NUTRACEUTICALS ROLE IN MANAGEMENT OF UROLITHIASIS

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Abstract

Urolithiasis is a third major urological disease represented by severe pain and obstructs urine flow due to the formation of stones in kidneys. Calcium oxalate is the major types of stone amongst the types of stones in urolithiasis and it is responsible for 80% of the cases. Treatment available in current scenario for stones include surgical methods (percutaneous lithotripsy, extracorporeal shock wave lithotripsy and transurethral lithotripsy) which are expensive and may lead to decrease in renal functions, haemorrhage and hypertension and they also, do not prevent recurrence rates. Drugs which are prescribed for the treatment of stones generally provide symptomatic relief and are not effective in all patients.Nutraceuticals possessing both medicinal and nutritional value can be an alternative in the management of urolithiasis to the current treatments available. Present review provides some nutraceuticals of herbal origin possessing potential to prevent and treat urolithiasis due to the presence of wide variety of phytochemicals.

Keywords: Nutraceuticals, urolithiasis, antiurolithiatic agents, herbs, phytochemicals

Introduction

Nutraceutical is the combination of word "nutrient" and "pharmaceutical". It is a part of food/ food supplements which occurs naturally and provide nutritional, medicinal and health benefits in prevention and treatment of diseases along with playing essential role in normal functioning of the body. Nutraceuticals are characterized as dietary fibres, polyphenols, probiotics, spices, antioxidants, vitamins and polyunsaturated fatty acids. Since antiquity they are used in the treatment of several diseases like cancer, heart disease, diabetes, arthritis, obesity, cholesterol etc. The nutraceuticals contain several phytoconstituents like saponins, bet-carotene, lycopene, lutein, polyphenolics (curcumin, glucosinolates, flavones, flavones, flavanols); dietary fibres (insoluble fibre, soluble fibre, sulphides/ thiol); fatty acids (omega 3 fatty acid, monosaturated fatty acid, minerals, polyols sugar alcohols) etc[1].They originates from different sources like plants (in dehydrated, ash and hard-pressed form), animal and marine sources. Nutraceuticals are well absorbed and have a long half-life with fewer adverse effects as compared to synthetic drugs and one can buy them without any prescription. India being a home to many herbs and species nutraceuticals is easily accessible in India as ayurvedic medicines and is marketed under different brand names. The Dietary Supplement Health and Education Act (1994) regulate the marketing of human nutraceuticals supplements. Results generated during the drug development phase are evaluated to check the therapeutic effect of drugs but for food safety evaluation there were no guidelines in past but in recent years, due to risen concerns regarded food content have generated guidelines for food related products[2]**.** The traditional nutraceuticals are classified as chemical constituents (herbs, nutrients, phytochemicals), probiotic microorganism and nutraceuticals enzyme. Herbs are one of the nutraceuticals types which are short in length, green in colour and they have non-woody soft stems. Since, the beginning of human civilization they were an important part of humanity due to their nutritional and medicinal benefits. Medicinal plants had made numerous contributions for the safeguard of health of individual from providing food supplements to the treatment and prevention of diseases. One such disease which in ancient times was treated with numerous herbal formulations (decoction, infusion/juice) is urolithiasis**.** In today's scenario treatment of urolithiasis include surgical methods (percutaneous lithotripsy, extracorporeal shock wave lithotripsy and transurethral lithotripsy) which are expensive and lead to decrease in renal function, haemorrhage and hypertension and they also, do not prevent recurrence. Few medications are also prescribed to resolve the pain and easy passage of stones like allopurinol, citrate, cystone and thiazide diuretics but they are not effective in all patients.So there is an urgent requisite to explore and develop a potent antiurolithiatic drug.

Urolithiasis

Urolithiasis is characterized by stone formation in urinary tract which obstructs urine flow and gives a severe pain sensation. In past 30 years, incidence of urolithiasis has been increased significantly and had led it to rank third in most common urological diseases. Risk factors for the development of urolithiasis can be grouped into two broad categories i.e. intrinsic factors and extrinsic factors.

