti-oxidant activity by scavenging DPPH (2,2-Diphenyl-1-picrylhydrazyl), Hydrogen peroxide, chelating metal ions and nitric oxide (NOx) (Sujana et al., 2021). Apart from that, notable suppression of lipid peroxidation was also seen as one of its major effects. The phytochemical investigation reassured the presence of flavonoids, steroids, alkaloids, and terpenoids with other biological activities (Kpemissi et al., 2019).

Sonchus oleraceus

The sow thistle or puha is an herbal plant native to Central Asia and Europe but now can be found across the globe. The shoots of this plant are used frequently in preparing herbal compounds for managing medical conditions such as hepatitis, pneumonia and diarrhea (Sujana et al., 2021). The herbal shoots of puha plant, which are rich source of antioxidants, α-tocopherol, flavonoids (luteolin and apigenin), essential fatty acids and carotenoids, are common ingredient of routine diet of people in New Zealand and other native regions (Whyte et al., 2001). A lab investigation held in 2006 demonstrated that antioxidant activity of puha leaves is three folds compared to blueberries (Gould et al., 2006).

In another research aimed to analyze 27 non-cultivated edible plant species in Ilaly, puha was recognized as a third richest herbal reservoir of low-molecular-weight anti-oxidants (Pieroni et al., 2002). Another pharmacological analysis performed by (Yin et al., 2007) depicted that anti-oxidant characteristics of *Sonchus oleraceus* are attributed to numerous phenolic compounds present in leaves. Also, 70% methanolic extract of leaves was most potent and suitable mixture from which antioxidants and other phytoconstituents can be separated effectively (Yin et al., 2007). In a recent investigation performed on mice in 2018, the plant's nephroprotective properties were analyzed in ischemia induced in 45 minutes with nephrotic pedicle occlusion,

subsequently leading to a recovery duration of 15 hours. The findings suggested that ischemic mice treated with *Sonchus oleraceus* extract at 300mg/kg exhibited noteworthy reduction in levels of malondialdehyde (MDA), blood-urea nitrogen (BUN), creatinine, IL-1β, IL-6 and TNF-α. Furthermore, histopathological analysis elicited ameliorated renal injuries in extract-treated group of mice (Torres-González et al., 2018).

GASTRIC DISEASES AND MEDICINAL PLANTS

Among the gastric disorders, peptic ulcer disease, gastric carcinoma and gastro-intestinal reflex disease (GERD) have been a prime threat to world populations for the past half-century (Javadzadeh & Hamedeyaz, 2014). It has caused high morbidness and considerable mortality (Rauws, 1993). There is a disparity in the etiology of peptic ulcer disease and shielding factors (bicarbonate, prostaglandin, mucin, NO, a few aggressive agents, and various other growth factors (Shahid et al., 2018). Procurement and prevalence of acid-related diseases are attainable by increasing gastric pH levels and enhancing mucosal preservation (Amandeep et al., 2012).

Numerous environmental and genetic factors also contribute to the induction and progression of GI disorders such as sedentary lifestyle, diet (excess alcohol intake, spicy food, unhygienic snacks, etc.), smoking, drugs (e.g. NSAIDS), vulnerability to numerous bacterial infections, unprotected sex, emotional distress, and psychological factors (Brooks, 1985). *Helicobacter (H.) pylori* is also one of the paramount factors and increases GI susceptibility to peptic ulcer disorder (Schmeda-Hirschmann & Yesilada, 2005). So, the main therapeutic goal regarding the treatment of peptic ulcer is the elimination of *H. pylori* from the Gastric cavity (Shipa et al., 2022). Before the *H. pylori* bacteria had been detected causing inflammation in the stomach, acid secretion increased leading to the damaged gastric mucosa (Geetha & Saranya, 2012). For treatment purposes, anti-microbial drugs such as amoxicillin, metronidazole, clarithromycin, and tetracycline; proton pump inhibitors (PPI) also inhibit the H^+, K^+, ATPase pump e.g. omeprazole, esomeprazole, lansoprazole, etc; H_2 receptor antagonists including ranitidine, cimetidine, famotidine, etc and bismuth salt is suggested for damaging the bacterial cell wall (Mota et al., 2009). Though humans have used herbal medicines since ancient times, even after the development of occidental medicine, herbal medicine is still a crucial requirement for ideal public management (Demir et al., 2009). Many plants have been reported in the literature for having gastroprotective effects (Table 2).

