



ANTIUROLITHIATIC EFFECTS OF MEDICINAL PLANTS: A REVIEW

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ABSTRACT

Kidney stone formation is a complex that results from a succession of several physicochemical events including supersaturation, nucleation, growth, aggregation and retention within the kidneys. Urinary stones affect 10-12 % of the population in industrialized countries. The problem of the stone formation is considered as a medical challenge due to its high rate of recurrence and also due to multifactorial etiology. So, in the present review aims to give data highlighting the present trends in research of medicinal plants accredited with antiurolithiatic activity. This article may help investigators to develop effective drug for urolithiasis.

Keywords: Antiurolithiatic, Calcium oxalate, Kidney stones, Medicinal plants, Renal calculi, Nephrolithiasis

INTRODUCTION

Formation and recurrence of kidney stones, one of the biggest challenges faced by urologists today, remains a major source of morbidity in humans [1]. This increasing urological disorder of human health affecting about 12% of the world population has been associated with an increased risk of end-stage renal failure. This growing trend

is believed to be associated with changes in lifestyle modifications such as lack of physical activity and dietary habits and global warming. Recurrent stone formation is a common problem with all types of stones and therefore an important part of the medical care of patients with stone disease [2].

In the United States, kidney stone affects 1 in 11 people, and it is estimated that 600,000 Americans suffer from urinary stones every year. In Indian population, about 12% of them are expected to have urinary stones and out of which 50% may end up with loss of kidney functions [3]. The prevalence of urolithiasis is on the rise due to various changes in the socio-demographic and other etiological factors in the north-eastern states of India in general and Manipur in particular [4]. Stone formation in the kidney is one of the oldest and most wide spread diseases known to man. Urinary calculi have been found in the tombs of Egyptian mummies dating back to 4000 BC and in the graves of North American Indians from 1500 to 1000 B.C. Reference to Stone formation is also documented in the early Sanskrit documents during 3000 and 2000 B.C [5].

In general, urolithiasis affects all age groups from less than 1 year old to more than 70, with a male to female ratio of 2:1. The peak age for the development of calcium oxalate stones was between 50–60 years. The risk of stone formation is generally high in men; however, it is becoming more common in young women. Men are at greatest risk of developing kidney stones with incidence and prevalence rates between 2–4 times that of women which could be due to the larger muscle mass of men as compared to women. This higher rate of occurrence in men than in women can also be due to enhancing

capacity of testosterone and inhibiting capacity of oestrogen in stone formation. Also, the increase daily breakdown of the tissues in men could result in increased metabolic waste and a predisposition to stone formation. The other more significant cause may be because of the male urinary tract being more complicated than the female urinary tract. Estrogen may also help to prevent the formation of calcium stones by keeping urine alkaline and raising protective citrate levels. However, recently there are reports of dramatic increase during the period from 1997 to 2002 in the prevalence of stone disease among females and a change from a 1.7:1 to 1.3:1 male to female ratio. The increasing incidence of nephrolithiasis in women might be due to lifestyle associated risk factors, such as obesity. Some reports have described that vegetarian are at lower risk for stone formation in contrast to non-vegetarians [1]. Globally, kidney stone disease prevalence and recurrence rates are increasing, with limited options of effective drugs. Urolithiasis affects about 12% of the world population at some stage in their lifetime. It affects all ages, sexes, and races but occurs more frequently in men than in women within the age of 20–49 years. If patients do not apply metaphylaxis, the relapsing rate of secondary stone formations is estimated to be 10–23% per year, 50% in 5–10 years, and 75% in 20 years of the patient. However,

life time recurrence rate is higher in males, although the incidence of nephrolithiasis is growing among females. Therefore, prophylactic management is of great importance to manage urolithiasis. Recent studies have reported that the prevalence of urolithiasis has been increasing in the past decades in both developed and developing countries. This growing trend is believed to be associated with changes in lifestyle modifications such as lack of physical activity and dietary habits and global warming. In the United States, kidney stone affects 1 in 11 people, and it is estimated that 600,000 Americans suffer from urinary stones every year. In Indian population, about 12% of them are expected to have urinary stones and out of which 50% may end up with loss of kidney functions [3].