Intrinsic factor include gender, age, ethnic differences, family or personal history while extrinsic factors include environmental factors, western diets, less amount of water intake, increased sodium, meat and oxalate intake, reduced calcium and fruits intake, metabolic disorders, BMI and urinary tract infections[3]. Males are at more risk and prevalence rate of occurring stone in males is 2-3 times higher as compared to females. By the age of seventy 11-16% mens and 7-8% women experience symptoms of urolithiasis which include intense pain, vomiting, hematuria and nausea. People aged between 20-50 years accounts for 70% of urolithiasis cases with 50% reoccurrence rate. In 15% of the cases reoccurrence occurs in first year of treatment and in 30-50% cases it is likely to reoccur within 10 years. Prevalence rates of urolithiasis are increasing with time in year 2004; it was only 5.2% which was doubled in year 2017.

Stone composition and formation mechanism

The stone formed in urolithiasis are composed of insoluble salts in which calcium oxalate is responsible for causing urolithiasis in more than 80% of patients. The remaining stone are comprised of uric acid, cystine and magnesium ammonium phosphate (struvite). Composition of kidney stone along with their percentage of occurrence has been mentiontioned in Table 1. In humans uric acid (UA) is synthesized in liver, kidneys, muscles etc and it is an end product of purines. Further uric acid is not oxidized into more soluble compound in humans due to lack of hepatic enzyme uricase and their disposal occurs in uric acid form via kidneys[4]. Urine pH also plays an important role in solubility and precipitation of uric acid as acidic pH leads to UA precipitation[5, 6].

Table 1: Composition of Kidney stone

S.No	Composition	Percent
1	Calcium oxalate and phosphate	80%
2	Uric acid	6%
3	Struvite	10%
4	Cystine	1%

Formation of stones in urolithiatic patient occurs due to aggregation of solute particles such as oxalates, uric acid, calcium, phosphate etc in supersaturated urine when levels of crystal development factors get increased in urine as compared to inhibiting factors this mechanism of stone formation is known as crystal aggregation. In this mechanism, salt in the urine forms crystals and aggregates with amorphous protein (matrix). Crystals precipitate and start accumulating causing them to grow into clumps which are large enough to cause symptoms. In the second mechanism (usually calcium oxalate stone deposition) dental calculus material appears in calcium phosphate sockets in the kidney papillae, mostly Randall’s plaques (consisting mostly of calcium phosphate).

Steps involved in formation of stones.

1. **Supersaturation:** Solutes dissolve in urine until a saturation point has not being reached. When saturation point is reached liquid starts to transform into solid phase and this step is facilitated by nucleation centers namely red blood cells, urinary casts and epithelial cells. They form the areas for crystal collection.
2. **Crystal nucleation**: due to the formation of areas for crystal collection, atoms arrange themselves in a lattice to form crystals and this process of formation of lattice is known as crystal nucleation.
3. **Crystal growth:** After the formation of crystals, atoms further aggregate themselves to form larger cluster of crystals which is known a crystal growth.
4. **Crystal retention:** Next step following the crystal growth is crystal retention in which formed stone adhere to urinary system[7].

Phytochemicals role in management of urolithiasis

Phytochemicals are the plant derived large class of compounds which are responsible for a wide range of protective effects. On the basis of their chemical structure, they are classified as phenolic acid, flavonoids and lignans/ stilbenes. Flavonoids which are polyphenolic secondary metabolites inhibit the oxalate production in urolithiasis and they also increase the bioavailability of nitric acid to cleave calcium via the cGMP (3', 5' cyclic guanosine monophosphate) pathway. Polysaccharides which are the large carbohydrate molecules act by decreasing blood urinary nitrogen (BUN) and creatinine level. They also reduce the nucleation and aggregation of calcium oxalate crystals[8].Saponins (triterpenoids glycosides) dissolves kidney stone by breaking the crystals of the calcium oxalate into monohydrate[16] while alkaloids (nitrogen containing organic base) prevents stone growth and collection in early stages. It creates a matrix like material on its surface which changes the shape and texture of stone. Another class of complex organic chemicals is lignins which prevent stone growth and collection in early stages and on its surface; it creates a matrix like material which changes the shape and texture of stone. Glycosides are the naturally occurring compounds and produce one or more sugar on hydrolysis. They prevent and reduce the formation of kidney stone and citric acid reduces the supersaturation of the urine by binding with urinary calcium.

