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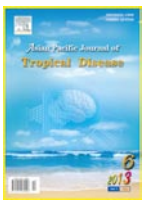

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Pathophysiology of kidney, gallbladder and urinary stones treatment with herbal and allopathic medicine: A review

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PEER REVIEW

Peer reviewer

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Comments

It is a systematic review that clearly focuses on first explaining the pathophysiological pathways of kidney, gall bladder and urinary stones followed by the medicinal plants that can be exploited to develop new therapeutic entities. The compilation of medicinal plants and their properties provides much clarity about the topic.
Details on Page 503

ABSTRACT

Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of various ailments. Today large number of population suffers from kidney stone, gall stone and urinary calculi. Stone disease has gained increasing significance due to changes in living conditions *i.e.* industrialization and malnutrition. Changes in prevalence and incidence, the occurrence of stone types and stone location, and the manner of stone removal are explained. Medicinal plants are used from centuries due to its safety, efficacy, cultural acceptability and lesser side effects as compared to synthetic drugs. The present article deals with measures to be adopted for the potential of medicinal plants in stone dissolving activity. The problem of urinary stones or calculi is a very ancient one and many remedies have been employed during the ages these stones are found in all parts of the urinary tract, the kidney, the ureters and the urinary bladder and may vary considerably in size. In the present article, an attempt has been made to emphasis on herbal option for urinary stone.

KEYWORDS

Medicinal plants, Kidney stone, Gall stone, Urinary calculi

1. Introduction

Nature bestowed our country with an enormous wealth of medicinal plants. Plants have been used as traditional healthcare system from the centuries. The WHO has listed 20 000 medicinal plants globally in which contribution of India is 15-20%[1]. The WHO reported that 80% of global countries depend on the medicinal plants[2]. A large body of evidence has collected to show potential of medicinal plants used in various traditional systems. In the last few years more than 13 000 plants have been studied for the various diseases and ailments all over the world[3]. Kidney stones are also major disorders prevailing all over the world. About 75% of kidney stones are composed of calcium oxalate crystals[4].

Gall stone mainly affects people in global countries. More than half a million people are affected annually in United States and more than 50 000 people in Canada. Canada endures surgical treatment to remove their gall bladder because of gall stone. About 80 % of all the gall stones has evidence for no symptoms and may continue for years[5]. Also, the over use of synthetic drugs, which

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results in higher incidence of adverse drug reactions, has motivated humans to return to nature for safe remedies. The origins, according to many, can be sourced to the World Health Organization's Canberre conference in 1976, which promoted the concept of 'Traditional' medicines for the developing countries[6].

The problem of urinary stones or calculi is a very ancient one and many remedies have been employed during the ages these stones are found in all parts of the urinary tract, the kidney, the ureters and the urinary bladder and may vary considerably in size, Linacre, who had founded the college of physicians, died of urinary stone in 1518 in London, a condition he could diagnose but could not be true[7].

2. Pathophysiology

2.1. Kidney stone

Kidney stone are called as renal calculi. They are crystal aggregations formed in the kidneys. Kidney stones normally leave the body by the route of urine stream, and many stones are produced and conceded without causing symptoms. If stones grow to plenty size before passage, on the order of at least 2-3 millimeters, they can cause barrier of the ureter[8]. The whole summary kidney stone path physiology is given in Figure 1 and Table 1.

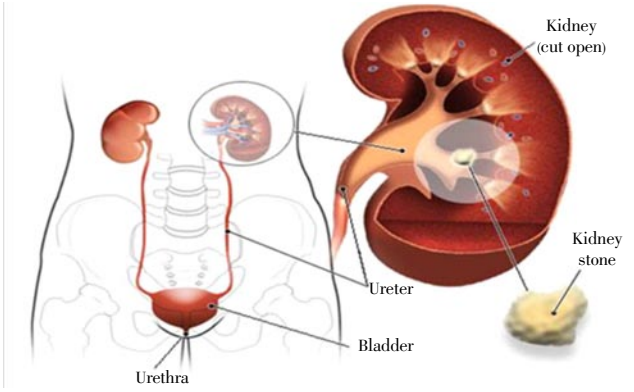


Figure 1. Kidney stone.

