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Review Article

A REVIEW ON PHYTOCONSTITUENTS FOR NEPHROPROTECTIVE ACTIVITY

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ABSTRACT

Kidney harm is most vital health issues and lots of herbal medicines are involved in case of kidney injury. World health organization (WHO) estimate that eightieth of total population used herbal drugs for some characteristic of primary health care while not any facet effects. Herbal medicine has emerged as a skilled approach with sensible values in handling various diseases and developing an affordable phytotherapy to treat severe kidney diseases. The use of herbs as nephroprotective is a major avenue in Indian perspectives particularly for treating kidneys damage, which require to be explored more successfully as there are many literatures available on these aspects. The current review is aimed toward collecting information on promising active phytoconstituents like alkaloids, benzoquinones, catechols, carotenoids, flavonoids, glycosides, flavonol glycosides, steroid glycosides, glycoalkaloids, terpenoids, monoterpenoids, diterpenoids, triterpene saponins, sterols and polyphenols from medicinal plants that are tested in nephroprotective models exploitation fashionable scientific system.

Keywords: Kidney, Nephrotoxic, Nephroprotective, Medicinal plants, Phytoconstituents.

INTRODUCTION

The incidence of kidney failure or chronic kidney failure has doubled over the last 15 years. It is estimated that currently, there are over one million people worldwide who are alive on dialysis or with a functioning graft. Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin (Porter *et al.*, 1981). The crisis of kidney shortage is a global phenomenon and it is worst in Asian countries (Surekha *et al.*, 2010). Kidney disease is the ninth leading cause of death. Approximately, 19 million adults have chronic kidney disease and an estimated 80,000 persons have chronic kidney failure diagnosed annually in India. Till date for end stage renal failure, renal replacement is the only therapy. In case, of non-availability of kidney, dialysis is the only alternative, which unfortunately is severely limited by several constraints including a good amount of expenditure. A number of potent therapeutic drugs like aminoglycoside antibiotics, NSAID's, chemotherapeutic agents and chemical reagents like ethylene glycol, carbon tetrachloride, sodium oxalate and heavy metals such as lead, mercury, cadmium and arsenic can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome, rapid decline in renal function resulting in abnormal retention of serum creatinine and blood urea, which must be excreted. According to WHO survey 80% of the population living in the developing countries relies almost exclusively on traditional medicine for their primary health care needs. The chemical constituents obtained from plants may be

pharmacological screened for developing novel agents. Phytochemicals are compounds found in plants that are not required for normal functioning of the body, but have a beneficial effect on health or play an active role in amelioration of diseases (Cordeiro *et al.*, 2011). From different regions, varied plant species having potent nephroprotective activity area unit portrayed at intervals the subsequent section. This review highlights on the chemo profiles from totally different regions of world for treating excretory organ diseases with major thrust on their active constituents.

Nephroprotective Phytoconstituents from Different Medicinal Plants

Aerva lanata

Aerva lanata (Linn.) belongs to the Amaranthaceae. Plant is prostate to decumbent, generally erect herb, 30-60 cm tall, wooly, tomentose throughout. It is distributed throughout Tropical India as a common weed in fields and is additionally found in Africa, Sri Lanka and Philippines. In traditional system of medicine, it is used as diuretic and anthelmintic, expectorant and in the treatment of pathology. The leaves of *Aerva lanata* are used as sap for eye-complaints; an infusion is given to cure diarrhea and kidney stone; and also the root is employed in snake bite treatment (Juss 2011). The foremost important bioactive a compounds of the plant includes alkaloids, flavonoids, tannins and phenolic compounds. The plant is employed for arresting hemorrhage during pregnancy, burn healing, as an anti-inflammatory, headache, skin diseases, to dissolve kidney and gall bladder stones, for uterus clearance after delivery and to forestall lactation (Anita *et al.*, 2013). The ethanolic extract of *Aerva lanata* possesses marked nephroprotective activity with stripped toxicity because of the flavonol glycoside like kaempferol-3-rhamnoside & kaempferol-3-rhamnogalactoside which supplied a promising role within the treatment of acute nephritic injury caused by nephrotoxins like cisplatin and antibiotics (Shirwaikar *et al.*, 2004) was cited in table 1 and table 2.

Andrographis paniculata

Andrographis paniculata belongs to the family Acanthaceae, is a tracheophyte ordinarily referred to as 'King of bitters', and is wide cultivated in Southern Asia. Most leaves and roots are historically used over the centuries for various medicinal purposes in Asia and Europe as folklore remedy for wide spectrum of ailment or as herbal supplement for treatment of common cold. It is a rich source of diterpenoids and 2'-oxygenated flavonoids as well as andrographolide, neoandrographolide and stigmasterol. Extensive research has revealed that it has a broad range of pharmacological activities like anti-tumor, anti-inflammatory, anti-viral, anti-diarrhoeal, anti-malarial, hepatoprotective, cardiovascular and immunostimulatory activities (Jarukamjorn & Nemoto 2008). The protective effect of chloroform extract of *Andrographis paniculata* against nephrotoxicity because of diterpenoid like Andrographidoids (Rao, 2006) was specified in table 1 and 2.

Artemisia annua

Artemisia annua (Asteraceae) is native to China, where it is referred to as qinghao (green herb) and has been used for over a period of 500 years to treat symptoms related to fever and protozoal infection. In China, it was traditionally used to treat fever and hemorrhoids. It is conjointly utilized in the crafting of aromatic wreaths, as a flavoring for spirits like vermouth, and as essential oil for the fragrance business. Sweet wormwood is that the main supply of artemisinin, a crucial natural sesquiterpene lactone with antiprotozoal drug impact against inclined and multi-drug resistant plasmodium species. Sweet wormwood leaves (Zheng and Wang, 2001) and crude extracts are a good supply of antioxidants (Cai *et al.*, 2004). This high antioxidant capability is perhaps due to the high content (Bilia *et al.*, 2006) and variety of its leaf flavonoids, together with the recently reported C-glycosyl flavonoids as possible component of the antioxidant and antiviral activity (Han *et al.*, 2008). The nephroprotective effect of ethanol extract is due to the terpenoids like artemisia ketone, α-pinene, 1,8-cineole (Randjelovic et al., 2013) of *Artemisia annua L* (table 1 and 2).

Berberis vulgaris

Berberis vulgaris is a woody plant of Berberidaceae family, native to central and southern Europe, northwest continent and western Asia. It is been used extensively as a medicative plant in ancient drugs. It contains organic acids and phenol compounds that contain anthocyanin and antioxidant pigments as well as phenolase, polyphenolase and glycosidase enzymes. Berbamin is an iso-kinolin alkaloid and exists in bark of its root, which is a strong antioxidant and is helpful in treating fibrosis caused by anti-cancer medicines like bleomycin (Minaiya *et al*., 2011). Pharmacologic properties embrace tonic, antimicrobial, antiemetic, antipyretic, antipruritic and cholagogue actions and it has been used in some cases like cholecystitis, cholelithiasis, jaundice, dysentery, leishmaniasis, malaria and gall stones (Javadzadeh *et al*., 2012). Berberine, an alkaloid is one of the active principles in *Berberis vulgaris* possessing the nephroprotective activity (Jyothilakshmi *et al.*, 2013), was stated in table 1 and 2.