Aegle marmelos

It is usually known as the Bael tree is an average-sized tree of tropical and sub-tropical regions (Kothari et al., 2011). Some parts of this plant have therapeutic potential to treat gastric issues such as dysentery, diarrhea, dyspepsia, and diabetes mellitus (Das & Roy, 2012.). According to previous studies, different parts of *Aegle (A.) marmelos* have the potential for numerous therapeutic characteristics like anti-pyretic, anti-fungal, anti-viral, anti-bacterial, anti-malarial, anti-inflammatory, anti-hyperlipidemic and radioprotective effects (Rana et al., 1997). For instance, the 50% ethanolic root extract depicted dose-dependent action against ulcer in various acute and chronic gastric ulcer models in rats (Verma, 2010). The extract remarkably decreased the severity index of ulcers by notably reducing superoxide dismutase, and lipid peroxidation, and elevating the catalase activities. Phytochemical analysis of *A. marmelos* exhibited promising results for saponins, terpenoids, steroids, alkaloids, tannins and flavonoids (Kim et al., 2015).

Withania somnifera

Commonly known as Dunal or Ashwagandha; has been commonly used as a domestic remedy for various diseases (Singh et al., 2011). It is a nutritional supplement comprised of a variety of nutrients that retains anti-inflammatory, sedatives, anti-oxidant, anti-microbial, anti-hepatotoxic, anti-stress, anti-tumor, and anti-diabetic potential with rejuvenating characteristics (Umadevi et al., 2012). *Withania* (*W.) somifera* also ameliorates the damage and inflammation caused by scorpion stings and snake bites and also relieves the symptoms of conjunctivitis, epilepsy, leprosy, senile dementia, insomnia, Parkinson's disease, rheumatism, GERD, gastric ulcer, dyspepsia, and gynecological disorders (Singh et al., 2011). Previous research suggested that two chief phytoconstituents Withaferin A and Withanolide could inhibit the *H. pylori*-induced production of biomarkers such as IL-1β in dendritic cells and can be used as advanced preventive and therapeutic agents in ailments such as peptic carcinoma (Hannan et al., 2012).

Asparagus racemosus

It is an undershrub wrapped with spines and contains various succulent tuberous roots bearing short rootstocks (Sairam et al., 2003). It is collected from numerous tropical and sub-tropical regions such as Africa, Asia, India, Australia etc. The medicinal uses of several parts of *Asparagus racemosus* have been reported in the traditional medicinal system of the mentioned regions as an indigenous medicinal herb (Goyal & Sairam, 2002). The unique combination of phytoconstituents in this plant can be used for its diuretic, anodyne, cardioprotective, adaptogenic, aphrodisiac, and galactagogue effects (Nwafor et al., 2000). Particularly, exploring its gastro-protective and neuroprotective potential, the plant has depicted promising results in the management of peptic ulcer, dysentery, diarrhea, rheumatism, drug or narcotic withdrawal syndrome, neurodegenerative disorders, and nervous breakdowns due to its potent anti-oxidant and immunostimulant effects (Bopana & Saxena 2007). According to previous research, the plant has primarily shown its phytoestrogen properties and ameliorates premenstrual and menopausal symptoms (Nwafor & Okwuasaba, 2003). In some other studies, the extract of plant root was tested for its anti-tumor effect, which was significant, since it enhanced the levels of several factors responsible for protecting mucus such as cellular life span, has elicited the noteworthy antioxidant effect without stimulating pepsin and acid secretion thus leading to melioration of peptic carcinoma. Another species of *Asparagus* genus known as *Asparagus pubescens* which is an evergreen herb, has been acknowledged widely for its therapeutic effects (anti-inflammatory and analgesic) in the