2.2. Mechanism of stone formation

Age, Profession, Nutrition, Climate, Inheritance, Sex, Mentality, Constitutions, Race

⇩

Abnormal renal morphology, Disturbed urine flow, Urinary tract infection, Metabolic abnormalities, Genetic factors

⇩

Increased excretion stone forming constituents, Decreased excretion of inhibitors of crystallizations

⇩

Physico-chemical change in the state of supersaturation

⇩

Abnormal crystalluria, Crystal's aggregations, Crystal's growth

⇩

Formation of stone[20]

2.3. Lithiasis

A kidney stone is a hard mass developed from crystals that separate from the urine within the urinary tract. Normally, urine contains chemicals that prevent or inhibit the crystals from urinary tract. These crystals remain tiny enough; they will travel through the urinary tract and pass out of the body in the urine without being noticed. A less common type of stone is caused by infection in the urinary tract. This stone is called struvite or infection stone. Another type of stone, uric acid stones, are a bit less common, and cystine stones rare[8]. Kidney stones are composed of inorganic and organic crystals amalgamated with proteins. Crystallisation and subsequent lithogenesis can happen with many solutes in the urine. Calcareous stones are still by far the most common nephroliths, 17 % accounting for more than 80% of stones[21].

2.4. Gall bladder stone

Gallstones are collections of cholesterol, bile pigment, which can form in the gallbladder or surrounded by the bile ducts of the liver. In the United States, the most universal category of gallstones is made of cholesterol. Cholesterol

Table 1
Kidney stone.

Etiology	Types	Symptoms
Kidney stones caused by basic metabolic conditions like renal tubular acidosis, modularly sponge kidney, Dent's disease and hyperparathyroidism[9].	Calcium oxalate crystals: 80%	Colicky pain: loin to groin, described as the worst pain ever experienced
	Urate (uric acid) crystals: 5-10%	Hematuria: blood in the urine, due to minor damage to inside wall of kidney, ureter and/or urethra
	Struvite crystals: Mg, NH_4 and PO_4, crystals	Pyuria: pus in the urine[10-12]
		Dysuria: burning on urination
	Calcium phosphate and cystine crystals	Oliguria: reduced urinary volume
		Nausea/vomiting: embryological link with intestine, stimulates vomiting center
		Hydronephrosis
		Post renal azotemia: kidney stone blocks ureter[13-19]

stones are mainly causes due to difference in the production of cholesterol or the secretion of bile. Pigmented stones are mainly composed of bilirubin, which is an element formed due to the normal breakdown of red blood cells. Bilirubin gallstones are more common in Asia and Africa but they are seen in diseases that break red blood cells such a sickle cell anemia[22]. The whole summary gallbladder stone path physiology is given in Figure 2 and Table 2.

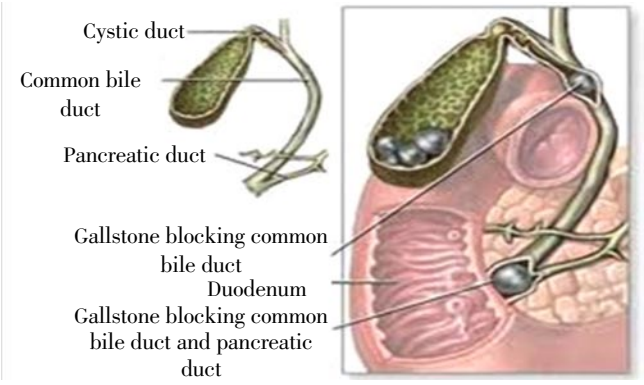
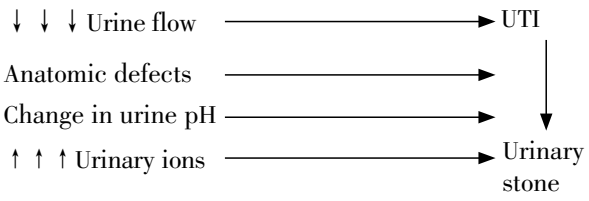


Figure 2. Gall bladder stone.

2.5. Urinary stone

Urinary calculi is composed of hard mineral masses lodged anywhere in the urinary tract. The urinary tract consists of organs which filter blood to eradicate liquid waste (urine) that is excreted from the body i.e. kidneys, ureter, bladder and urethra. The stones firstly form in the kidney and then it travel to other parts of the urinary tract where they may become trapped in smaller tubes *e.g.* bladder stones, ureteric stones and kidney stones.

2.6. Path physiology of urinary stones



The condition may be extremely painful[28]. Urolithiasis

Table 2
Gall bladder stone.