Some nutraceuticals having potential to treat urolithiasis:

1. ***Aerva javanica*:** Synonym of this herb is Khar Buta, Phatarphod, Desert cotton, Javanese wool plant. It belongs to family Amaranthaceae. It is abundantly found in Bhavnagar, Gujarat(India), Burma, Baluchistan, Sind, Deccan, Egypt, Arabia, tropical Africa and Cape Verde Islands during rainy season. The various chemical constituents present in the plant are steroids, saponins, terpenoids, lipids, flavonoids, tannins etc. Due to the presence of saponins this herb can break the crystals of calcium oxalate into monohydrate[9]. *Aerva javanica* is used in the treatment of rheumatoid arthritis, UTIs and as antimicrobial and antifungal agents.

2. ***Abutilon indicum*** (Synonyms: *Sida indica*) commonly known as Indian mallows or country mallow. It is known as Khansi in Sanskrit, Kandghi in hindi, Petari in Bengali, Tutturu Benda in Telugu and Panirara and turri in Mudra and petri in Marathi and Uram in Malayalam. In Persian it is named as Darakhtahan, in Kannada it is Tutti and in Arabic it is Masthul gola. It

belongs to family Malvaceae which widely grows in tropical (India, Sri Lanka and African countries) and subtropical countries (America and Australia. This plant contain carbohydrates (such as galactose and galacturonic acid), raffinose, oils (stearic acid and palmitic acid) and unsaturated fats (such as ferulic acid, sulfuric acid, maleic acid, leucine, asparagine, histidine, tyrosine, glycine etc). The active ingredients found in plants are flavonoids, alkaloids, saponins and mucilage's. Other compounds which are also present in this herb are caffeic & fumaric acids, vanillin, p-coumaric acid, p-hydroxybenzoic acid, quercetin etc and due to the presence of quercetin it increases urine volume output in urolithiasis. It is used in hyperglycaemia, diarrhoea, ulcer, analgesic, hyperlipidemia, convulsion, arthritis, fungal & bacterial infection and as immunomodulator, estrogenic and diuretics[10].

3. ***Aegle marmelos*** (Synonyms: *Belou marmelos, Crateva marmelos, Maja, Bael, Lao, kuralam, sir phal, mapin, Trae mam, belbum*) belongs to the family Rutaceae. They are widely distributed in tropical and subtropical regions of Asia (Punjab, India) and Western Ghats. This plant consists of alkaloids, terpenoids, flavonoids and coumarins and due to the presence of flavanoids this has the potential to prevent calcium oxalate formation. Whole plant is used as analgesic, antipyretic, anti-inflammatory, anticancer, antidiabetic, antidiarrheal, antifungal, antihyperlipidemic, antihistamine, antimicrobial, antiulcerogenic, antiviral etc.

4. ***Amaranthus spinosus*** commonly known as Katewail chaulai/Kantabhaji (in Hindi) and pigweed (in English). This herb belongs to family Amaranthaceae. It is found intropical and subtropical regionsof world (India, USA, Africa, Southeast Asia, SriLanka, Northern America, Philippines, Maldives and Cambodia. This plant is rich inalkaloids, amino acid, flavonoids, glycosides, lipid, phenolic acids, terpenoids, carotenoids, saponins, catechuic, tannins, beralains, amaranthine, quercetin, hydroxycinnamates, iso- amaranthine, kaempferol, glycosides etc. Due to the presence of flavanoids this can prevent calcium oxalate formation and due to the presence of saponins this herb can also dissolve kidney's stone by breaking the crystals of the calcium oxalate into monohydrate. Leaves of this herb are used for the treatment of pain, stomach, burning sensation, wounds, ache, jaundice, laxative, vegetables, antioxidant; seed used for menstruation, bone broken, loose motion, bleeding internally, food; root used for urinary tract, inflammation, wound, burn, menorrhagia, emollient and its whole plant is used in jaundice and snake bite.