Studies on the geographic variation in the prevalence of kidney stone disease have shown a 50% higher prevalence in the southeast (the 'kidney stone belt') than the northwest, possibly associated with a changing state of dehydration related to high summertime temperatures and resulting in a low urine volume. Given the temperature rise worldwide due to the effects of global warming, it has been predicted that there could be an increase of 1.6–2.2 million lifetime cases of kidney stone by 2050, particularly in the southeast regions of the USA [6].

A large number of people are suffering from urinary stone problem all over the globe. Not only the humans but animals and birds also suffer from the urinary stone problem. The occurrence in some areas is so alarming that they are known as Stone Belts. Urinary stone disease is a common disorder estimated to occur in approximately 12% of the population, with a recurrence rate of 7081% in males, and 4760% in females. Approximately 50% of patients with previous urinary calculi have a recurrence within 10 years. Stone disease is 2-3 times more common in males than in females. Most urinary calculi occur in patients aged 20 to 49 years [7].

LITERATURE SEARCH

METHODOLOGY

In this study, at first, the search was done by keywords such as “nephrolithiasis”, or “kidney stone” or “urolithiasis”, or “renal calculi”, or “renal stone”, CaOx stones, medicinal plants and herbal therapy from electronic databases such as Google Scholar, PubMed, Science Direct, etc. Related articles were selected for review.

RESULTS

The number of identified plants according to the results obtained, but only in vivo study was included. Additional information is shown in **Table 1**.

Table 1: In vivo studies of Medicinal Plants against nephrolithiasis

Sr. No	Name	Parts and Family	Extracts/Fraction	Urolithiasis Model	Days of study	Maximum tolerated dose (MTD)/Therapeutic doses (mg/kg)	Constituents/Possible mechanism responsible for this effect
1.	<i>Abelmoschus moschatus</i> [8]	Seed (Malvaceae)	Chloroform Methanolic	Surgical implantations of zinc disc	7	100, 200, 400	Diuretic, Antioxidant, Free-radical scavenging properties
2.	<i>Adiantum capillus veneris</i> [9]	Fronds (Unani system)	Hydro alcoholic (50%-50%)	0.75% EG and 1% AC	21	127.6 255.2	Anti-inflammatory, Antimicrobial, Antioxidant activities
3.	<i>Aerva Javanica</i> [10]	Plant powders (Amaranthaceae)	Alcoholic Aqueous Ethyl acetate	0.75% EG	28	2000/ 200 400	Increased diuresis and lowering the urinary concentrations of stone forming constituents.
4.	<i>Agaricus bisporus (button mushroom)</i> [11]	Dried fruiting bodies (Agaricaceae)	Aqueous	0.75% EG	49	100	Affecting NF-κB activation, extrinsic apoptosis and intrinsic apoptosis pathways.
5.	<i>Alcea rosea</i> [12]	Root (Malvaceae)	Hydroalcoholic ethanol (70%)	1% EG	28	170	Diuretic, anti-inflammatory effects
6.	<i>Alphonsea sclerocarpa</i> [13]	Leaves (Annonaceae)	Ethanolic	0.75% EG	28	2000/ 250 500	Increased diuresis and lowering of urinary concentrations of stone-forming constituents
7.	<i>Ammi visnaga</i> [14]	Fruits (Apiaceae)	Aqueous	0.75% EG and 1% AC	14	125, 250, 500	
			Khellin visnagin			5, 10	
8.	<i>Angelica sinensis polysaccharide</i> [15]	Roots (Umbelliferae)	Aqueous	1% EG	28	80 320	ROS modulatory effect
9.	<i>Annona squamosa</i> Linn. [16]	Leaves (Annonaceae)	Ethanolic	0.75% EG	28	250 500	Improving the renal antioxidant status and cell membrane integrity, inhibition of crystal nucleation, aggregation, and growth, by increasing urine volume, pH, and anticalcifying activity and regulation of oxalate metabolism.
10.	<i>Benincasa hispida</i> [17]	Seeds (Cucurbitaceae)	Ethanolic	0.75% EG	34	250 500	Increased diuresis and lowering of urinary concentrations of stone forming constituents
11.	<i>Berberis trifoliata (Mahonia trifoliata)</i> [18]	Leaves (Berberidaceae)	Methanolic	zinc disc implantation	20	50, 100, 150	Excretion of small particles from the kidney and reduce the chance of them being retained in the urinary tract.