Camellia sinensis

The tea plant, *Camellia sinensis*, is a member of the Theaceae family, and black, oolong, and green tea are produced from its leaves. Chinese *Camellia sinensis* is native to mainland china, south and southeast Asia, however it is nowadays cultivated across the planet in tropical and subtropical areas especially green tea. The chemical constituents found in tea are flavanols or catechins. The main catechins in green tea are epicatechin, epicatechin-3-gallate, epigallocatechin, and epigallocatechin-3-gallate. They are demonstrated to possess vital antioxidant, anticarcinogenic, anti-inflammatory, thermogenic, probiotic, and antimicrobial properties in various human, animal, and in vitro studies (Namita *et al.*, 2012). The protective effect of catechins against nephrotoxicity (Bhattacharya *et al.*, 2013) was mentioned in table 1 and 2.

Cassia auriculata

Cassia auriculata Linn. commonly called tanner's cassia, belongs to the family Fabaceae. It is a common plant in Asia, profoundly employed in Ayurvedic medicine as a tonic, astringent and as a remedy for diabetes, conjunctivitis and ophthalmia (Joy *et al.*, 2012). It contains chemical constituents like fatty acid esters, fatty acid amide, triterpene, diterpene alcohols and phytol in the leaf part, terpenoids, tannin, flavanouds, saponin, cardiac glycosides and steroids within the flower and Grape seed oil, n-Hexadecanoic acid, 9-Octadecenoic acid, (E)-, E, Z 1, 3, 12-Nonadecatriene , stearic acid in its seeds(Raj *et al.*, 2012). The shrub is extremely popular for its attractive yellow flowers which are used in the treatment of skin disorders and body odor. Its bark is used as an astringent, leaves and fruits as anthelminthic, seeds accustomed treat in eye troubles and roots are utilized in skin diseases (Sushma *et al.*, 2012). Its pharmacologic activities embrace antidiabetic and anti-pyretic (Pari & Latha, 2002), hepatoprotective (Ganapathy *et al.*, 2011), bactericidal (Maneemegalai *et al.*, 2010), anti-oxidant (Kumaran *et al.*, 2007), and anthelmintic (Satish *et al.*, 2009). Quercetin and Rutin are the two flavonoids in *Cassia auriculata* (Annie *et al.*, 2005) that play a key role in nephroprotection (Table 1 & 2).

Ceratonia siliqua

Ceratonia siliqua belongs to the Leguminosae is an evergreen shrub or tree up to 10 m high, crown broad semi-spherical, thick trunk, brown rough bark and sturdy branches. It is a durable evergreen and thermophilic tree thriving in habitats with delicate Mediterranean climates. It grows well in warm temperate and semitropical areas, tolerates hot and humid coastal areas. Its chemical constituents embrace carob polyphenols, tanins etc. Tannins extracted from the pulp act as antidiarrhoetic. Ground pulp and seed endosperm are employed in the preparation of pharmaceutical product. Technical applications of carob bean gum include cosmetics, pharmaceuticals, film emulsions, paints, polishes, ceramics and adhesives (Konate *et al.*, 2007). Carob polyphenols are the important phytoconstituents in *Ceratonia siliqua* that shows defensive effect in nephrotoxicity (*Ben et al.*, 2011) was mentioned below table 1.

Cordyceps cicadae

Cordyceps cicadae is an Ascomycetes fungus belonging to the family Clavicipitacea. In nature, it is found solely at high altitudes on the himalayan plateau and is therefore difficult to harvest. Due to such difficulties, *Cordyceps* has always been one amongst the most expensive medicative 'herbs'. It has been used in ancient Chinese medicine ever since to treat kidney, lung, and heart ailments, male and female sexual dysfunction, fatigue, cancer, hiccups, and heavy injury, to relieve pain, and the symptoms of tuberculosis and hemorrhoids, to restore general health and appetite, and to promote longevity (Holliday & Wasser, 2005). The chemical constituents embody cordycepin (3'-deoxyadenosine) and its derivatives, ergosterol, polysaccharides, a glycoprotein and peptides containing α-amino isobutyric acid. Scientifically pharmacologic activities embrace anti-cancer, immunomodulatory, insecticidal, anti-microbial, hypolipidaemic, hypoglycemic, anti-arrhythmic, anti-hypolibidinism, anti-aging, neuroprotective and renoprotection (Paterson, 2008). A sterol called ergosterol is present in *Cordyceps cicadae* (Paterson, 2008) which is responsible for nephroprotective action (table 1 and 2).

Crocus sativus

Crocus sativus Linn. (Family: Iridaceae) is a flowering plant in the crocus family and is commonly known as saffron. It is widely used as spice and as a coloring and flavoring agent in the preparation of various foods and cosmetics. It is native to Iran and Greece. It is now cultivated largely in Southern Europe, Tibet and other countries. It is a grass like tuber plant with purple or lilac colored flowers. The stigmas of the plant are mainly used for its medicinal properties extensively in traditional medicine for various purposes, as an aphrodisiac, antispasmodic, expectorant, for treatment of stomach ailments, reducing stomachache and for relieving tension. Chemical studies on stigmas of *Crocus* reported that it possesses carotenoids like crocetin, its glycosidic forms are digentiobioside (crocin), gentiobioside, glucoside, gentioglucoside and diglucoside. Carotenoids, anthocyanins, flavonoids, vitamins are also found in it. Crocin is reported to have anti-carcinogenic activity, anti-oxidant activity, anti-tussive activity and anti-hyperlipidemic acivity (Bhargava, 2011). Crocin is a glycoside which plays a significant role in treatment of cisplatin-Induced acute renal failure (Naghizadeh *et al.*, 2010) was given below in table 1 and 2.

Curcuma longa

Curcuma longa, a perennial herb and member of the family Zingiberaceae (ginger) family, grows to a height of 3 to 5 feet and is cultivated extensively in Asia, India, China, and different countries with a tropical climate. Curcumin is that the principal curcuminoid of the popular Indian spice turmeric, which is a member of the ginger family. The other two curcuminoids are desmethoxycurcumin and bisdesmethoxycurcumin. The curcuminoids are polyphenols and are liable for the yellow color of turmeric. Dried *Curcuma longa* is the supply of the spice turmeric. Turmeric is employed extensively in foods for its flavor and color, still as having an extended tradition of use within the Chinese and ayurvedic systems of medication for the treatment of flatulence, jaundice, expelling difficulties, hematuria, hemorrhage, and colic. Curcumin has antioxidant, anti-inflammatory, antiviral and antifungal actions (Bush *et al.*, 2001). Scientific studies showed that curcumin exhibits nephroprotective action (Venkatesan *et al*., 2000), which was stated in table 1 and 2.

Nigella sativa

Nigella sativa belongs to the family Ranunculaceae is a little elegant herb, largely found and cultivated in Syrian Arab Republic, Lebanon, Israel and Southern Europe. Historically the seeds and its oil are employed in many diseases. The seeds are considered as bitter, appetizer, stimulant, diuretic, thermogenic, carminative, deodent, expectorant and purgative (Paarakh, 2010). Oil is a local anaesthetic. The foremost necessary active compounds are Thymoquinone, Thymohydroquinone, dithymoquinone, p-cymene, carvacrol, 4-terpinol, t-anethol, sesquiterpene longifolene and phenol (Aftab Ahmad *et al.*, 2013). It has a wide spectrum of its pharmacological actions that

embrace antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, gastroprotective, anti-oxidant properties (Nickavar *et al.*, 2003). Thymoquinone is one of the important phytoconstituents constituent in *Nigella sativa* that plays a major role in the treatment of gentamicin induced nephrotoxicity (Aftab Ahmad, 2013) which was cited in table 1 and 2.