5. ***Amaranthus viridis*** is an annual herb native to America. It is one of the members of Genus Amaranth and family Amaranthaceae. Amaranth comprised of seventy species and every species of this family have some economic value. Other species of Amaranthaceae family are *Amaranthus cruentus, Amranthus caudate, Amranthus tricolor, Amranthus retroflexus, Amranthus hybridus, Amranthus hypochondriacus* etc. It is commonly known as Chowlai and amaranth crop. It has both nutritional and medicinal properties due to which it is considered as a precious plant. Existence of this plant is known from ancient times and their leaves and seeds were used as foods, cereals and weeds. It was considered as a divine plant therefore was able to found place in several religious ceremonies. *A. viridis* contains flavonoids, steroids, phenols, triterpenoids, tannins and saponin. Due to the presence of saponins this herb can dissolve

kidney stone by breaking the crystals of the calcium oxalate into monohydrate. It is also used in the treatment of inflammation, dysentery, constipation, wound healing, diuretics, hyperlipidemia, diabeties and hepatotoxicity.

6. ***Amaranthus caudatus*:** (Synonyms: *Herbare kiwicha*) belongs to the family Amaranthaceae. They are widely distributed in South and Central America, Europe, Asia, Africa, Australia and India[11]. The various chemical components present in the leaves such as potassium, sodium, magnesium, calcium, iron, phosphorus, zinc, vitamin, protein. This herb also contains amino acids, fatty acids, polyphenolic acid (rutin, isoquniline and nicotine) and phenolic compounds (ellagic acid, rutin, gallic acid). The seeds used to treatheavy bleeding, bleed internally; Root used to treat gonorrhea; leaves used as a good soothing agent and the whole herb used in the treatment of urinary tract inflammation, appetite, astringent, piles, gonorrhoea, snake bite, leprosy, high blood pressure, heart disease, constipation, fever, anemia, kidney disease and as a high nutritional food. This herb can be used in the prevention of calcium oxalate formation due to the presence of polyphenols.

7. ***Apium graveolens*** (Synonyms: celery, karnaulli, ajmod) belongs to the family Apiceae. They are widely distributed in the India (north-western Himalayas, Punjab, Haryana and western Uttar Pradesh), Sweden, Egypt, Algeria and Ethiopia. The leaf and stalk consist of vitamin A, B, C; fat; fibers; protein; calcium; iron; phosphorus. It also composes of essential oil such as delta limonene, saliene, various sesquiterpene. This plant used as an antifungal, antihypertension, antibacterial, diuretics, chemotherapy, antianxiety, anti-inflammatory, urarthritis and as a nutritious drink[12]. It also has antioxidant property due to which this herb can be useful in calcium oxalate prevention.

8. ***Achyranthes aspera*** (Synonyms: Aghata, Latjira, Safad Aghedo, Shiru-kadaladi, Uttaraene, Kadaladi, Kutri, Chirchitaa, Apaamaarga, Khare-vazhum, Atkumah, Mosotillo) commonly known aslatjeera and rough chaff tree. The synonyms of this herb are Aghata, Latjira, Safad Aghedo, Shiru-kadaladi, Uttaraene, Kutri, Chirchitaa, Apaamaarga, Khare-vazhum, Atkumah, Mosotillo. It belongs to the family Amaranthaceae. They are widely distributed in India, south Andaman Islands, topical Asia, Africa, Australia, Ceylon, America and Baluchistan. The seeds of this herb contain saponin which can break crystals of calcium oxalate and therefore it has the ability to dissolve kidney stones. They are also used to treat several conditions such as hyperglycemic, cancer, inflammation, liver disease, arthritic, microbial infection, depression, urinary tract infection, heart disease, allergy, hyperlipidemic, coughing and asthma.

9. ***Beta vulgaris*** belongs to the family Amaranthaceae. They are widely distributed in Mediterranean, Europe (Atlantic coast) and India. Leaves of this plant contain phytoconstituents such as polyunsaturated fatty acid, phenol, mineral element such as Ca, Mg. Due to the presence of phenols it can prevent calcium oxalate formation. This herbs is used in treating certain conditions such as wounds, indigestion, blood disorder, fungal infection, hyperglycemic, inflammation, cancer etc[13].