12.	<i>Berberis vulgaris</i> [19]	Roots (Berberidaceae)	Aqueous-Methanol n-butanol fraction Aqueous fraction	0.75% EG and 1% AC	21	50 10,40	Inhibition of calcium oxalate crystallization and antioxidant activity
13.	<i>Bergenia ciliata</i> Haw [20]	Rhizomes (Saxifragaceae)	Hydro-methanol	0.75% EG	28	3000/150, 300	Antioxidant activity, lowering of urinary concentrations of stone-forming constituents.
14.	<i>Bergenia ligulate</i> [21]	Rhizome (Saxifragaceae)	Aqueous-Methanolic (70% methanol in water (v/v))	0.75% EG and 1% AC	21	5, 10	CaC ₂ O ₄ crystal inhibition, diuretic, hypermagnesuric and antioxidant effects
15.	<i>Biophytum sensitivum</i> (L.) DC [22]	Whole plant material (Oxalidaceae)	Methanolic	zinc disc-implanted	7	100, 200, 400	Diuretic, antioxidant and anti-inflammatory effects
16.	<i>Blumea balsamifera</i> (Sambong) [23]	Leaves (Asteraceae)	Decoction	0.75% EG and 2% AC	21	50%, 100%, 200% sambong	Diuretic, direct chemolytic effect.
17.	<i>Boldoa purpurascens</i> Cav. [24]	Leaves (Nyctaginaceae)	Aqueous	0.75% EG and 2% AC	10	100, 200, 400	Antioxidant, anti-inflammatory, antimicrobia inhibition of all phases of CaOx stone formation (nucleation, growth and aggregation),
18.	<i>Bombax ceiba</i> L [25]	Fruits (Bombacaceae)	Ethanol Aqueous	0.75% EG	28	400	Increased diuresis and lowering of urinary concentrations of stone forming constituents.
19.	<i>Bryophyllum pinnatum</i> Lam. [26]	Leaves (Crassulaceae)	Hydroalcoholic	NaOx, 70 mg/kg, i.p	14	50, 100, 200	Antioxidant nephroprotective properties as well as a reduction in urinary stone forming constituent concentrations
20.	<i>Caffeic acid</i> [27]			0.75% EG and 1% AC	28	20, 40	
21.	<i>Cerasus Avium</i> [28]	Stem (Rosaceae)	Aqueous	1% EG	30	200 400	Anti-inflammatory, Antioxidant, Antibacterial, Anti-fat properties.
22.	<i>Chenopodium album</i> Linn. [29]	Leaves (Chenopodiaceae)	Methanolic Aqueous	0.75% EG	28	2000/100, 200, 400	Inhibitory effect on crystallization and stone dissolution
23.	<i>Cissampelos pareira</i> [30]	Roots (Menispermaceae)	Alcoholic	0.75% EG and 2% AC	10	2,000/100, 200, 400	Combination of antioxidant, diuretic, hypocalciuric, hypermagnesiemia and urine alkalinizing activities
24.	<i>Citrullus Lanatus</i> (watermelon) [31]	Fruits (Cucurbitacea)	Ethanol	0.75% EG and 1% AC	21	200	Steroids and long chain alkanes
25.	<i>Citrus medica</i> Linn [32]	Fresh unripe fruits (Rutaceae)	Flavanoid rich fraction	0.75% EG	28	320 µg/kg, 380	Increased diuresis, lowering of urinary concentrations of stone forming