Etiology	Types	Symptoms
Gallstones may be caused by a combination of factors, including inherited body chemistry, body weight, gall bladder motility (movement) and perhaps diet[23].	Calcium oxalate crystals: in about 80% of cases	Biliary colic: a person will experience intense pain in the upper abdominal region that gradually increases for approximately thirty minutes to several hours.
	Urate (uric acid) crystals: 5-10%	Murphy's sign: gallbladder is inflamed, the patient will hastily stop inhaling due to the pain.
	Struvite crystals: Mg, NH_4 and PO_4, Crystals	Low grade fever: yellowing of the skin or eyes.
	Calcium phosphate and cystine crystals	Other symptoms: include intolerance of fatty foods, belching, gas, abdominal bloating and indigestion[24-27].

Table 3
Urinary stone.

Etiology	Types	Symptoms
Urinary stone caused by bacterial infection[31] Kidney stones form as a result of physicochemical or genetic derangements leading to super saturation of the urine with stone-forming salts or, less commonly, from recurrent urinary tract infection with urease producing bacteria like *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Enterobacter* spp., *Serratia* spp., *Staphylococcus aureus*, *Staphylococcus epidermitis*. Three conditions must coexist for the formation of struvite calculi. 1. Alkaline urine. 2. The presence of urea or ammonia in the urine. 3. Higher concentration of minerals in the urine[32-34]. Urine from healthy humans consists of a large quantity of nitrogenous compounds, including 0.5 mol/L urea, as well as inorganic ions. Urine is neutral to slightly acidic, and under these conditions, ammonia becomes protonated with the concomitant generation of hydroxide, which increases urine pH.	Calcium oxalate crystals: in about 80% of cases	Recurrent UTI: Younger children should be a pointer and deserves further investigation.
	Urate (uric acid) crystals: 5-10%	Crying on micturation: Crying or pain on micturation (in older children) is also a common presenting feature and this may start early in life. The child may also tug at the penis during micturation.
	Struvite crystals: Mg, NH4 and PO_4, Crystals	Urinary retention: This may be the initial symptom of urinary stones.
	Calcium phosphate and cystine crystals	Pain/Colic: Frank renal colic is a feature in adolescents but acute generalized abdominal. Pain is commoner in younger children and diagnosis is done on work-up for UTI[35].
	Bacterial ureas alkalinizes urine:There by causing:	Gross hematuria: This alarming symptom in combination with colics is the main presenting features of urinary stones in older.
	i: Supersaturation with respect to struvite and calcium phosphate	Nausea and vomiting: Unexplained nausea and vomiting may be due to stones and a deeper probing into the history may reveal more symptoms.
	ii: Formation of struvite and apatite crystals. Urease-induced Supersaturation appears to be the primary cause of infection-induced urinary stones.	Fever: Fever may occur in children with urinary stones especially if associated with UTI.
		Other symptoms include: frequency, tugging or pulling at the phallus, spontaneous passage of stones[36].

is complex encompassing several physicochemical events occurring sequentially or concurrently. Where by calcium oxalate crystals are retained in the kidney and form renal stones remain incompletely understood. UTI is an important predisposing factor in infants and younger children. The organisms commonly isolated are urease splitting species of *Proteus*, *Klebsellia*, *Pseudomonas*, *Staphylococcus* and some anaerobes. These microbes split urea leading to an increase in the urinary pH, which in turn raises the urinary concentration of magnesium ammonium phosphate ions creating a favourable environment for stone formation.

2.7. Chemistry of urinary stones

The chemical composition of urinary stones in children is similar to those found in adults. About one-half are calcium oxalate, calcium phosphate account for 15-25%, while 10-15% is mixed (calcium oxalate and calcium phosphate). The others are struvite (magnesium ammonium, phosphate) 15-30%, cystine 6-10%, and uric acid 2-10%[29,30].

Due to their relative high densities (based on their calcium content), most of these stones are visible on plain radiographs but some better than others.

The whole summary Urinary stone path physiology is given in Figure 3 and Table 3.

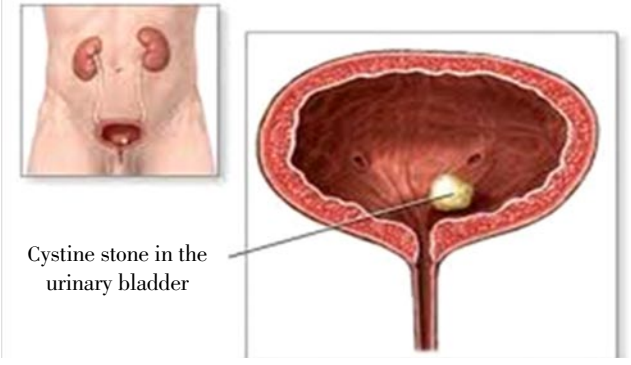


Figure 3. Urinary stone.