Panax ginseng

Panax ginseng belongs to Araliaceae family and is found everywhere in East Asia and Russia. It is over-harvested in different areas of Asia. It is cultivated in Korea, China, and Japan for use as a medicinal herb. It is a shade-loving, deciduous perennial plant with five-fingered leaves, tiny white flowers and yellowish-brown roots (Ernst, 2010). Its chemical constituents embody triterpene glycosides, or saponins, usually called ginsenosides. Though ginseng has been employed by Asian cultures for thousands of years for conditions like fatigue, mental stress, blood sugar regulation, improving libido, and supporting longevity, modern clinical studies have targeted on the making use of of *ginseng* in cancer prevention, blood sugar regulation, fatigue, and immunomodulation in human health and disease (Yun, 2001). Ginsenosides Rh4 and Rk3 significantly abridged the cisplatin-induced nephrotoxicity (Aek *et al.*, 2006) was additionally mentioned in table 1 and 2.

Phoenix dactylifera

Date palm (*Phoenix dactylifera L.*) is a monocotyledon plant within the palm tree family and is one in all the oldest fruit crops fully grown within the arid regions of the Arabian Peninsula, North Africa, and the Middle East. Later they were also introduced to new production areas in Australia, India, Pakistan, Mexico, southern Africa, South America, and the United States. Dates are main income basis and staple food for local populations in many countries in which they are cultivated (Chao; Krueger 2007). Its medicine activities embody antiviral, antifungal, antioxidant, antihyperlidimic and hepatoprotective activity. These activities are as a result of the high contents of antioxidant in date fruit such as the coumaric acid and ferulic acid. It also contains flavonoids, sterols, procyanidins, carotenoids, anthocyanins, sugar (Ismail *et al.*, 2013). Quercetin is one of the active principles in date palm, which possess protective effects against thegentamicin-induced nephrotoxicity (Abdel-Raheem *et al.*, 2009) in rats is mentioned more in table 1 and 2.

Picrorhiza kurroa

Picrorhiza kurroa (family: Scrophulariaaceae) is a little perennial herb that grows in northwest India on the slopes of the Himalayas between 3000 and 5000 meters. It is found in Southeast Tibet, North Burma and West China. It is a very important herb in the traditional Ayurvedic system of medicine, and has been used to treat liver troubles and bronchial problems, dyspepsia, bilious fever, chronic dysentery, and scorpion sting. Kutkin is the active principal of *Picrorhiza kurroa* and is comprised of kutkoside and iridoid organic compound picrosides I, II, and III. Different known active constituents are apocynin, drosin, and nine cucurbitacin glycosides. It is scientifically evidenced to possess hepatoprotective, anticholestatic, antioxidant and immune-modulating activity (Yadav & Khandelwal, 2009). Kutkoside and Picroside are the active constituents in *Picrorhizakurroa* that are responsible for nephroprotective action (Yadav & Khandelwal, 2009), were cited in table 1 and 2.

Polyporus umbellatus

Polyporus umbellatus (family: Polyporaceae) is one of the commonly used and precious medicinal fungi, with sclerotia being widely used for many years as an anti-diuretic agent as well as an antidote in oriental countries, especially in China, Korea and Japan. In ancient medication, it was used to cure edema and had a high effect. It's mainly compositions contain phytosterol, polysaccharides, protein, etc. Phytosterols of *Polyporus umbellatus* include ergosterol, 22-tetren-3-one (ergone), ergosta-7, 22-dien-3-one, ergosta-7 and 22-dien-3-ol. It also contains some other compounds belonging to different classes of

natural products, such as long chain fatty acids, anthraquinones, nucleosides, etc. It polysaccharides has good effect to to anti-tumor, prevent radiation, help to cure rheumatism, edema, lung or stomach cancer, enhancing immune function, reducing transaminase, inhibition of virus replication, and repair of liver damage (Liu & Guom, 2009). Ergone exhibited a fine nephroprotective effect against aristolochic acid or adenine-induced nephrotoxicity in rats (Zhao, 2013), was indicated in table 1 and 2.

Ramulus mori

Ramulus mori (young twigs of mulberry tree L.) belongs to Moraceae is a fast-growing deciduous plant that grows under completely different climate like tropical, semitropic and temperate. Mulberry is valued for its foliage that constitutes the foremost important feed for silkworms. In ancient Chinese medicine it is used for the treatment of joint pain. Chemical constituents of this plant are stilbenes, cis-mulberrosideA, resveratrol and flavonoids like rutin, quercetin and morin. The pharmacological actions of this plant are found to be anti-inflammatory, potential analgesic activity and anti-rheumatoid activity (Zhang & Shi, 2010). Ethanolic extract of *Ramulus mori* showed nephroprotective effect because of active constituents like Rutin, Quercetin (Zhu *et al*., 2004), Morin (Wang *et al*., 2010) and mulberroside A (Wang *et al*., 2011), which were mentioned in table 1 and 2.

Satureja khuzestanica

Satureja khuzestanica is an endemic plant of Iran that is widely distributed in the Southern part of Iran (Jamzad Z, 1994). It is notable for its medical uses as analgesic and antiseptic in folk medication (Zargari, 1990). Carvacrol is that the major active constituent in genus *Satureja khozistanica*. The other vital constituents are myrcene, para-cymene, terpinene, linalool, 4-terpineol, eugenol and caryophyllene compounds. Pharmacological activities embrace antiviral (Abad *et al*., 1999), antinociceptive (Hajhashemi *et al*., 2000), anti-inflammatory (Amanlou *et al*., 2005), antibacterial (Yamasaki *et al*., 1998), antifungal (Azaz *et al*., 2002), antimicrobial (Amanlou *et al*., 2004), antispasmodic and antidiarrhea (Hajhashemi *et al*., 2002). Nephroprotective action of this plant is a result of monoterpenoid like Carvacrol in it (*Tavafi et al.*, 2011), which is mentioned in table 1 and 2.

Solanum xanthocarpum

Solanum xanthocarpum belongs to the family Solanaceae. It is an annual herbaceous plant comprising 90 genera and 2000-3000 species. In ancient systems of medicine, different parts like leaves, stem, flower, root, seeds of *Solanum xanthocarpum* or the plant as a whole are used (Singh & Singh, 2010). The reported chemical constituents are carpesterol, gluco alkaloid solanocarpine, solanine-S, solasodine, solasonine, stigmasterol, campesterol, cholesterol, sitosteryl-glucoside, solasurine. It also contains methyl ester of caffeic acid, isochlorogenic acid, neochlorogenic acid, chlorogenic acids (fruit), apigenin, sitosterol (flower), solanocarpine and amino acids (seeds); coumarins etc.. The drug of this plant is used as anti-asthmatic, hypoglycaemic, anti-inflammatory, antitumor, anti-tussive, antipyretic, antispasmodic, anti-histaminic, hypotensive and cytotoxic activity (Roshy Joseph *et al*., 2012). Ethanol, butanol and water extracts of *Solanum xanthocarpum* showed nephroprotective activity which is because of a glycoalkaloid called Solasodine (Patel *et al.*, 2012), which is cited in table 1 and 2.

Zingiber officinale

Ginger (*Zingiber officinale Roscoe*, Zingiberacae) is one amongst the vital medicinal plant that naturally occurs in several country like Asian country, China, South East Asia, West Indies, Mexico and other parts of the planet (Ghosh *et al*., 2011). The pungency of ginger is due to gingerol, an oily liquid consisting of homologous phenols, which is produced in the plant from phenylalanine, malonate and hexonate. The British Herbal Compendium reported its action as carminative, antiemetic, spasmolytic, peripheral circulatory stimulant and anti-inflammatory (Malhotra *et al*., 2003). Aqueous and ethanolic extracts of *Zingiber officinale* contains Gingerols, which showed protective effect against anticancer drug doxorubicin-induced acute nephrotoxicity (Ajith *et al.*, 2008), and was mentioned in table 1

and 2. Phytoconstituents and their structures were further mentioned in table 2.