10. ***Bombax ceiba*** commonly known as semal, simabal, simul, Indian kapok, katsavar, Indian bombax, red silk and cotton tree. It belongs to the family Bombacaceae. This plant is widely distributed in Asia, India, tropical Asia, Africa and Australia. Flower contains large amount of essential oil, kaempferol and quercetin and the bark contains saponins and tannins. Other chemical constituents like alkaloids, coumarins, proteins, flavonoids and amino acid. Due to the presence of flavanoids it can prevent calcium oxalate formation in urolithiasis. This herb is used as an antioxidant, antihypertensive, antiangiogenic, analgesic, antimicrobial, antibacterial, anticancer, antiobesity, anti-acne and antipyretic. They also used as a food source[14].

11. ***Berberis vulgaris*** commonly known as berberis. They belong to the family berberidaceae which widely grown in Asia, Africa, Europe, North and South America. This herbcontains phenols, anthocyanin, protein, elements (copper, zinc, iron, potassium, calcium, manganese), alkaloids and triterpenes. The main phytoconstituents are berberine and beramine. The possible mechanism of action of this herb containing phenol can be prevention of calcium oxalate formation in urolithiasis. They are used in treating certain conditions such as hypertension, inflammation, malarial, hyperglycemic condition, sedative, vomiting, pyretic and arrhythmia[15].

12. ***Bryophyllum pinnatum*** commonly known as Salisb, Lam, Pers, Clus and Oken. It belongs to the family Crassulaceae which are widely distributed in India, Madagascar and southern Africa. This herb contains alkaloids, tannins, flavonoids and saponins. They are used as a wound healing drug, antidiabetic drug, anti-hypertensive, chemotherapy, anti-inflammatory and diuretic. It is also used as a food supplement. This herb could be beneficial in treatment of kidney stones as it can dissolve stones due to the presence of saponins[16,17].

13. ***Capsicum annum*** belongs to the family Solanaceae. They are widely distributed in Central America, India (Andhra Pradesh, Maharashtra, Karnataka, Tamil Nadu and Rajasthan). They are rich in vitamin C, A and E content. The chief constituents present in the seeds are dihyrocapsaicin, nordihyrocapsacin, homocapaisin and homocapsaicin. They are used in the treatment of neuralgia, rheumatic, non-allergic rhinitis and flatus-relieving. Due to the presence of capsaicin it can increase the urine volume. And due to the presence of flavonoids it can prevent calcium oxalate formation[18,19].

14. ***Cassia fistula*** commonly known as baundaralati, Goldern shower, Garmala, Sunaari, Nripadruma, Sonhali, Bahava, Amaltaas). It belongs to the family Fabaceae which are widely distributed in Thailand, Bangladesh, India, China, Hong Kong, Philippines, Malaysia and Indonesia. This herb contains large amount of phenolic antioxidant like flavonoids and anthraquinones. Other constituents such as alkaloids, saponin, tannins, terpenoidsand steroids. They are used as an antidiabetic drug, antiulcer, antitumor, antioxidant, antitussive, anti-inflammatory, CNS stimulant, disinfectant and wound healing medicines[20].

15. ***Citrus medica*** belongs to the family Rutaceae. They are widely distributed in Himalaya region (Gadwall to Sikkim), Assam, Central and Western Ghats in India; America; Medes; Persia and Assyria. The phytoconstituents present in the leaves and peel oil are Linalool, citronellal, citronellyl acetate, citronellic acid, isopulegol; Z, E-citral and citrine. This herb has the potential to dissolve calcium oxalate due to the presence of citrate.They are eaten as a fruit in various part of the world. This herb used in the treatment of sea sickness, intestinal disorder, pulmonary troubles, dysentery, rheumatoid arthritis, appetite and stomach-ache[21].

16. ***Citrus aurantium*** commonly known as Bitter orange which belongs to the family Rutaceae. This herb contains vitamin, terpenoids, alkaloids, minerals and flavonoids (flavones, flavanones, anthocyanins and flavanols). C. *aurantium* are used as a cytotoxic drug, anxiolytic and sedative, antidiabetic, antiobesity, antimicrobial drug, antioxidant, pesticide and antiulcer drug. The possible mechanism of action of this herb containing flavonoids is to prevent calcium oxalate formation.