3. Herbal drugs

3.1. Pashanbheda drugs

An attempt has been made during the last decade to study the identical, chemistry, pharmacology and clinical investigations of Pashanbheda plants used for dissolving kidney stones[37].

Pashanbheda is a drug mentioned in the Ayurvedic system of medicine for various ailments but mainly as a diuretic and lithotriptic. It is said to have properly of breaking and disintegrating the stones and is widely used drug. However, its identity is yet debatable. Many diuretic and other plants such as *Alternanthera sessalis* and *Aerva spp.* In South India[38]. *Rotula aquatica* in Mysore[39], *Ammaunia baceifera* in Kerala[38], *Bauhinia racemosa*, *Coleus spp.*, *Bryophyllum spp.*, *Didymocarpus pedicellata*, *Ocimum basilicum* in Bengal[40] and many other have been referred to as Pashanbheda from time to time. Now *Bergenia ligulata syn. Saxifrega ligulata* is being widely accepted under this name. Chemical efficiency of *Bergenia ligulata* is dissolving the urinary stones fully justifies the use of various names attributed to it, *viz.*, Pashanbheda, Pashana, Asmaribheda, Ashmabhid, Ashmabhed, Nagabhid, Upalbhedak, Parwatbhed and Shilabhed (dissolving or piercing stones or slabs) etc[41].

The very first mention of this drug in Ayurvedic literature is Charak Samhita (210 BC-170 AD) under the name Pashanbhed. It is recommended for painful micturition, for curing abdominal tumour and for breaking up calculi, Sushruta Samhita (170 AD- 340 BC) mentions the drug under various synonyms in Chikitsa silianam- under the name Pashanbhed for uric acid calculi and Ashnibhid for biliary calculi. In Sushruta Samhita, decoction of Pashanbhed, Ashmantaka, Satavari, Vrihati, Bhalluka, Varuna (Crataeva nurvula), kulatha, kola and kataka seeds have been described for the patients of Vataja Ashmari, while Kusa, Ashmabhid, Patala, Trikantaka, Sirisha, Punarnava and Silajatu and Meduka flower for Pittaja Ashmari have been mentioned[42]. Ashtang Hridaya (341 AD-434 AD) mentions the drugs in chiktsit Sthanam- Upalbhed for extreme pain due to obstructed micturition, Pashanbhed for uric acid calculi and ashmabid for biliary calculi. In Susruta Samhita "Kurantika" or "Sitivaraka" (*Celosia argental*) is tested in 'Viratarvadigana', which is said to have specific action in urinary diseases, *viz.*, calculi (ashmari), gravels (sarkara), dysuria (*mutra krichhra*) and suppression of urine etc. *Aerva spp.*, *Ammania baccifera* and *Nothosasrva brachiata* have been reported from South India as lithotriptic plants[43].*Celosia argental* in Indian system of medicine is considered to be specific for the tratment of ashmari *i.e.*, urinary stone. Aqueous decoction is used for the dissolution and excretion of stones[44]. *Didymocarpus pedicellata*, commonly known as Patharphodi or Shila pushp is useful for stones of kidney and bladder, while *Homonoia riparia*, known as Pashanbhed or kshudra Pashanbhed is useful in vesical calculi. *Rotula aqualica syn. Rhabdia lycioides*, also known as Pashanbhed is useful for stones in bladder. *Bergenia ligulata, syn. Saxifraga ligulata*, known as Pashanbheda have strong diuretic and lithotriptic activities but *Kalanchoe pinnala syn. Bryophyllum calycinum* known as Pashanbhed in Bengal, and others have no diuretic or lithotriptic activity *Bridelia Montana* also known as Pashanbhed has also not shown any such activites[45]. Tribulus terrestris fruits have also been found useful in diuretic and kidney stones[46].

Effective cure of urinary calculi have been prescribed by practitioners in unani system of medicine[47], while in Homoeopathic system of medicine, *Berberis vulgaris, cantharis spp.*, and *Lycopodium spp.* are being use.

Table 4

Lists of plant drugs used in kidney stone, gall stone, urinary calculi[48-52].