Miscellaneous Phytoconstituents for Nephroprotective Activity

Ascorbic acid (Vitamin C)

Vitamin C is a vitamin, which means the human body does not store it. It is found in foods like citrus fruits, broccoli, and tomatoes. It is associate inhibitor that blocks a number of the harm caused by free radicals, substances that harm deoxyribonucleic acid. The build-up of free radicals over time could contribute to the aging method and therefore the development of health conditions like cancer, heart condition, and inflammatory disease (Davies *et al.*, 1991). Scientific studies discovered that Ascorbic acid is also found to have Nephroprotective activity (Huang *et al*., 2000).

Caffeic acid phenylethyl ester

Caffeic acid phenylethyl organic compound is a vigorous part of propolis from bee hives. It is better-known to own antimitogenic, anticarcinogenic, medicine, and immunomodulatory properties. It is a potent and specific inhibitor of nuclear transcription factor (NF-κB) activation (Sudina *et al*., 1993). Recent studies revealed that it also exhibits nephroprotective activity (Ozen *et al*., 2006).

Capsaicin

Capsaicin is that the ingredient found in numerous sorts of hot peppers, like cayenne peppers, that creates the peppers spicy hot. Once a chemical irritant capsaicin cream or ointment is employed on the skin (topical use), it helps relieve pain. If hot peppers are taken as dietary supplements, the chemical irritant could improve the digestion by increasing the organic process fluids within the abdomen associated by fighting microorganism that would cause an infection. It facilitates forestall cardiovascular disease. It also stimulates the circulatory system and lowers blood cholesterin levels. It additionally helps forestall natural action and hardening of arteries (atherosclerosis). It acts as associate inhibitor, protects the cells of the body from harm by harmful molecules referred to as free radicals. It obstructs microbial infections. It also strengthens respiratory organ tissues and facilitates to treat respiratory disorder (Nelson, 1919). Modern research showed that capsaicin is also proven to have nephroprotective activity (Shimeda *et al.*, 2005).

Desferoxamine

Deferoxamine (also referred to as desferrioxamine B, desferoxamine B, DFO-B, DFOA, DFB or desferal) is being a microorganism siderophore created by the action of bacteria *Actinomycetes*. Its medical applications as a chelating agent accustomed take away excess iron from the body (Miller *et al*., 1989). By removing excess iron, the agent reduces the injury done to varied organs and tissues, like the liver (Lee et al., 2007). This agent is additionally of times accustomed treat hemochromatosis, an illness of iron accumulation which will be either genetic or uninheritable. Deferoxamine has conjointly been utilized in the treatment of a patient with aceruloplasminemia (Miyajima *et al.*, 1997). Scientific research showed that Deferoxamine also has nephroprotective acivity (Kadikoylu *et al*., 2004).

DL-α- Lipoic acid

Lipoic acid (LA) is associate organosulfur compound derived from octanoic acid (Reljanovic *et al*., 1999). Lipoic acid is found in the majority of foods and slightly in kidney, heart, liver, spinach, broccoli, and yeast extract (Durrani *et al*., 2010). Lipoic acid is used in clinical trials like accelerate chronic wound healing (Alleva *et al*., 2005), reduce levels of asymmetric dimethylarginine (ADMA) in diabetic end-stage urinal disease patients on hemodialysis (Chang *et al*., 2007), prevent or slow the progression of Alzheimer's sickness (Holmquist *et al*., 2007), and reducing the inflammation (Zhang *et al.*, 2007). Studies showed that DL-α- Lipoic acid also has nephroprotective activity (Obrosova *et al.*, 2003).

Edarabone

Edarabone (3-methyl-1-phenyl-2-pyrazolin-5-one), a strong antioxidative radical scavenger, is that the exclusively drug presently out there in

clinical practice for the treatment of cerebral infarction (Satoh *et al.*, 2002). But, later on scientific studies manifested that it also possess nephroprotective activity (Satoh *et al.*, 2003).

Lupeol

Lupeol, a triterpene, is that the principal constituent found in edible vegetables and fruits such as white cabbage, pepper, cucumber, tomato, carrot, pea, bitter root, soy bean, ivy gourd, black tea, figs, strawberries red grapes, mulberries, date palm and guava. Lupeol has been found to possess a large vary of medicative properties that embrace conditions like inflammation, arthritis, diabetes, cardiovascular ailments, kidney disease, hepatic toxicity, microbial infections and cancer (Al-Rehaily *et al*., 2001; Fernández *et al*., 2001; Chaturvedi *et al*., 2008; Sudhahar *et al*., 2008). Scientific studies revealed that lupeol is a possessor of nephroprotective activity (Nagaraj *et al*., 2000).

Lycopene

Lycopene (from the Neo-Latin word Lycopersicum, touching on the tomato species) is a bright red carotene and carotenoid pigment and phytochemical found in tomatoes and other red fruits and vegetables, like red carrots, red bell peppers, watermelons and papayas. In line with one preliminary study, consumption tomato paste for 3 months decreases sun injury by U.V radiation by 30 minutes through the action of lycopene (Rizwan *et al*., 2011). Scientific research on lycopene showed that it also exhibits nephroprotective action (Atessahin *et al*., 2005).

Pyridoxamine

Pyridoxamine is a vitamer within the B-complex vitamin family, which incorporates B-complex vitamin and pyridoxamine (Roje, 2007). Pyridoxamine is transformed to the biologically active form of B-complex vitamin, B-complex vitamin 5-phosphate, through the B-complex vitamin salvage pathway. Pyridoxamine inhibits the Maillard reaction and can block the formation of advanced glycation endproducts, which are related to medical complications of diabetes (Ahmed *et al*., 2007). In alternative diagnosis analysis, pyridoxamine is also effective in treating diabetic neuropathy and retinopathy associated with diabetes and kidney stone disease (Voziyan *et al*., 2005). Studies proved that pyridoxamine has nephroprotective activity (Metz *et al*., 2003).

Resveratrol

Resveratrol is a stilbenoid, a polyphenolic compound found in grapes, red wine, purple grape juice, peanuts, and some berries (Soleas *et al*., 1997). Most analysis on resveratrol has been done on animals, not people. Research in mice given resveratrol suggests that the antioxidant may additionally facilitate protect them from fat and diabetes, both of that are which sturdy risk factors for cardiopathy. In mouse and rat experiments, telomere lengthening, telomerase activity enhancement, anti-inflammatory, blood sugar-lowering and different beneficial cardiovascular effects of resveratrol have been reported (Strong *et al.*, 2003). Most recent research manifested that resveratrol also has nephroprotective activity (Mannari *et al*., 2010).

Taurine

Taurine, or 2-aminoethanesulfonic acid, was originally discovered in ox (Bostaurus) bile and was named after taurus, or bull. A nonessential amino acid-like compound, taurine is found in high abundance within the tissues of many animals, particularly ocean animals, and in much lower concentrations in plants, fungi, and in a few microorganisms. As an amine, taurine is vital in several metabolic processes of the body, as well as stabilizing cell membranes in electrically active tissues, like the brain and heart. It conjointly has functions within the gallbladder, eyes, and blood vessels, and may have some inhibitor and detoxifying properties (Huxtable RJ, 1992). Scientific studies revealed that taurine is possessor of nephroprotective activities (Trachtman *et al.*, 1993).