Table 2. Gastroprotective effects of various medicinal plants

Botanical name	Part used	Active constituents	Pharmacological effects	References
Aegle marmelos	Methanolic extract of unripe fruit, fruit juice with mucilages	Alloimperatorin, imperation, methyl ether, marmin, marmelide, marmesin, umbeliferone, skimmianine, umbelliferine, scoporone, armelide, xanthotoxol, scopoletin, psoralen	Decrease the intestinal propulsion, suppress oxidative stress, and restore the levels of mucosal thickness, catalase activity, superoxide dismutase, and glutathione levels.	Rao et al., 2003
Withania somnifera	Root powder, leaves extract, methanolic extract of whole powder plant	Withaferin-A	Inhibit *H. pylori*-induced production of IL-1β in dendritic cells,	Sabina et al., 2009
Asparagus racemosus	Root powder	Vitamins (A, B1, B2, C, and E), folic acid, essential fatty acid, gamma linileinic acid, diosgenin, arginine, tyrosine, quercetin 3-glucuronides, Kaepfrol, Sarsapogeni, etc.	Immunostimulants, and antiulcer, restore levels of lipid peroxidation and reduce oxidative stress	Shameem & Majeedi, 2020
Ficus religiosa	Ethanolic extract of stem bark, hydroalcoholic extract leaves	Friedelin, lupeol, quercetin-3-galactoside, leucodelphinidin, gallocatechin, leucopelargonidin-3-O-β-D-glucopyranoside, α-cadinol, α-eudesmol, β-eudesmol, β-sitosterol, stigmasterol, β-sitosterol-d-glucoside	Anti-secretary and cytoprotective properties, anti-cancer effects	Murugesu et al., 2021
Benincasa hispida	Methanolic extract of seeds and fruit	Triterpenes, tannins, proteins	Free radical scavenging, normalizing catalase and MDA levels	Majeed et al., 2015

treatment of common GI disorders [gastritis, diarrhea, GERD, etc. (Singh et al., 2011)].

Ficus religiosa

Commonly known as Bodhi or Peepal tree, is found excessively in the Sub-continent of Asia in regions of Pakistan, Bengal, central India, and some areas of China. Over the centuries, it has been used frequently as indigenous medicine for many infectious diseases and disorders associated with the GI tract, endocrine system, and central Nervous System (Saha & Goswami, 2010). For instance, it has been commonly prescribed by herbalists and traditional medicinal practitioners for the management of asthma, inflammation, diabetes, gastric ailments, duodenal ulcers, and sexual disorders (Abhilash et al., 2014). Results reported from past pharmacological investigations held to explore the therapeutic potential of its bioactive metabolites suggested its promising potential against neuroinflammation, neuropsychiatric, stress-related disorders, and antimicrobial infections (especially affecting intestinal flora). In another lab investigation involving rats, several parts of *Ficus religiosa* showed significant results regarding gastro-protective effects due to its cytoprotective characteristics and anti-secretory effect (Thorat et al., 2013).

Benincasa hispida

It is a renowned member of Cucurbitaceae family, and is vastly used for its therapeutic effects in case of hepatic diseases, fever, renal dysfunction and neural diseases (Al-Snafi, 2013). In a lab trial, albino rats were induced with gastric ulcers by ethanol administration, and methanolic extract of *Benincasa hispida* fruit was administered to them in combination with petroleum ether to investigate their gastroprotective properties (Grover et al., 2001). The outcomes of this study elicited the significant contribution of this extract in restoring the catalase and malondialdehyde (MDA) levels by suppressing the pathway of lipid peroxidation. Hence, the anti-ulcer activity of this plant can be attributed to its free radical scavenging action (Rachchh & Jain, 2008). A further dose-dependent study conducted by (Gill et al., 2011) has depicted the anti-ulcer and antioxidant effect of methanolic extract of plant seeds in ulcerous rats. The extract remarkably ameliorated the ulcer stage by lowering the total acidity, ulcer index and gastric residual volume. Albeit, the intensity of gastroprotective activity at 300mg/kg dose was in concordance with the therapeutic dose of popular WHO approved anti-ulcer agent ranitidine (Gill et al., 2011). Phytochemical investigations had demonstrated the existence of tannins, carbohydrates, triterpenes, amino acids and proteins in plant extract were the cause of its potent antioxidant and gastroprotective effects (Majeed et al., 2015).