17. ***Centella asiatica***is commonly known as Gotu kola and Tiger herb. They belong to the family Apiaceae. They are widely distributed in India, China, Indonesia, Malaysia, Madagascar and Africa. This herb contains triterpene saponosides, flavonoids (quercetin,rutin), phenolic acid and polysaccharides. They are used as an immunosuppressant, anti-bacterial, anti-oxidant, anti-inflammatory, antiulcer, hepatoprotective, antidiabetic, chemotherapy, antiviral and antifungal. The possible mechanism of action of this herb containing phenol is to prevent calcium oxalate formation[22].

18. ***Didymocarpus pedicellata*** commonly known as Stone flower, Muskan and shilapushpa. They are widely distributed in India (Pithoragarh in Kumaon Himalayas). They containseveral chemical constituents such as essential oil, tannins, carbohydrates, steroids, flavonoids, alkaloids, terpenoids, carbohydrates, fat, fiber, silica, chlorophyll a and b and mineral (sodium, potassium, calcium, lithium, iron, zinc, manganese, Sulphur and nitrogen). They are used in the treatment of kidney stone (may be due to the presence of flavonoids which can prevent calcium oxalate formation), cancer, cough, Alzheimer's disease, asthma, Parkinson's disease, viral infection, bacterial infection and diabetes[23].

19. ***Dactus carota*** commonly known as carrot belonging to the family Apiaceae. They are widely distributed in Asia (southwest or near west), Australia, South America, Africa and Mediterranean region[24]. They consist of polyacetylenes, phenol, carotenoids, tocopherol and ascorbic acid and due to the presence of phenol it can prevent calcium oxalate formation. They are used in the treatment of HIV infection, hypertension, anemia, eye related problem, acne, wounds and injuries[25].

20. ***Elettaria cardamomum*** commonly known as "Queen of Spices". This herb belongs to the family Zingiberaceae which are widely distributed in the South India and West Malesia. The main phytochemical present such as saponins, cardiac glycosides, alkaloids, anthraquinones, polyphenols and tannins. Seed consists of phenols, terpenoids, flavonoids, protein, starch and sterols and due to presence of flavanoids they can prevent calcium oxalate formation. They are used as an antimicrobial, anti-inflammatory, cardioprotective, antihypertensive, anti-oxidient, chemotherapy, antituberculosis and anti-proliferative. They are also used as food flavoring component and in Spices[26].

21. ***Equisetum arvense*** commonly known as horsetail. They belong to the family Equisetales which are widely distributed in Asia, USA, Canada, Iran, Himalayas of Iraq, Turkey, Japan and China. This herb consists of protein, amino acid, alkaloids, phytosterols, phenol, flavonoids, triterpenoids, saponins, volatile oil, carbohydrates and protein. They are used in several medical conditions such as kidney stone, profuse menstruation, hair fall, rhematic arthritis, nasal disease, g.i.t disease, wound and inflammation**.** The possible mechanism of action of this herb containing phenol is to prevent calcium oxalate formation[27].

22. ***Eleusine coracona*** commonly known as Finger millet, Tamba, Kpana, Chargari, Ragi, Madua. They belong to the family poaceae. The Geographical distribution is in Africa, Southern India, Ethiopia and Asia. Seeds contain polyphenols such as tannic acid, caffeic acid, vanillic acid, gallic acid and chlorogenic acid. Other constituents such as amino acid, alkaloids, tannins, terpenoids, saponin, basalms, cardiac glycosides and phenols. They are used as a cancer drug, antimicrobial drug, antiaging drug, antilithiatic drug, anti-inflammatory drug, in liver disease, anti-diabetic drug and anti-bacteria. The possible antiurolithiatic mechanism of this herb can be prevention of stone growth due to presence of alkaloids[28,29].

23. ***Ficus carica*** belongs to the family Moraceae. They are widely distributed in Mediterranean, Algeria, Morocco, Turkey and Egypt. Leaves of this herb contain volatile oil. The pulps and peel contains flavonoids, tannins, phenol and anthocyanins and due to the presence of flavanoids this herb can prevent calcium oxalate formation. They are used in the treatment of acne, inflammation, pyretic, cancer, bacterial infection, liver disease, diabetes, Alzheimer disease, fungal disease, tuberculosis and obesity[30].