Vitamin E

Vitamin E is fat-soluble compound that includes both tocopherols and tocotrienols (Brigelius *et al*., 1999). As a fat-soluble antioxidant, it stops the assembly of reactive oxygen species shaped when fat undergoes oxidation (Herrera *et al*., 2001).

Vitamin E has several biological functions, the antioxidant operate being the foremost vital and best known. Its alternative functions embody enzymatic activities, gene expression, and neurological functions. The most vital function of vitamin E has been suggested to be in cell signaling (Azzi, 2007). Deficiency vitamin E causes spinocerebellar ataxia, myopathies, peripheral neuropathy, ataxia, skeletal myopathy, retinopathy, impairment of the immune response and red blood cell destruction (Traber *et al*., 2007). Scientific research on vitamin E showed that it is also has a power of nephroprotective activity (Bursell *et al*., 1999).

Xanthorrhizol

Xanthorrhizol may be a sesquiterpenoid compound extracted from *Curcuma xanthorrhiza*. Historically, it absolutely was found to possess antibacterial, anticancer and anti-inflammatory activity (Ismail et al., 2005). The stem has additionally been used to treat inflammation in postpartum uterine bleeding. Recent studies also proved that it possess nephroprotective activity (Kim *et al*., 2005). Miscellaneous phytoconstituents compounds and their structures were further mentioned in table 4.

CONCLUSION

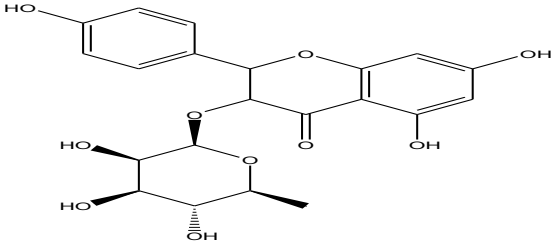
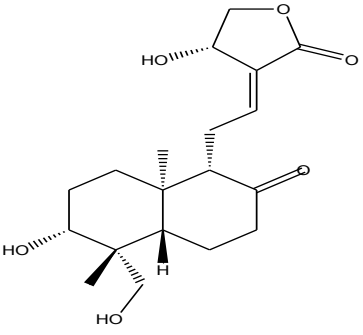
From this study, it is clear that the so many herbal plants active constituents play an important role against nephrotoxicity caused by numerous agents (drugs, chemicals etc.).The nephroprotective activity is in all probably due to the presence of assorted active constituents like alkaloids, benzoquinones, catechols, carotenoids, flavonoids, glycosides, flavonol glycosides, steroid glycosides, glycoalkaloids, terpenoids, monoterpenoids, diterpenoids, triterpene saponins, sterols and polyphenols in all few herbal plants have been reported for its significant nephroprotective activity in animal models. The results of this study indicate that extracts of leaves and other parts of some medicinal plants have good potentials for use in kidney damage. The present review study gives evidential nature of nephroprotection in some medicinal plants against experimentally induced nephrotoxicity. Hence, the review of the study concluded that the plants containing these phytoconstituents possesses nephroprotective activity and it has been proven by different animal models which gives many links to develop the future trials.

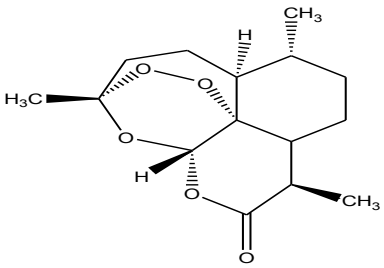
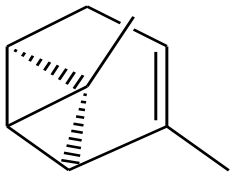
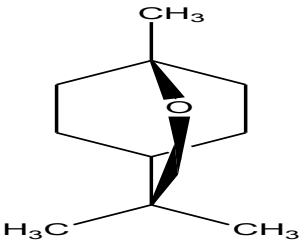
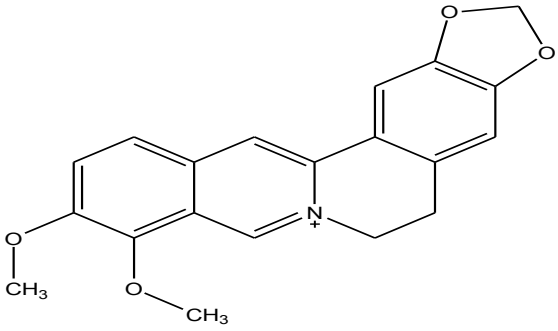
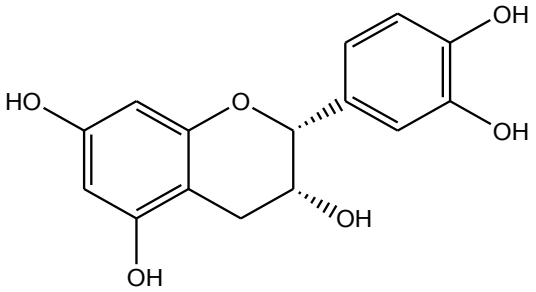
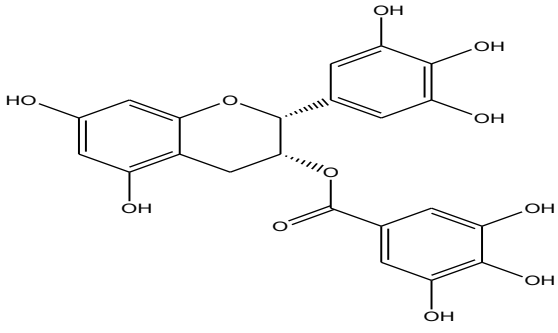
Table 1: Phytoconstituents from Medicinal plants for Nephroprotective activity