						µg/kg, 440 µg/kg	constituents and increase in inhibitors level,
26.	<i>Copaifera langsdorffii</i> [33]	Leaves (Fabaceae)	Hydroalcoholic (Aqueous ethanol 7:3)	CaOx pellets	48	20	Flavonoid heterosides and other phenolic compounds
27.	<i>Costus igneus</i> [34]	Stem (Costaceae)	Aqueous	0.75% EG	28	1,000/100	
	Ethanollic		Lupeol			500/50 100	
			stigmasterol			500/50 100	
28.	<i>Costus spiralis Roscoe</i> [35]	Brazilian folk medicine (Zingiberaceae)	Aqueous	Implantation of a zinc disc	56	0.25 and 0.5 g/kg	Increased diuresis and excretion of urinary salt forming stones.
29.	<i>Crataeva nurvala</i> [36]	Bark Root (Capparaceae)	Methanolic	0.75% EG and 2% AC	10	150, 300	Lupeol
30.	<i>Crocus sativus</i> L. (saffron) [37]	Powder (Iridaceae)	Aqueous	0.75 % EG and 1 % AC	30	25, 50 and 100	Antioxidant property and lowering of some urinary concentrations of stone forming constituents.
31.	<i>Cynodon dactylon</i> [38]	Roots (Poaceae)	Ethanollic	1 % EG	28	3.2 12.6	
32.	<i>Desmodium styracifolium and Pyrrosiae petiolosa</i> [39]	Chinese herbs	Aqueous	calculi producing diet (CPD),	21	275, 550, 1100	By rising urinary Citrate excretion, decreasing urinary calcium, diuresis, and antioxidative effects.
						150, 300, 600	
33.	<i>Desmodium styracifolium</i> [40]	Aerial part (Fabaceae)	Petroleum ether	1 % EG and 2 % AC	28	2.16	Inhibition of CaOx crystal aggregation as well as the alleviation of oxidative injury
			Chloroform			1.008	
			Ethyl acetate			0.576	
			n-butyl alcohol			1.584	
34.	<i>Dichrostachys cinerea</i> [41]	Root (Fabaceae)	Ethanollic	0.75% EG	28	2000/ 200 400	
35.	<i>Diosmin</i> [42]			0.75% EG and 2% AC	15	10 g/kg/ 10 20	Antioxidant, anti-inflammatory effects and protective effects of microcirculation.
36.	<i>Dolichos biflorus and Crataeva nurvala</i> [43]	(Seed + bark) (Fabaceae + Capparidaceae)	Hydroalcoholic Aqueous	0.75% EG	35	[D.b + C.n: 1:1] [D.b + C.n: 3:1] 500mg/kg	
37.	<i>Dolichos biflorus</i> [44]	Seeds (Fabaceae)	70% hydro-alcoholic	0.75% EG		3000 150, 300	
38.	<i>Foeniculum vulgare (Fennel)</i> [45]	Seeds (Umbelliferae)	Ethanollic	1% EG	14	100 200 300	Flavonoids, phenols, and various fatty acids antioxidant nature
39.	<i>Ferulic acid</i> [46]	-----	-----	0.75 % EG	28	40 80	Its antioxidant nature