S. No.	Botanicals name	Common name	Part use	Used
1.	*Alhagi mannifera* (Leguminosae)	Camels thorn	Roots	For kidney pebbles and Sands
2.	*Armoracia lopathifolia* (Brassicaceae)	Horse radish	Seeds	Diuretic, Kidney Stones
3	*Aerva javanica* (Amaranthaceae)	No Common Name	Seed heads	HerbDiuretic,Purgetive, Demulcent
4.	*Aerva lanata* (Amaranthaceae)	Gorkhabundi	Leaves	Cough,Sorethroat, Diabtes, Lithiasis
5.	*Ammannia baccifera* (Lythraceae)	Dadamari,	Root	Ringworm, Parasitic skin affection, Anti-typhoid, Anti-tubercular properties
6.	*Arctostaphylos ura ursi* (Asteraceaer)	Bearberry	Fruits	Diuretic, Diaphoretic,Gout,Skin affection
7.	*Ascyrum hypericoides* (Asclepidaceae)	Ascus	Root/ Leaves	Emetic and Catharatic
8.	*Asparagus racemosus* (Liliaceae)	Satavar	Root	Herb tonic,Diuretic,Galactagogue
9.	*Abutilon indicum* (L.) Sweet (Malvaceae)	Indian Mallow	Seed & Leaf extract	Extract is given for urinary disorder
10.	*Abutilon indicum* (L.) (Malvaceae)	Indian Mallow	Leaves	Juice taken twice daily for two weeks
11.	*Aegle marmelose*(L.) (Rutaceae)	Wood apple, Bael	Leaves and fruit	1 spoon of Fruit pulp powder is taken orally with coconut milk for 14 days to dissolve kidney stones
12.	*Amaranthus spinosus* (L.) (Amaranthaceae)	Spiny amaranth	Root or plant	1 cup of whole plant is taken
13.	*Amaranthus viridis* (L.) (Amaranthaceae)	Slender Amaranth, Green Amaranth.	All parts	Given in kidney stone
14.	*Argemone maxicana* (L.) (Papaveracea)	Slender Amaranth	Root	Root powder is given for burning urination
15.	*Ageratum conyzoides* (L.) (Asteraceae)	Goat Weed	Leaves	Leaf extract is given twice a day
16.	*Amaranthus caudatus* (L.) (Amaranthaceae)	Love-lies-bleeding	Leaves	Extract is given in kidney stone
17.	*Asphodelus tenuifolius* (Cav.) (Liliaceae)	Weed of fields	Leaves	Decoction of leaves
18.	*Apium graveolens* (Apiaceae)	Lavender	Flowers	Decrease cholesterol level, Condiment.
19.	*Barbarea vulgaris* (Brassicacaea)	Rocket	Roots Leaves	For kidney stone
20.	*Berginia ligulata* (Saxifragaceae)	Pasanabheda	Rhizomes	Astringent.Diuretic, Lithontriptic
21.	*Bridolia montana* (Euphobiaceae)	Chikitsa silianam	Bark	Bark Astringent,Anthelminetic
22.		Sugar beet	Rhizomes	Daily two glass of rhizomes juice is given in kidney stone
23.	*Bombex ceiba* (L.)(Bombacaceae)	Cotton tree	Stem and bark	Given for urinary problems
24.	*Borhaavia difffusa* (Nyctagenaceae)	Hogweed, Punarnava	Root	Root decoction is given daily for one month in kidney stone
25.	*Blumea balsamifera* (Asteraceae)	Sambong	Flowering plant	Diuretic, common cold, urolithiasis expectorant, an anti-diarrheal
26.	*Capsella Bursa-pastori* (Brassicaceae)	Shepherd's-purse	Entire plant	Diuretic, For bladder & kidney spasm
27.	*Cucumis sativus* (Cucurbitaceae)	Cucu	Leaves	Kidney stones, Emollient
28.	*Caesalpinia huga* (Caesalpinioceae)	Nicker nut	Root	Root Diuretic, Lithontriptic
29.	*Citrus japonica* (Rutaceae)	Celery	Whole plant	Antispasmodic, Eczema
30.	*Celosia argentla* (Amararanthacea)	Plumed cockscomb	Leaves /Stem	Diarrhoea,Eye troubles, Sore mouth
31.	*Chelidonium majus* (Papaveraceae)	Chel	Leaves	Diuretic,Antispasmodic, bitter
32.	*Cassia fistula* (L.) (Caesalpinioideae)	Golden shower tree	Fruit	Fruit powder is given with water for 3-4 month to expel the kidney stone
33.	*Ceropegia bulbos* (L.) (Asclepidaceace)	Caudiciform	Tubers	Decoction of tubers is used to remove urinary bladder stone
34.	*Chenopodium album* (L.) (Chenopodiaceae)	Lamb´s Quarters	Leaves	Cokked leaves is given in urinary trouble
35.	*Coculus hirsutus*(L.) (Menispeermacea)	Cocculus Indicus	Leaves	Leaf dried powder is given during burning urination
36.	*Corbichonia decumbens*(Forrsk.) (Molluginacae)	Forssk	Leaves	Crushed leaves given orally
37.	*Costus speciosus* (koen.) (Costaceae)	Keukand	Tubers	Decoction of tubers orally for stones
38.	*Cynodon dactylon* (L.) (Poaceae)	Dog´s tooth grass	Root	Root decoction is given in case of urolithiasis
39.	*Chimaphila numbellata* (Cruciferae)	Prince´s pine	Flower	Diuretic,Expectorant, Stimulant
40.	*Curcuma longa* (Zingiberaceae)	Haldi	Rhizome	Diuretic,Choleretic, Hepatoprotective
41.	*Desmodium styracifolium* (Papilionaceae)	Osbeck	Rhizome	Roots Emmenagogue, Stomachic
42.	*Didymocarpus pedicellata*	Stone Flower	Leaves	Lithontriptic
43.	*Daucas carota*(L.) (Apiaceae)	Wild carrot	Rhizome	One glass juice is given fornight to remove kidney stone
44.	*Digera Muricata*(L.) (Amaranthaceae)	Digera Muricata	Leaves	Once in a day for urinary complains
45.	*Diospyros melaoxylon* (Rox) (Ebenaceae)	Digera Muricata	Fruit and bark	Fruit is given in urinary disorders
46.	*Dolichos biflorus* (Leguminaceae)	Horse gram	Seeds	Diuretic,Astringent, Tonic