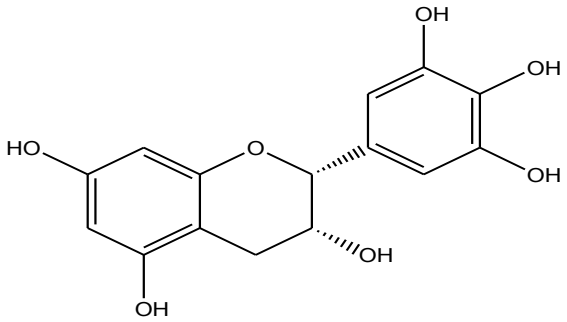
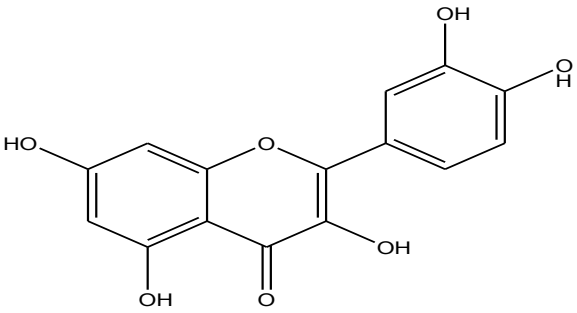
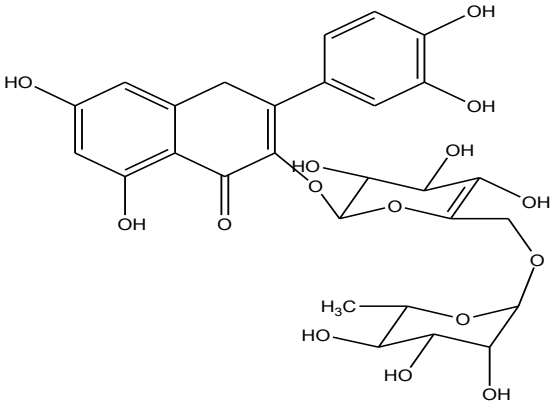
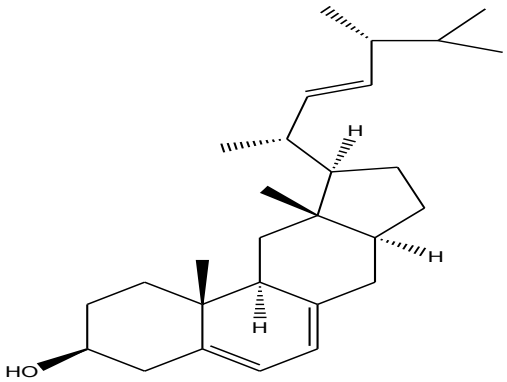
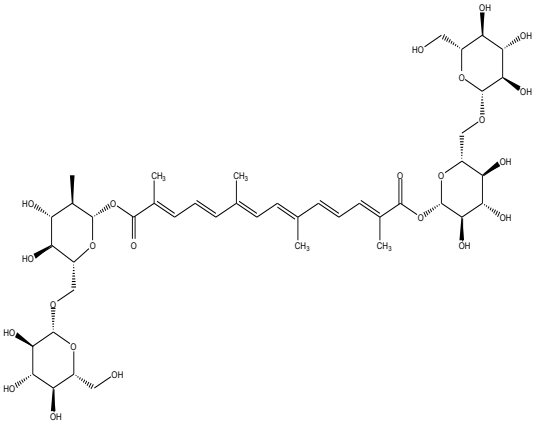
Name and family	Family	Major constituent	Specific constituent	References
Aerva lanata	Amaranthaceae	Flavonol glycoside	Kaempferol-3-rhamnoside & kaempferol- 3-rhamnogalactoside	Shirwaikar et al., 2004
Andrographis paniculata	Acanthaceae	Diterpenoid	Andrographidoids	Rao, 2006
Artemisia annua L.	Asteraceae	Terpenoid	Artemisiaketone, α-pinene &1,8-cineole	Randjelovic et al., 2013
Berberis vulgaris	Berberidaceae	Alkaloids	Berberine	Jyothilakshmi et al., 2013
Camellia sinensis	Theaceae	Flavonoids	Epicatechin, epicatechingallate, epigallocatechin, epigallocatechingallate	Bhattacharya et al., 2013
Cassia auriculata	Fabaceae	Flavonoids	Quercetin & Rutin	Annie et al., 2005
Ceratonia siliqua	Leguminosae	Polyphenol	Carob polyphenols	Ben et al., 2011

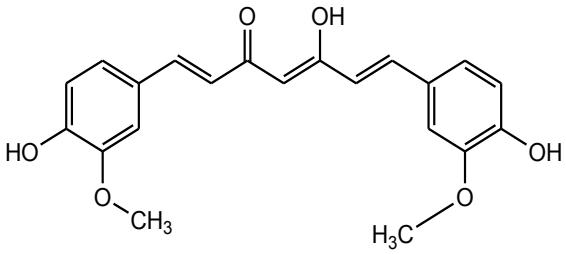
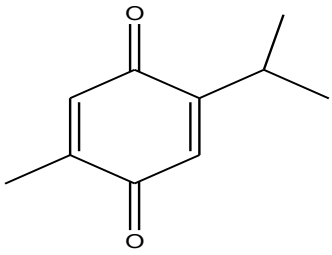
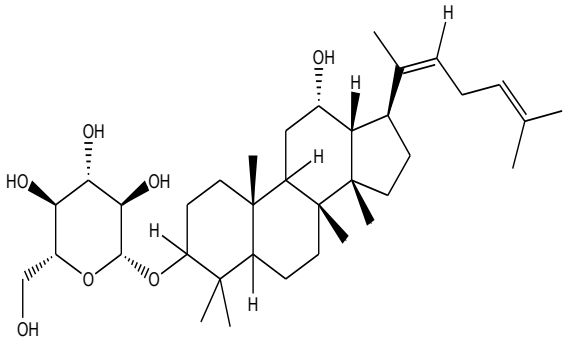
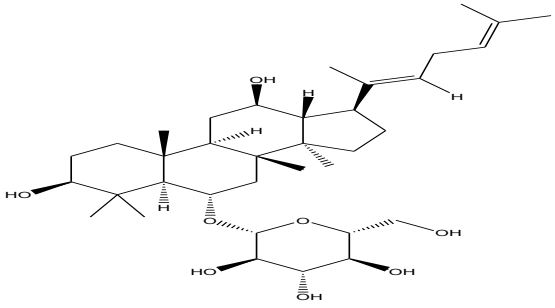
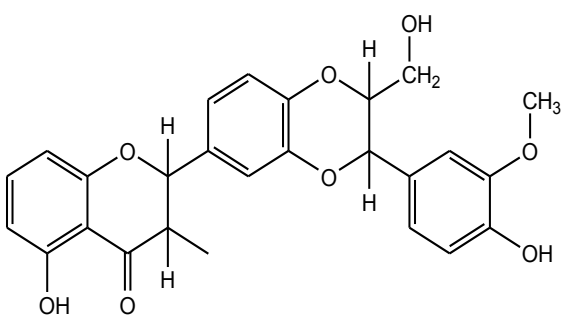
Cordyceps cicadae	Clavicipitacea	Sterol	Ergosterol	Paterson, 2008
Crocus sativus L.	Iridaceae	Carotenoid	Crocin	Naghizadeh et al., 2010
Curcuma longa	Zingiberaceae	Terpenoid	Curcumin	Venkatesan et al., 2000
Nigella sativa	Ranunculaceae	Benzoquinones	Thymoquinone	Aftab Ahmad, 2013
Panax ginseng	Araliaceae	Steroid glycosides, triterpenesaponins	Ginsenosides Rh4 & Rh3	Aek et al., 2006
Phoenix dactylifera L.	Arecaceae	Flavonoids	Quercetin	Abdel-Raheem et al., 2009
Picrorhiza kurroa	Scrophulariaceae	Glycosides	Picroside I and Kutkoside	Yadav & Khandelwal, 2009
Polyporus umbellatus	Polyporaceae	Alkaloids	Ergone	Zhao, 2013
Ramulus mori	Moraceae	Flavonoids, flavonol, Diglucoside	Rutin, quercetin, morin, mulberroside A.	Zhu et al., 2004; Wang et al., 2010; Wang et al., 2011
Satureja khuzestanica	Lamiaceae	Monoterpenoid	Carvacrol	Tavafi et al., 2011
Solanum xanthocarpum	Solanaceae	Glycoalkaloid	Solasodine	Patel et al., 2012
Zingiber officinale	Zingiberaceae	Catechols	Gingerols	Ajith et al., 2008

Table 2: Structure of Phytoconstituents with IUPAC name

Source	Active constituent	Chemical name (IUPAC name)	Structure
Aerva lanata	Kaempferol	5,7-Dihydroxy-2-(4-hydroxyphenyl)-3-[(2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxychromen-4-one	
Andrographis paniculata	Andrographiloid	(S,E)-dihydro-3-(2-((1R,2R,4aS,5R,8aS)-decahydro-2-hydroxy-1-(hydroxymethyl)-1,4a-dimethyl-6-methyl enenapthalen-5-yl) ethylidene)-4-hydroxyfuran-2(3H)-one	