40..	<i>Flos carthami (Carthamus tinctorius)</i> [47]	Chinese medicine Asteraceae	-----	0.75% EG	28	300 600 1,200	
41.	<i>Glechoma longituba</i> [48]	Aerial part (Labiatae)	Aqueous	1 % EG	28	220 440 880	Increasing antioxidant levels, decreasing urinary stone-forming constituents and urolithiasis-related protein expression, and elevating urinary citrate levels.
42.	<i>Glochidion velutinum</i> [49]	Leaves (Euphorbiaceae)	Methanolic	0.75% EG and 1% AC	21	250 500	Inhibition of CaOx crystal formation and its effect on the urinary concentration of stone-forming constituents
43.	<i>Gomphocarpus fruticosus</i> [50]	Ethiopian folk medicine Leaves (Apocynaceae)	Petroleum ether, chloroform, ethyl acetate, butanol, water	0.75% EG and 1% AC	28	200	
44.	<i>Gymnema sylvestre R.Br</i> [51]	Leaves (Apocynaceae)	Ethanollic	0.75% EG and 1% AC	28	4000 200, 400	Potent diuretic activity and presence of phytochemicals such as alkaloids, phenols, flavonoids, saponins
45.	<i>Helichrysum graveolens (M.Bieb.) Sweet</i> [52]	Flowers (Asteraceae)	Aqueous	NaOx, 70 mg/kg, i.p	10	62.5, 125	High phenolic contents
	<i>Helichrysum stoechas ssp. barellieri (Ten.) Nyman (HS)</i>					78, 156	
46.	<i>Helichrysum plicatum DC. subsp. Plicatum</i> [53]	Flowers (Compositae)	water: absolute ethanol (1:1)	1% EG and 1% AC	21	125, 250 500	A rich flavonoid content, such as helichrysin A and B, apigenin, naringenin, isostragalol, and isosalopurposide (So, antioxidant activity)
47.	<i>Herniaria hirsute</i> [54]	Caryophyllaceae		0.75% EG	21	1ml of decoction	
48.	<i>Hibiscus sabdariVa L.</i> [55]	Calyces (Malvaceae)	Aqueous	0.75% EG and 2 % AC	28	2010/ 250, 500, 750	Increased diuresis and lowering of urinary concentrations of stone-forming constituents.
49.	<i>Holarrhena antidysenterica</i> [56]	Seeds (Apocynaceae)	Aqueous-methanolic extract	0.75% EG and 1% AC	21	30 100	Multiple pathways including inhibition of the CaOx crystal aggregation, antioxidant and epithelial cell protective effects
50.	<i>Homonía riparia</i> [57]	Roots (Euphorbiaceae)	Ethanol	Rat feed mixed with 3% w/w glycolic acid	30	8 g/kg 2 g/kg	

51.	<i>Hordeum vulgare</i> [58]	Seeds (Poaceae)	Ethanolic	0.75% EG	28	5/ 100 250 500	Diuretic, antioxidant, nephroprotective property, and lowering the concentration of urinary stone-forming constituents.
52.	<i>Hygrophila spinosa</i> [59]	Whole plants (Acanthaceae)	Aqueous	0.75% EG	28	200	The alkaloids, phytosterols, mucilage and fixed oil
53.	<i>Hypericum Perforatum L.</i> [60]	Leaves (Hypericaceae)	Hydroalcoholic	1% EG with 0.5 % AC	28	300 500	Diuretic activity
54.	<i>Ichnocarpus frutescens</i> ^[61]	Roots (Apocynaceae)	Ethyl acetate	0.75% EG	28		
55.	<i>Indigofera tinctoria</i> [62]	Roots (Fabaceae)	Ethanolic	0.75% EG	30	2000/ 200 400	Inhibiting the synthesis of oxalate
56.	<i>Ipomoea eriocarpa</i> [63]	Leaves (Convolvulaceae)	Ethanol	1 % EG and 1% AC	28	200	To increased diuresis and lowering of urinary concentrations of stone-forming components.
57.	<i>Ipomoea reniformis</i> [64]	Leaves (Convolvulaceae)	Ethanolic	0.75% EG	28	200 400	Presence of flavonoids
58.	<i>Jasminum auriculatum Vahl</i> [65]	Flowers (Oleaceae)	Aqueous Alcohol	0.75% EG	28	2500 250	Increased diuresis and lowering of urinary concentrations of stone forming constituents
59.	<i>Lagenaria siceraria</i> [66]	Fruit powder (Cucurbitaceae)	Fruit powder suspension	NaOx, 70 mg/kg, i.p	7	500	Flavonoid and triterpenes present in <i>LSFP</i> might have been responsible for the reduction of CaOx crystal aggregation and stone formation in kidney
60.	<i>Lantana camara</i> [67]	Roots (Verbenaceae)	Ethanolic Oleanolic acid	Zinc disc implantations	10	200 60 80 100	
61.	<i>Launaea Procumbens</i> [68]	Leaves (Asteraceae)	Methanolic	0.75% EG and 1% AC	21	150 300	Antioxidant, Nephroprotective properties and also lowering the concentration of urinary stone-forming constituents.
62.	<i>Lemon juice</i> ^[69]			0.75% EG and 2 % AC	10	6 µl lemon juice solution/g body weight	
63.	<i>Lupeol (Crataeva nurvala. Buch Ham.)</i> [70]	-----	-----	zinc implantation	15	35	