CONCLUSION

A comprehensive assessment of the gastroprotective and nephroprotective properties of the herbal plants included above has been discussed. Since the kidney and gastric organs are some of the few most important organs of the human body, without their proper functioning, survival is not possible. The disorders related to these organs are treated with these herbal plants and their formulations in traditional medical systems. For the treatment of acute and chronic disorders, herbal therapies are beneficial despite the vast amount of accessible knowledge and availability of occidental medicines. It is necessary to create potent formulations employing native herbal plants that are backed by relevant pharmacological research and clinical trials, as no one medication can treat all forms of ailments completely and Western medicine has certain unavoidable medicines.

REFERENCES

Moneim AEA, MS Othman & AM Aref, 2014. *Azadirachta indica* attenuates cisplatin-induced nephrotoxicity and oxidative stress. BioMed Research International 2014:647131. https://doi.org/10.1155/2014/647131

Abhilash G, YJ Maheswari, A Gopal et al., 2014. Review on some medicinal plants with hepato-protective activities. Research Journal of Pharmacognosy and Phytochemistry 22:33.

Al-Snafi AE, 2016. The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia* - A review. IOSR Journal of Pharmacy 6:64-75.

Alzohairy MA, 2016. Therapeutics role of *Azadirachta indica* (Neem) and their active constituents in diseases prevention and treatment. Evidence-Based Complementary and Alternative Medicine 2016:7382506. https://doi.org/10.1155/2016/7382506

Amandeep K, S Robin, S Ramica et al., 2012. Peptic ulcer: A review on etiology and pathogenesis. International Research Journal of Pharmacy 3:34-8.

Ameen AA, EF El-Haggar & GG Mohamed, 2023. Contemplation impact of pulp seeds *Cucurbita Pepo* L. and its paste on oxidative stress in rats. Journal of Advanced Zoology 44.477

Arany I, GP Kaushal, D Portilla et al., 2008. Cellular mechanisms of nephrotoxicity. In: Clinical Nephrotoxins: Renal Injury from Drugs and Chemicals (De Broe ME, GA Porter, WM Bennett & G Deray, eds): Springer, Boston, USA, pp. 155-70. https://doi.org/10.1007/978-0-387-84843-3_8

Barnett LM & BS Cummings, 2018. Nephrotoxicity and renal pathophysiology: a contemporary perspective. Toxicological Sciences 164:379-90. https://doi.org/10.1093/toxsci/kfy159

Bopana N & S Saxena, 2007. *Asparagus racemosus* - Ethnopharmacological evaluation and conservation needs. Journal of Ethnopharmacology 110:1-15. https://doi.org/10.1016/j.jep.2007.01.001

Brooks FP, 1985. The pathophysiology of peptic ulcer disease. Digestive Diseases and Sciences 30:15-29. https://doi.org/10.1007/BF01309381

Caili FU, S Huan & LI Quanhong, 2006. A review on pharmacological activities and utilization technologies of pumpkin. Plant Foods for Human Nutrition 61:70-7. https://doi.org/10.1007/s11130-006-0016-6

Campagne O, DE Mager, D Brazeau et al., 2019. The impact of tacrolimus exposure on extrarenal adverse effects in adult renal transplant recipients. British Journal of Clinical Pharmacology 85:516-29. https://doi.org/10.1111/bcp.13811

Coulson S, A Rao, SL Beck et al., 2013. A phase II randomised double-blind placebo-controlled clinical trial investigating the efficacy and safety of ProstateEZE Max: a herbal medicine preparation for the management of symptoms of benign prostatic hypertrophy. Complementary Therapies in Medicine 21:172-9. https://doi.org/10.1016/j.ctim.2013.01.007

Das SK & C Roy, 2012. The protective role of *Aegle marmelos* on aspirin-induced gastro-duodenal ulceration in albino rat model: a possible involvement of antioxidants. Saudi Journal of Gastroenterology 18:188-94. https://doi.org/10.4103/1319-3767.96452