Artemisia annua L.	Artemisia ketone	2,5,5-Trimethyl-2,6-heptadien-4-one	
Artemisia annua L.	alpha-pinene	(1*S*, 5*S*)-2,6,6-Trimethyl bicyclo[3.1.1]hept-2-ene ((−)-α-Pinene)	
Artemisia annua L.	1, 8-cineole	1,3,3-Trimethyl-2-oxabicyclo-[2,2,2]-octane	
Berberis vulgaris	Berberine	5,6-dihydro-9,10dimethoxybenzo[g]-1,3-benzodioxolo[5,6-a]quinolizinium	
Camellia sinensis	Epicatechin	(2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-1-benzopyran-3,5,7-triol	
Camellia sinensis	Epicatechingallate	[(2R,3R)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl]3,4,5-trihydroxy benzoate	

Camellia sinensis	Epigallocatechin (EGC)	(2R,3R)-2-(3,4,5-trihydroxy phenyl)3,4-dihydro-2H-1 benzopyran-3,5,7-triol	
Cassia auriculata	Quercetin	2-(3,4-dihydroxyphenyl)-3,5,7- trihydroxy-4*H*-chromen-4-one	
Cassia auriculata	Rutin	2-(3,4-dihydroxyphenyl)-5,7 dihydroxy-3-[α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranosyloxy]-4*H*-chromen-4-one	
Cordyceps cicadae	Ergosterol	ergosta-5,7,22-trien-3β-ol	
Crocus sativus L.	Crocin	Bis[(2S,3R,4S,5S,6R)-3,4,5 trihydroxy-6-({[(2R,3R,4S,5S,6R) 3,4,5-trihydroxy-6(hydroxymethyl) tetrahydro-2H-pyran-2-yl]oxy} methyl)tetrahydro-2H-pyran-2-yl] (2E,4E,6E,8E,10E,12E,14E)2,6,11,15-	

		tetramethyl-2,4,6,8,10,12,14-hexadeca heptaenedioate	
Curcuma longa	Curcumin	(1E,6E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione	
Nigella sativa	Thymoquinone (TQ)	2-Isopropyl-5-methylbenzo-1,4-quinone	
Panax ginseng	Ginsenosides Rh3	(2R,3S,4S,5R,6R)-2(hydroxymethyl)-6-[[(8R,10R,12S,13R,14S,17S)-12-hydroxy-4,4,8,10,14-pentamethyl-17-[(2Z)-6-methylhepta-2,5-dien-2-yl]-2,3,5,6,7,9,11,12,13,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl]oxy]oxane-3,4,5-triol	
Panax ginseng	Ginsenosides Rh4	2-({5,16-dihydroxy-2,6,6,10,11-pentamethyl-14-[(2E)-6-methylhepta-2,5-dien-2-yl]tetracyclo[8.7.0.0^{2}.0^{11},1^{5}]heptadecan-8-yl} oxy)-6(hydroxymethyl) oxane-3,4,5-triol	
Picrorhiza kurroa	Kutkin	beta-d-Glucopyranoside, 1a,1b,2,5a,6,6a hexahydro-6-hydroxy-1a(hydroxymethyl)oxireno[4,5] cyclopenta[1,2-c]pyran-2-yl,6-(3-phenyl-2-propenoate),[1aS [1aalpha, 1bbeta,2beta(E),5abeta,	

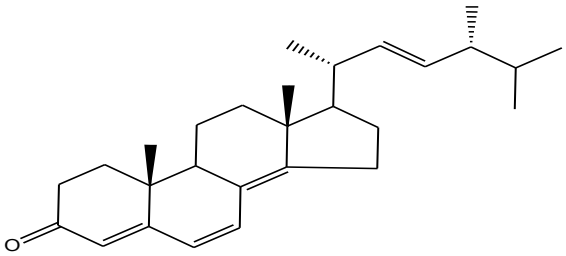
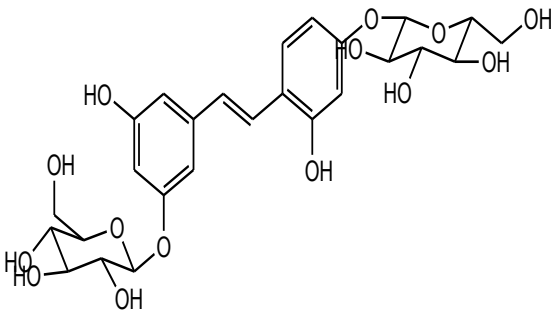
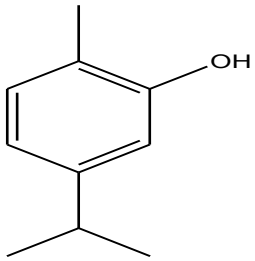
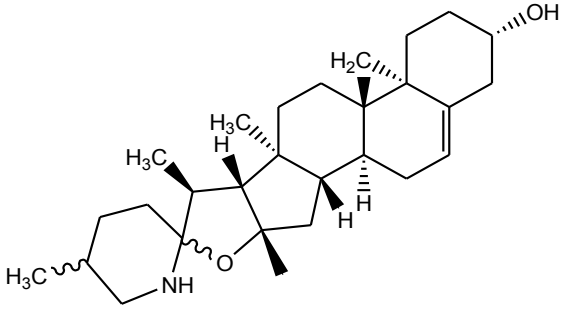
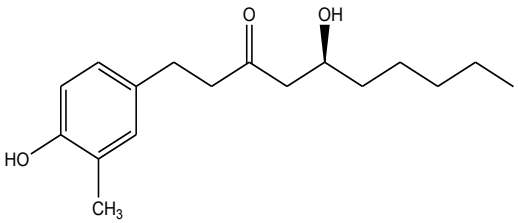
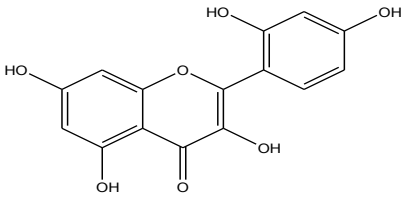
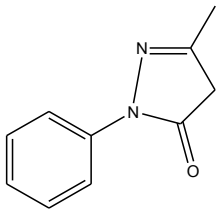
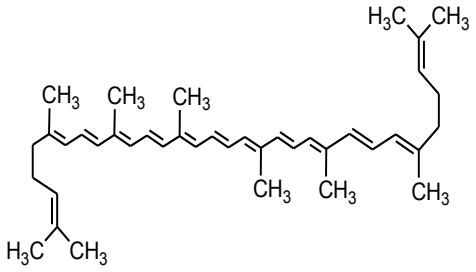
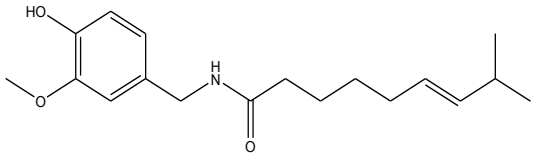
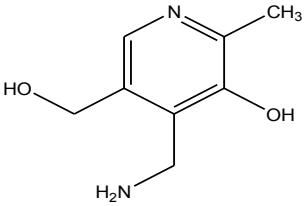
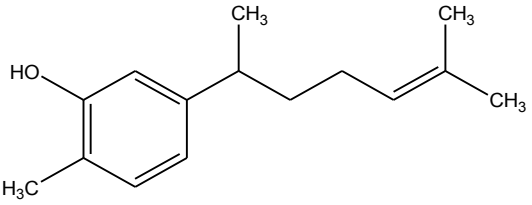
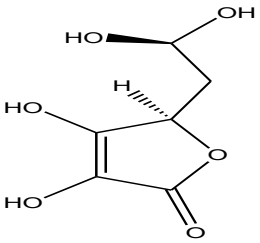
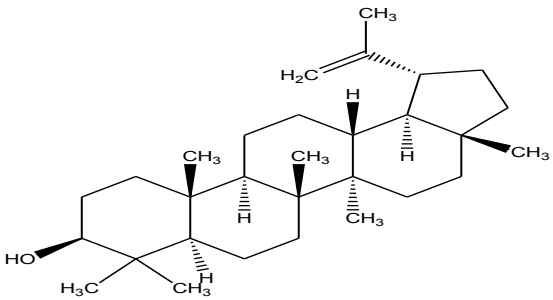
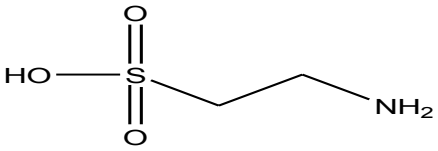
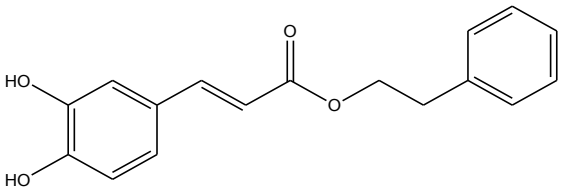
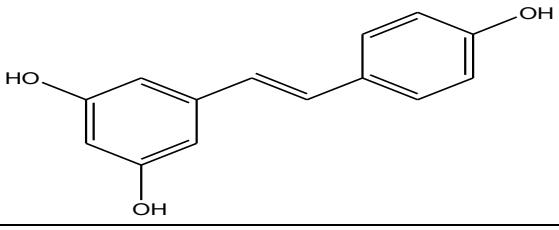
		6beta,6aalpha.	
Polyporus umbellatus	Ergone	Tetrasodium-2-[2-[bis(2-oxido-2-oxoethyl)amino]ethyl-(2-oxido-2-oxoethyl)amino]acetate	
Ramulus mori	Mulberroside-A	(2S,3R,4S,5S,6R)-2-[3-hydroxy-4 [(E)-2-[3-hydroxy-5 [(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]ethenyl]phenoxy]-6-(hydroxymethyl)oxane-3,4,5-triol	
Satureja khuzestanica	Carvacrol	5-isopropyl-2-methylphenol-2-Methyl-5-(1-methylethyl)-phenol	
Solanum xanthocarpum	Solasodine	(3β,22α,25*R*)-Spirosol-5-en-3-ol	
Zingiber officinale	Gingerols(polyphenols)	(*S*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-3-decanone	
Ramulus mori	Morin	3,5,7-trihydroxy-2-(2,4-dihydroxy phenyl)-4H-chromen-4-one	