Table 2: List of some nutraceuticals having antiurolithiatic potential

S No.	Herbal Plants	Mechanism of action	Chemical constituents	Uses
1.	*Aerva Javanica*	Dissolve kidney stone.	Steroids, terpenoids, lipids, saponin and flavonoids.	Antimicrobial, antifungal, UTI, and rheumatoid arthritis
2.	*Abutilon Indicum*	Dissolve kidney stone.	Stearic acid, palmitic acid, flavonoids,alkaloids, saponinsand mucilage's.	Hyperglycaemic, diarrhoeal, ulcer, analgesic, hyperlipidemic, convulsant, arthritic, immunomodulatory, estrogenic, fungal infection and as diuretics.
3.	*Aegle Marmelos*	Prevent calcium oxalate formation	Alkaloids, terpenoids, flavonoids and coumarins	Analgesic, antipyretic, anti-inflammatory, anticancer, antidiabetic antidiarrheal, antihyperlipidemic, antihistamine, and antimicrobial
4.	*Amaranthus spinosus*	Prevent calcium oxalate formation	Alkaloids, amino acid, flavonoids, glycosides, lipid, phenolic acids, terpenoids, carotenoids, saponins, catechic tannins	Menorrhagia, pain, stomach, burning sensation, wounds, ache, jaundice, laxative, vegetables, antioxidant, and for menstruation
5.	*Amaranthus Viridis*	Dissolving kidney stone by breaking the crystals	Flavonoids, steroids, phenols, triterpenoids, tannins, and saponin.	Dysentery, constipation, wound healing and diuretics.
6.	*Amaranthus caudatus*	Prevent calcium oxalate formation	Potassium, sodium, magnesium, calcium, iron, phosphorus, zinc, vitamin, amino acids, fatty acids.	Urinary tract inflammation, diarrhoea, appetizer, astringent, piles, gonorrhoea, pyretic, snake bite, and leprotic.
7.	*Apium Graveolens*	Helps in calcium oxalate prevention.	Vitamin A, B, C; fat; fibres; protein; moisture; calcium; iron; phosphorus, essential oil.	Antifungal, antihypertension, antibacterial, diuretics, chemotherapy, anxiety, menstrualdistress, and to reinstate sexual strength imperial
8.	*Achyranthes Aspera*	Dissolving kidney stone	Saponin A, B; 10-octacosamine, 10-triocsanone and 4-triacntanone	Hyperglycaemic, cancer, inflammation, liver disease, arthritic, microbial infection, depression, and urinary tract infection.

9.	*Beta Vulgaris*	Prevent calcium oxalate formation.	Polyunsaturated fatty acid, phenolic compounds, mineral element such as Ca, Mg	Wounds, indigestion, blood disorder, fungal infection, hyperglycaemic, inflammation, and cancer
10.	*Bombax Ceiba*	Dissolving kidney stone by breaking the crystals of the calcium oxalate into monohydrate	Saponins, tannins, gums, lupeol, free beta-sitosterol, hentriacontanol, large amount of essential oil, kaempferol and quercetin	Antioxidant, antiangiogenic, analgesic, antimicrobial, anticancer, antiobesity, anti-acne, in heart disease, and antipyretic
11.	*Berberis Vulgaris*	Prevents stone growth and collection in early stages and on its surface	Phenols, anthocyanin, protein, dextrose, carotenoid, malic acid, pectin, tartaric acid, resin, elements (copper, zinc, iron, potassium, calcium, manganese), alkaloids and triterpenes	Hypertension, inflammation, malarial, hyperglycaemic condition, sedative, vomiting, pyretic, and arrhythmia
12.	*Bryophyllum pinnatum*	Dissolving kidney stone by breaking the crystals	Alkaloids, tannins, flavonoids and saponins	Wound healing drug, antidiabetic drug, anti-hypertensive, liver disease; chemotherapy, anti-inflammatory, uterine tract disease, and diuretic
13.	*Capsicum Annum*	Increase the urine volume.	Vitaminc, A, E; dihyrocapsaicin, nordihyrocapsacin, homocapaisin, homocapsaicin	Neuralgy, rheumatic and non-allergic rhinitis and flatus-relieving.
14.	*Cassia fistula*	Prevents stone growth and collection in early stages and on its surface.	Alkaloids, reducing sugar, saponin, tannins, terpenoids, phlobatanin and steroids	Antidiabetic, ulcer treatment, antitumour, antioxidant, antitussive, anti-inflammatory, CNS stimulant, and disinfectant
15.	*Citrus medica*	Inhibit stone formation.	Linalool, Gamma-terpinene, citronellal, citronellol, r-cymene, geranial, citronellyl acetate	Sea sickness, intestinal disorder, pulmonary troubles, dysentery, rheumatoid arthritis, and as appetite stimulant
16.	*Citrus Aurantium*	Inhibit oxalate production and increase	Vitamin, terpenoids, alkaloids, minerals and flavonoids	Diabetic, antiobesity, antimicrobial drug, antioxidant, pesticidal and antiulcer drug