Mota KSDL, GEN Dias, MEF Pinto et al., 2009. Flavonoids with gastroprotective activity. Molecules 14:979-1012. https://doi.org/10.3390/molecules14030979

Demir S, M Yılmaz, M Köseoğlu et al., 2009. Peptic ulcer disease. The Lancet 374:1449-61. https://doi.org/10.1016/S0140-6736(09)60938-7

Devi J & RB Sharma, 2023. Medicinal Importance of *Azadirachta indica*: An Overview. Journal of Drug Delivery and Therapeutics 13:159-65. https://doi.org/10.22270/jddt.v13i6.5992

Dwyer JT, PM Coates & MJ Smith, 2018. Dietary supplements: regulatory challenges and research resources. Nutrients 10:41. https://doi.org/10.3390/nu10010041

Edwin UW, MO Domnic & DR Norman, 2023. Restorative effects of *Azadicarachta indica* on the kidney histomorphometry in cisplatin treated Wister albino rats. Anatomy Journal of Africa 12:2448-54. https://doi.org/10.4314/aja.v12i2.13

Eneh FU, GC Ugochukwu & CM Okoye, 2018. Effect of ethanol extract of *Cucurbita pepo* leaves on the lipid profile of Wistar albino rats. Asian Journal of Research in Biochemistry 2:1-7. https://doi.org/10.9734/ajrb/2018/v2i4601

Geetha A & P Saranya, 2012. A study on the gastroprotective effect of *Andrographis paniculata* and andrographolide in rats subjected to pylorus ligation. Journal of Pharmacy Research 5:787-91.

Gill NS, K Dhiman, P Sharma et al., 2011. Evaluation of free radical scavenging and antiulcer potential of methanolic extract of *Benincasa hispida* seeds. Research Journal of Medicinal Plant 5:596-604. https://doi.org/10.3923/rjmp.2011.596.604

Gould KS, K Thodey, M Philpott et al., 2006. Antioxidant activities of extracts from traditional Maori food plants. New Zealand Journal of Botany 44:1-4. https://doi.org/10.1080/0028825X.2006.9513001

Goyal RK & K Sairam, 2002. Anti-ulcer drugs from indigenous sources with emphasis on *Musa sapientum*, Tamrabhasma, *Asparagus racemosus* and *Zingiber officinale*. Indian Journal of Pharmacology 34:100-10.

Grover JK, G Adiga, V Vats et al., 2001. Extracts of *Benincasa hispida* prevent development of experimental ulcers. Journal of Ethnopharmacology, 78:159-64. https://doi.org/10.1016/S0378-8741(01)00334-8

Hannan JMA, L Ali, J Khaleque et al., 2012. Antihyperglycaemic activity of *Asparagus racemosus* roots is partly mediated by inhibition of carbohydrate digestion and absorption, and enhancement of cellular insulin action. British Journal of Nutrition 107:1316-23. https://doi.org/10.1017/S0007114511004284

Haque S, 2013. Kidney failure and its management with dialysis and nephroprotective herbal drugs. Indian Journal of Canine Practice Volume 5:10.

Hoitsma AJ, JF Wetzels & RA Koene, 1991. Drug-induced nephrotoxicity: aetiology, clinical features and management. Drug Safety 6:131-47. https://doi.org/10.2165/00002018-199106020-00004

Janda K, I Gutowska, M Geszke-Moritz et al., 2021. The common cichory (*Cichorium intybus* L.) as a source of extracts with health-promoting properties-a review. Molecules 26:1814. https://doi.org/10.3390/molecules26061814

Javadzadeh Y & S Hamedeyaz, 2014. Floating drug delivery systems for eradication of helicobacter pylori in treatment of peptic ulcer disease. Trends in Helicobacter pylori Infection 1:13. https://doi.org/10.5772/57353

Javed G, R Javaid & F Ahmed, 2020. Kasni (Cichorium intybus): a Unani hepatoprotective drug. Journal of Drug Delivery and Therapeutics 10:238-241. https://doi.org/10.22270/jddt.v10i4.4162

Kanj D, K Raafat, A El-Lakany et al., 2019. Phytochemical compounds of Cichorium intybus by exploring its antioxidant and antidiabetic activities. Pharmacognosy Journal 11:248-57. https://doi.org/10.5530/pj.2019.11.39