Table 4, continued

Lists of plant drugs used in kidney stone, gall stone, urinary calculi[48-52].

S. No.	Botanicals name	Common name	Part use	Used
47.	*Elettaria cardamomum* (Zingiberaceae)	Cardamom	Seeds	Diuretic,Carmintive, Aromatic stimulant
48.	*Equisitum arvense* (Equisetaceae)	Horsetail	Seeds	Diuretic,Dropsy, Graval,Renal affection
49.	*Fogonia bruguieri* (Umbelliferae)	Fagonia	Fruit	Diuretic, Mildly carminative
50.	*Ficus carica* (Moraceae)	Fig	Fruit, latex	Destroy urinary & gall Stone
51.	*Garcinia pictoria* (Guttiferae)	Tamal. Pers.	Leaves	Dropsical affection
52.	*Gynocardia odorata* (Flacourtiaceae)	Coffee Plum	Fruit	Fish poision,Insecticidal,Skin aliments
53.	*Gomphrena celosioidest* (Amaranthaceae)	Gomphrena Weed	Whole plant	Juice is given twice a day for ten days
54.	*Grewia flavescens* (A.Juss) (Tiliaceae)	Sandpaper Raisin	Root	Decoction of root powder to stop bleeding in urine
55.	*Hygrophila spinosa* (Acanthaceae)	Gokulakanta	Leaves	Strongly Diuretic
56.	*Lavendula Officinalis* (Lamiaceae)	Ginger	Rhizomes	Stop bleeding, Ant rheumatism
57.	*Mentha piperita* (Lamiaceae)	Peppermint	Entire herb	Treatment in stone disease
58.	*Mimosa pudica* (Mimosaceae)	Touch-me-not	Leaves	Gravel, Urinary complaints
59.	*Ocimum* (Labiatae)	Holy Basil, tulsi	Leaves	Stomachic, alexipharmac, antipyretic, antihelminitic
60.	*Onosma bracteatum* (Boraginaceae)	Sedge	Leaves	Tonic,Demulcent, Diuretic, Spasmolytic
61.	*Olea europeae* (Oleaceae)	Olive	Oil	Treatment of kidney stone
62.	*Pavonia odorata* (Malvaceae)	Fragrant Swamp Mallow	Rhizomes, Leaves	Antipyretic, Stomachic, Refrigerent, Dysentery
63.	*Pimpinella anisum* (Umbelliferae)	Anise	Fruit	Antispasmodic, Diuretic, Treatment of kidney stones
64.	*Pedalium murea* (Pedaliaceae)	Burra Gokhru	Fruits	Decoction of fruit is used for urinary complains
65.	Phy1llanthus emblica(L.) (Euphorbiaceae)	Gooseberry or amla	Seed Powder	Given to avoid burning urination
66.	*Phyllanthus fraternus* (Webster.) (Euphorbiaceae)	Gulf leaf-flower	Whole plant	Plant extract is given orally for 3-4 day to dissolve the stones
67.	*Rosmarinus officinalis* (Lamiaceae)	Rosemary	Leaves	Relive menstrual cramps, increase, urine flow, and reduce kidney pain
68.	*Rubia cordifolia* (Rubiaceae)	Madder or Indian Madder	Leaves, Roots	Antidysentric,Antiseptic,Deobstruent
69.	*Solanum surattence* (Solanaceae)	Yellow-Berried Nightshade	Roots	Root decoction is given for seven day
70.	*Santalum album* (Solanaceae)	White sandal	Oil	For urinary bladder.
71.	*Tectona grandis* (Verbenaceae)	Teak	Wood	Urinary discharge
72.	*Theobroma cocao* (Malvaceae)	Cacoa	Seed	urinary tracts diseases