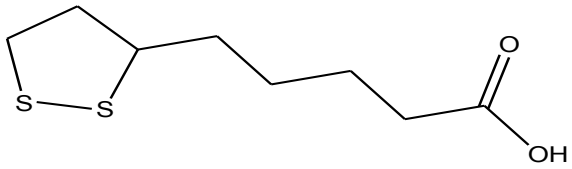
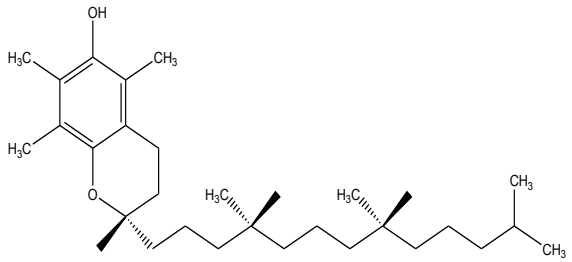
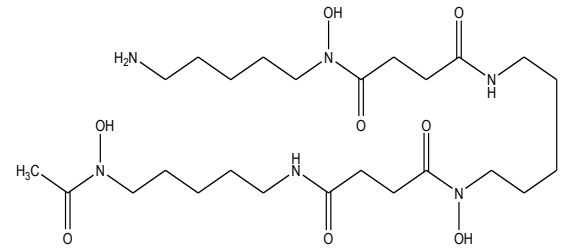
Table 3: Miscellaneous phytoconstituents for nephroprotective activity

Source	Compound	Reference
3-methyl-1-phenyl-2-pyrazolin-5-one	Edarabone	Satoh et al., 2003
Acacia visco	Lycopene	Atessahin et al., 2005
Capsicum annuum	Capsaicin	Shimeda et al., 2005
Carrots, walnuts, chicken and fish	Pyridoxamine	Metz et al., 2003
Curcuma xanthorrhiza	Xanthorrhizol	Kim et al., 2005
Kakadu plum and Camucamu Fruit	Ascorbic acid	Huang et al., 2000
Mango, *Acacia visco or Abronia villosa*	Lupeol	Nagaraj et al., 2000
Metabolic product of the amino acid cysteine	Taurine	Trachtman et al., 1993
Propolis	Caffeic acid phenethyl ester	Ozen et al., 2004
Ramulus mori	Resveratrol	Mannari et al., 2010
Spinach, broccoli, yeast extract.	DL-α-lipoic acid	Obrosova et al., 2003
Spinach, chard, and turnip greens, mustard greens, pepper, almonds, sunflower seeds, asparagus.	Vitamin E	Bursell et al., 1999
Streptomyces pilosus	Desferioxamine	Kadikoylu et al., 2004

Table 4: Structure of miscellaneous phytoconstituents with IUPAC name

Source	Phytoconstituent name	IUPAC Name	Structure
-	Edaravone	3-methyl-1-phenyl-1H-pyrazol-5(4H)-one	
Acacia visco	Lycopene	(6*E*,8*E*,10*E*,12*E*,14*E*,16*E*,18*E*,20*E*,22*E*,24*E*,26*E*)-2,6,10,14,19,23,27,31-Octamethyldotriaconta-2,6,8,10,12,14,16,18,20,22,24,26,30-tridecaene	

Capsicum annuum	Capsiacin	(E)-N-(4-hydroxy-3-methoxybenzyl)-8-methylnon-6-enamide	
Carrots, walnuts, chicken and fish	Pyridoxamine	4-(aminomethyl)-5-(hydroxymethyl)-2-methylpyridin-3-ol	
Curcuma xanthorrhiza	Xanthorrhizol	2-methyl-5-(6-methylhept-5-en-2-yl)phenol	
Kakadu plum and Camucamu Fruit	Ascorbic acid	(R)-3,4-dihydroxy-5-(2,2-dihydroxyethyl)furan-2-(5H)-one	
Mango, *Acacia visco or Abronia villosa*	Lupeol	(1R,3aR,5aR,5bR,7aR,9S,11aR,11bR,13aR,13bR)-3a,5a,5b,8,8,11a-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7a,9,10,11,11b,12,13,13a,13b-hexadecahydrocyclopenta[a]chrysen-9-ol	
Metabolic product of the amino acid Cysteine	Taurine	2-aminoethanesulfonic acid	
Propolis	Caffeic acid phenethyl ester	(E)-phenethyl 3-(3,4-dihydroxyphenyl)acrylate	
Ramulus mori	Resveratrol	5-[(E)-2-(4-hydroxyphenyl) ethenyl] benzene-1,3-diol	

Spinach, broccoli, yeast extract.	DL-α-lipoic acid	5-(1,2-dithiolan-3-yl) pentanoic acid	
Spinach, chard, and turnip greens, mustard greens, pepper, almonds , sunflower seeds, asparagus	Vitamin E	(S)-3,4-dihydro-2,5,7,8-tetramethyl-2-(4,4,8,8,12-pentamethyltridecyl)-2H-chromen-6-ol	
Streptomyces pilosus	Desferoxamine	N'-{5-[Acetyl(hydroxy)amino]pentyl}-N-[5-({4-[(5-aminopentyl)(hydroxy)amino]-4-oxobutanoyl}amino)pentyl]-N-hydroxysuccinamide	

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