Kesari AN, RK Gupta, SK Singh et al., 2006. Hypoglycemic and antihyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats. Journal of Ethnopharmacology 107:374-9. https://doi.org/10.1016/j.jep.2006.03.042

Kessler CS, A Morandi, A Kumar et al., 2019. Reliability of ayurvedic diagnosis for knee osteoarthritis patients: a nested diagnostic study within a randomized controlled trial. The Journal of Alternative and Complementary Medicine 25:910-9. https://doi.org/10.1089/acm.2018.0273

Khaliq T, F Mumtaz, I Javed et al., 2015. Nephroprotective potential of *Rosa damascena* Mill flowers, *Cichorium intybus* Linn Roots and their mixtures on gentamicin-induced toxicity in albino rabbits. Pakistan Veterinary Journal 35:43-7.

Kim JE, JY Lee, MJ Kang et al., 2015. Withaferin A inhibits helicobacter pylori-induced production of IL-1β in dendritic cells by regulating NF-κB and NLRP3 inflammasome activation. Immune Network 15:269-77. https://doi.org/10.4110/in.2015.15.6.269

Kothari S, V Mishra, S Bharat et al., 2011. Antimicrobial activity and phytochemical screening of serial extracts from leaves of *Aegle marmelos* (Linn.). Acta Poloniae Pharmaceutica 68:687-92.

Kpemissi M, K Eklu-Gadegbeku, VP Veerapur et al., 2019. Nephroprotective activity of *Combretum micranthum* G. Don in cisplatin induced nephrotoxicity in rats: In-vitro, in-vivo and in-silico experiments. Biomedicine and Pharmacotherapy 116:108961. https://doi.org/10.1016/j.biopha.2019.108961

Lin Z, B Zhang, X Liu et al., 2014. Effects of chicory insulin on serum metabolites of uric acid, lipids, glucose, and abdominal fat deposition in quails induced by purine-rich diets. Journal of Medicinal Food 17:1214-21. https://doi.org/10.1089/jmf.2013.2991

Mai W, A Wei, X Lin et al., 2021. Efficacy and safety of traditional Chinese medicine injection with mecobalamin in treating diabetic peripheral neuropathy: A protocol for systematic review and meta-analysis. Medicine 100:e23702. https://doi.org/10.1097/MD.0000000000023702

Majeed W, T Khaliq, B Aslam et al., 2015. Medicinal plants with gastroprotective potential. Bangladesh Journal of Pharmacology 10:588-603. https://doi.org/10.3329/bjp.v10i3.23578

Verma M, 2010. Investigation on antiulcer activity of Aegle marmelos root as experimental, biochemical and histological study. Journal of Pharmacy Research 3:2523-28.

Misurac JM, CA Knoderer, JD Leiser et al., 2013. Nonsteroidal anti-inflammatory drugs are an important cause of acute kidney injury in children. The Journal of Pediatrics 162:1153-9. https://doi.org/10.1016/j.jpeds.2012.11.069

Murugesu S, J Selamat & V Perumal, 2021. Phytochemistry, pharmacological properties, and recent applications of *Ficus benghalensis* and *Ficus religiosa*. Plants 10:2749. https://doi.org/10.3390/plants10122749

Negi K & A Mirza, 2020. Nephroprotective and therapeutic potential of traditional medicinal plants in renal diseases. Journal of Drug Research in Ayurvedic Sciences 5:175-83. https://doi.org/10.5005/jdras-10059-0079

Nwafor PA & FK Okwuasaba, 2003. Anti-nociceptive and anti-inflammatory effects of methanolic extract of *Asparagus pubescens* root in rodents. Journal of Ethnopharmacology 84:125-9. https://doi.org/10.1016/S0378-8741(02)00213-1

Nwafor PA, FK Okwuasaba & LG Binda, 2000. Antidiarrhoeal and antiulcerogenic effects of methanolic extract of Asparagus pubescens root in rats. Journal of Ethnopharmacology 72:421-7. https://doi.org/10.1016/S0378-8741(00)00261-0