73.	Tamarind indica (Fabaceae)	Tamarindus	Fruits	For kidney and gall stone
74.	*Tinospora cordifolia*(Wild L) (Menispermaceae)	Guduchi	Stem	Crushed stem to expel the stone
75.	*Tribulus terrestis*(L) (Zygophyllaceae)	Puncture Vine	Leaves	Used in treatment of kidney stone
76.	*Tridex procumbens*(L.) (Asteraceae)	Coat buttons	Leaves	Leaf paste is given for kidney stone
77.	*Tubiflora Acaulis*(L.F.) (Acanthaceae)	Kuntze	Leaves	Leaf powder with water is given for urinary complains
78.	*Urgina maritime* (Asparagaceae)	Squill bulb	Bulb leaves	Diuretic
79.	*Urtica dioica* (Urticaceae)	Stinging nettles	Roots	Diuretic.
80.	*Vernomia cineea* (Compositae)	Little iron weed	Leaves	Anthelmintic, Diarrhoea
81.	*Zingiber Officinale* (Zingiberaceae)	Ginger	Rhizomes	Stop bleeding, Ant rheumatism
82.	*Zea mays* (Poaceae)	Maize	Seeds Oil /Tassel	For bladder & Kidney spasm. Given orally to expel the stone

3.2. Herbal drugs used in kidney stone, gall stone, urinary calculi

Herbal drugs used in kidney stone, gall stone, urinary calculi are defined below in Table 4. Most of these remedies were taken from plant and proven to be useful. They are reported to be effective with no side effects[53,54].

3.3. Researchers reported for stone dissolving activity

1) Aqueous and alcohol extracts of *Jasminumauriculatum Vahl* (Oleaceae) flowers are reported for kidney stone[55]. 2) Aqueous of extracts of *Herniaria hirsuta L.* are reported for nephrolethiasic[56]. 3) Ethanolic extracts of leaves of

Table 5
List of synthetic drug used in treatment of stone diseases[67].

S.No	Drugs	Category	Mechanism of action	Uses
1.	Amiloride (Midamor)	Diuretics	Na^+ reabsorption in late distal tubule and collecting duct	Kidney diseases
2.	Allopurinol (Lupurin, Zyloprim)	Analogue of hypoxanthine	It inhibits xanthine oxidase and prevent the synthetic of urate	Urinary infections, Calculi.
3.	Cholestyramine (Questran)	Bile acid sequestrates	Increases in hepatic LDL receptors.	Kidney diseases.
4.	Cholic acid	Bile acid derivatives	It induces bile flow, feedback	Gall stone diseases.
5.	Digoxin (Lanoxin)	Cardiac glycoside	Inhibition of Na^+, K^+ ATPase	Ailments of kidney diseases
6.	Etidronate disodium	Bisphosphonate	It prevent hydroxyl apatite Dissolution	Kidney stones
7.	Fluvastatin (Lescol)	Statin	Reduction of LDL levels. It competitive inhibit	Gall stone diseases
8.	Gemfibrozil	Fibric acid derivatives	It reduces triglycerides through PPAR a moderated stimulation of Fatty acids oxidations	Gall bladder diseases
9.	Indinavir	Peptidomimetic hydroxyethylene	It reversely binds to the active site o	HIV diseases, Kidney diseases
10.	Zonisamide	Sulphonamide Derivatives		Ailments of stone diseases