		bioavailability of nitric acid		
17.	*Centella Asiatica*	Decreasing blood urinary nitrogen (BUN) and creatinine level,reduce the nucleation and aggregation of Calcium oxalate crystals.	Flavonoids, phenolic acid and polysaccharides	Anti-bacterial, anti-oxidant, anti-inflammatory, antiulcer, hepatoprotective, antidiabetic, chemotherapy, antiviral and antifungal
18.	*Didymocarpus Pedicellata*	Prevents stone growth and collection in early stages and on its surface.	Essential oil, tannins, carbohydrates, steroids, flavonoids, alkaloids terpenoids.	Kidney stone, cancer, cough, alzheimer's disease, asthma, parkinson's disease, viral, bacterial infection and diabetes
19.	*Dactus Carota*	Prevent calcium oxalate formation.	Polyacetylenes, phenolic carotenoids, beta-carotene, tocopherol and ascorbic acid.	Hiv infection, hypertension, anaemia, eye related problem, acne, wounds, injuries and boost immunity
20.	*Elettaria Cardamomum*	Inhibit oxalate production and increase bioavailability of nitric acid	Saponins, cardiac glycosides, alkaloids, anthraquinones, polyphenols, tannins, phenols, terpenoids, flavonoids, protein, starch sterols	Inflammation, cardiovascular disease, hypertension, anti-oxidient, chemotherapy, antituberculosis, anti-proliferative and digestive problem
21.	*Equisetum arvense*	Prevent calcium oxalate formation	Protein, amino acid, alkaloids, phytosterols, phenol, flavonoids, triterpenoids, saponins, volatile oil, carbohydrates and protein	Kidney stone, profuse menstruation, hair fall, rhematic arthritis, nasal disease, g.i.t disease, wound and inflammation
22.	*Eleusine Coracona*	Dissolving kidney stone by breaking the crystals	Mineral, calcium, fats, dietary fibres, protein, micronutrients, vitamin,	Mineral, calcium, fats, dietary fibres, protein, micronutrients, vitamin, carbohydrates and polyphenols.

			carbohydrates, polyphenols	
23.	*Ficus Carica*	Inhibit oxalate production	Flavonoids, volatile oil, amino acid, fiber, potassium, calcium and iron.	Acne, inflammation, pyretic, cancer, oxidant, bacterial infection

CONCLUTION AND FUTURE SCOPE

This review provides a number of traditional herbal nutraceuticals plant which have a potential to treat and prevent kidney stones. It also offers the geographical distribution, chemical constituents, and macroscopic characters of the herbal plants. These herbal plants are also used to treat multiple disorders like fungal infection, rheumatoid arthritis, microbial infection, hyperlipidemic, diarrhea, viral infection, constipation, dysentery, anemia, gonorrhoea, snake bite, cancer, allergy, depression, inflammation, acne, appetite, ulcer, Alzheimer's disease and Parkinson's disease. This review also concludes the possible mechanism of action of the herbal plants. In future pre- clinical studies can be performed to evaluate the antiurolithiatic potential of these herbs.

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