Oketch-Rabah HA, AL Roe, CV Rider et al., 2020. United States Pharmacopeia (USP) comprehensive review of the hepatotoxicity of green tea extracts. Toxicology reports 7:386-402. https://doi.org/10.1016/j.toxrep.2020.02.008

Pan SY, G Litscher, SH Gao et al., 2014. Historical perspective of traditional indigenous medical practices: the current renaissance and conservation of herbal resources. Evidence-Based Complementary and Alternative Medicine 2014:525340. https://doi.org/10.1155/2014/525340

Peterson CT, K Denniston & D Chopra, 2017. Therapeutic uses of triphala in ayurvedic medicine. The Journal of Alternative and Complementary Medicine 23:607-14. https://doi.org/10.1089/acm.2017.0083

Pfister B, J Jonsson & M Gustafsson, 2017. Drug-related problems and medication reviews among old people with dementia. BMC Pharmacology and Toxicology 18:1-11. https://doi.org/10.1186/s40360-017-0157-2

Pieroni A, V Janiak, CM Dürr et al., 2002. In vitro antioxidant activity of non-cultivated vegetables of ethnic Albanians in southern Italy. Phytotherapy Research 16:467-73. https://doi.org/10.1002/ptr.1243

Rachchh MA & SM Jain SM, 2008. Gastroprotective effect of *Benincasa hispida* fruit extract. Indian Journal of Pharmacology 40:271-5. https://doi.org/10.4103/0253-7613.45154

Rahmani A, A Almatroudi, F Alrumaihi et al., 2018. Pharmacological and therapeutic potential of neem (*Azadirachta indica*). Pharmacognosy Reviews 12:250-5. https://doi.org/10.4103/phrev.phrev_8_18

Rana BK, UP Singh & V Taneja, 1997. Antifungal activity and kinetics of inhibition by essential oil isolated from leaves of *Aegle marmelos*. Journal of Ethnopharmacology 57:29-34. https://doi.org/10.1016/S0378-8741(97)00044-5

Rao C, R Amresh, A Irfan et al., 2003. Protective effect of Aegle marmelos fruit in gastrointestinal dysfunction in rats. Pharmaceutical Biology 41:558-63. https://doi.org/10.1080/13880200390501190

Rastogi S, 2021. Emanating the specialty clinical practices in Ayurveda: Preliminary observations from an arthritis clinic and its implications. Journal of Ayurveda and Integrative Medicine 12:52-7. https://doi.org/10.1016/j.jaim.2019.09.009

Sabina E, S Chandel & MK Rasool, 2009. Evaluation of analgesic, antipyretic and ulcerogenic effect of Withaferin A. International Journal of Integrative Biology, 6:52-6.

Saha S & G Goswami, 2010. Study of anti ulcer activity of *Ficus religiosa* L. on experimentally induced gastric ulcers in rats. Asian Pacific Journal of Tropical Medicine 3:791-3. https://doi.org/10.1016/S1995-7645(10)60189-7

Sairam K, S Priyambada, NC Aryya et al., 2003. Gastroduodenal ulcer protective activity of *Asparagus racemosus*: an experimental, biochemical and histological study. Journal of Ethnopharmacology 86:1-10. https://doi.org/10.1016/S0378-8741(02)00342-2

Schmeda-Hirschmann G & E Yesilada, 2005. Traditional medicine and gastroprotective crude drugs. Journal of Ethnopharmacology 100:61-6. https://doi.org/10.1016/j.jep.2005.06.002

Seriana I, M Akmal, D Darusman et al., 2021. Neem leaf (*Azadirachta indica* A. Juss) ethanolic extract on the liver and kidney function of rats. The Scientific World Journal 2021:7970424. https://doi.org/10.1155/2021/7970424

Shabbir S, P Boruah, MFEA Kulyar et al., 2023. Nephroprotective effect of *Cinnamon cassia* and *Azadirachta indica* on titanium dioxide nanoparticles. Current Nanoscience 19:291-303. https://doi.org/10.2174/1573413718666220816084532

Shahid F, Z Farooqui & F Khan, 2018. Cisplatin-induced gastrointestinal toxicity: An update on possible mechanisms and on available gastroprotective strategies. European Journal of Pharmacology 827:49-57. https://doi.org/10.1016/j.ejphar.2018.03.009

Shameem I & SF Majeedi, 2020. A review on potential properties and therapeutic application of *Asparagus racemosus* wild. World Journal of Pharmceutical Research 9:2532-40.