hibiscus sabdariffa linn are used for kidney stone[57]. 4) The acute diuretic effect of the water extract of the aerial parts of *Retama raetam* (RR) is used for kidney ailments[58]. 5) The chronic diuretic effect of the water extract of the whole plant of *Spergularia purpurea* are used for kidney stone[59]. 6) Aqueous extracts *Rosmarinus officinalis* and *Centaurium erythraea* are used for kidney ailments[60]. 7) Ethanolic extract of *Ammannia baccifera (Bhatjambol)* was found to be effective in reducing the formation of urinary stones (prophylactic)[61]. 8) *Crateva nurvala (Varun)* were found to possess significant anti-hyperoxaluric and anti-hypercalciuric activity[62]. 9) The Aqueous extracts *Sesbania grandiflora* are used for antiurolithiatic[63]. 10) The Aqueous extract of the bark of *Raphanus sativus* was tested for its antiurolithiatic and diuretic activity[64].

3.4. Plants acting on gall stones

Different types of plants used in the treatment of gall stones are *Apium graveolens, Bauhinia cumanensis, Bauhinia excise, Costus scaber, Chamaesyce hirta, Cissus verticillata, Capraria biflora, Cocos nucifera, Eleusine indica, Ficus carica, Gomphrena globosa, Kalanchoe pinnata, Portulaca oleraceae, Solanum melongena*[65].

3.5. Challenges and future aspects of medicinal plants

Today medicinal plants are very important for the growth of new drugs. People are using herbal drugs because of its safety, efficacy and lesser side effects. Plants and plant products have utilized with varying success to cure and prevent diseases. At present demand of natural plants derived products are increasing day by day in global countries[66].

3.6. Allopathic medicines

Depending on the result of 24 hour urine collection, there are different treatment options for different stone types. Now there is convincing evidence that by treating specific biochemical abnormalities, the recurrence rate can be reduced. The three most commonly used classes of medications for stone prevention are enlisted here. List of synthetic drug used in treatment of stone diseases is given below in Table 5.

4. Conclusion

As evident from the above discussion, nature is the best combinatorial chemistv and has possible answers to all diseases for mankind. Medicinal plants play a vital role in stone diseases. The undesirable effect of the modern medicine has already diverted the attention of the people towards herbal medicines. To increase the acceptability and awareness among the people, there is an urgent need to develop trust and faith towards the safer indigenous system by establishing its validity in treatment for various diseases. Health care systems are going to become more and more expensive, therefore we have to introduce herbal medicine systems in our health care. Lets us hope that in future natural products will be competing modern medicines with added advantages of more safety and lower costs.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

The manuscript is mainly focused on understanding the pathophysiology of urinary stones and discussing the herbal treatments that can be used to cure the patients with urinary stones. Herbs have been look upon as the source of cure for many disorder including urinary stones from ancient time due to their vast medicinal properties.

Research frontiers

The work gives sufficient information for the readers as well as the researchers to exploit the naturally available medicinal plants as therapeutic drugs to combat with complications associated with kidney, gall bladder and urinary stones.

Related reports

Very few articles are available which describes the role of medicinal plants in treating kidney, gall bladder and urinary stones based on its pathophysiology. The present work is related to the previously published reports in the fact it gives detailed information of pathophysiology of kidney, gall bladder and urinary stones but the manuscript also covers the medicinal plants having potential to remove the stones.

Innovations & breakthroughs

The authors have compiled the medicinal properties of some native herbs and the active principles present in them that can be explored as therapeutic agents in chronic stone conditions, where the current conventional treatments are not satisfactory and are full of adverse effects. The herbs are suggested based on the pathophysiology of these stones, thereby suggesting the possible mechanism of action of these plants.

Applications

The work gives specific information regarding the chemistry and therapeutic utility of each herb that is being covered and can be explored foer their medicinal properties.

Peer review

It is a systematic review that clearly focuses on first explaining the pathophysiological pathways of kidney, gall bladder and urinary stones followed by the medicinal plants that can be exploited to develop new therapeutic entities. The compilation of medicinal plants and their properties in Table 4 provides much clarity about the topic.

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