Shipa SJ, L Khandokar, MS Bari et al., 2022. An insight into the anti-ulcerogenic potentials of medicinal herbs and their bioactive metabolites. Journal of Ethnopharmacology 293:115245. https://doi.org/10.1016/j.jep.2022.115245

Singh N, M Bhalla, P de Jager et al., 2011. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. African Journal of Traditional, Complementary and Alternative Medicines 8:208-13. https://doi.org/10.4314/ajtcam.v8i5S.9

Sujana D, NM Saptarini, SA Sumiwi et al., 2021. Nephroprotective activity of medicinal plants: A review on in silico-, in vitro-, and in vivo-based studies. Journal of Applied Pharmaceutical Science 11:113-27. https://doi.org/10.7324/JAPS.2021.1101016

Tahir M, N Sadiq, S Ahmed et a., 2018. Effects of aqueous and methanolic extracts of *Cichorium Intybus* seeds on gentamicin induced nephrotoxicity in rats. Journal of Islamic International Medical College 13:184-8.

Talele BD, RT Mahajan, MZ Chopda et al., 2012. Nephroprotective plants: a review. International Journal of Pharmacy and Pharmaceutical Science 4:8-16.

Thorat S, D Deshmukh, D Gaikwad et al., 2013. Anti-ulcer effect on the ethanol extract of the bark and root of *Ficus religoisa* linn. In different experimental ulcer models in rats. International Journal of Pharmaceutical Sciences and Research 4:1120.

Tienda-Vázquez MA, ZP Morreeuw, JE Sosa-Hernández et al., 2022. Nephroprotective plants: a review on the use in pre-renal and post-renal diseases. Plants 11:818. https://doi.org/10.3390/plants11060818

Tine Y, M Sene, C Gaye et al., 2024. *Combretum micranthum* G. Don (Combretaceae): A review on traditional uses, phytochemistry, pharmacology and toxicology. Chemistry and Biodiversity 21:e202301606. https://doi.org/10.1002/cbdv.202301606

Torres-González L, E Cienfuegos-Pecina, MM Perales-Quintana et al., 2018. Nephroprotective effect of *Sonchus oleraceus* extract against kidney injury induced by ischemia-reperfusion in wistar rats. Oxidative Medicine and Cellular Longevity 2018:9572803. https://doi.org/10.1155/2018/9572803

Umadevi M, R Rajeswari, CS Rahale et al., 2012. Traditional and medicinal uses of *Withania somnifera*. The Pharma Innovation 1:102.

Wang DC, H Xiang, D Li et al., 2008. Purine-containing cucurbitane triterpenoids from *Cucurbita pepo* cv dayangua. Phytochemistry 69:1434-8. https://doi.org/10.1016/j.phytochem.2008.01.019

Whyte R, JA Hudson, S Hasell et al., 2001. Traditional Maori food preparation methods and food safety. International Journal of Food Microbiology 69:183-90. https://doi.org/10.1016/S0168-1605(01)00547-5

Yin J, GJ Kwon & MH Wang, 2007. The antioxidant and cytotoxic activities of *Sonchus oleraceus* L. extracts. Nutrition Research and Practice 1:189-94. https://doi.org/10.4162/nrp.2007.1.3.189

Yoo S, K Kim, H Nam et al., 2018. Discovering health benefits of phytochemicals with integrated analysis of the molecular network, chemical properties and ethnopharmacological evidence. Nutrients 10:1042. https://doi.org/10.3390/nu10081042

Zaman R, A Alam, MA Jafri et al., 2017. Nephroprotective effect of beekh kasni (roots of *Cichorium intybus*) in the form of methanolic and aqueous extract in Gentamycin induced rat models. Journal of Pharmacognosy and Phytochemistry 6:337-41.