64.	<i>Mallotus philippinensis</i> Lam. [71]	Leaves (Euphorbiaceae)	Alcoholic	0.75% EG	28	2000 250 500	Alkaloids, triterpenoids and flavonoids
65.	<i>Malva Neglecta</i> Wallr [72]	Leaves (Malvaceae)	Aqueous	1% EG and 0.25% AC	28	200 800	Due to the components presented in this plant such as saponins, flavonoids, mucilage, and phenolic compounds.
66.	<i>Mangifera indica</i> [73]	Seeds (Anacardiaceae)	Aqueous methanol (20:80)	0.75% EG and 1% AC	25	250; 500 1000	To restoring the normal antioxidant levels, diuresis, hypocalciuria, hypermagnesemia, urinary alkalization and hypercitrauria.
67.	<i>Melia azedarach</i> ^[74] [75]	Leaves (Meliaceae)	Aqueous Ethanol	0.75% EG	28	250	
68.	<i>Mimusops elengi</i> [76]	Bark (Sapotaceae)	Petroleum ether extract Chloroform Alcohol	0.75% EG	28	2000/ 200	
69.	<i>Moringa oleifera</i> Lam [77]	Roots (Moringaceae)	Aqueous Alcoholic	0.75% EG	28	2000/ 200	Diuresis and lowering of urinary concentrations of stone forming constituents.
70.	<i>Moringa oleifera</i> Lam. [78]	Seeds (Moringaceae)	Aqueous alcoholic	0.75% EG and 1% AC	21	10 g/kg 100, 300, 500	Antioxidant potential, urine alkalinizing and diuretic effects
71.	<i>Musa paradisiaca pseudostem</i> [79]	Pseudostem (Musaceae)	Hydro-ethanol	0.75% EG and 1% AC	28	3000 100, 150, 200, 250, 300	Inhibiting various pathways involved in renal CaOx formation, antioxidant effect, and potential to inhibit biochemical parameters involving in impairment of renal function.
72.	<i>Nigella sativa</i> [80]	Seeds (Ranunculaceae)	Seeds oil	0.75% EG and 1% AC	25	5 ml/kg b.w	Antioxidant
73.	<i>Olive oil (Olea europaea)</i> [81]	Olive oil	Olive oil	0.75% EG	28	1.3 and 1.7 mL/kg	Antioxidant properties
74.	<i>Origanum vulgare</i> [82]	Aerial Part (Lamiaceae)	Aqueous-methanol (30:70)	0.75% EG and 1% AC	21	10 30	Combination of CaOx crystal inhibitory, diuretic, antioxidant, antispasmodic, epithelial cell protective, hypocalciuric 75.and hypercitrauric effects

75.	<i>Paronychia argentea</i> [83]	Aerial parts (Caryophyllaceae)	Aqueous	NaOx, 70 mg/kg, i.p	28	2000/ 250 500	Lowering of urinary concentrations of stone forming constituents, Antioxidant activity and free radical scavenging
			Butanolic			40/ 10 20	
76.	<i>Pedaliium murex</i> L. [84]	Whole plants (Pedaliaceae)	Ethyl acetate	Magnesium oxide (0.4%) 1.0 ml/rat/day	28	300	
77.	<i>Peperomia tetraphylla</i> [85]	Plant powdered material (Piperaceae)	Methanolic Chloroform	0.75% EG	28	200 400	
78.	<i>Pergularia daemia</i> [86]	Whole-Plant (Asclepediaceae)	Hydroalcoholic (50% alcohol)	0.75% EG	28	2000/ 400	Diuretic properties and lowering of urinary concentrations of stone-forming constituents, which may be attributed to the presence of alkaloids, triterpenoids and flavonoids.
79.	<i>Pericampylus glaucus</i> [87]	Leaves (Menispermaceae)	Ethanol	0.75% EG	30	2000 200 and 400	
80.	<i>Petroselinum Sativum</i> [88]	aerial parts and roots (Umbelliferae)	Aqueous	1% EG	30	200 600	Increasing diuresis and lowering urinary concentrations of stone forming constituents
81.	<i>Peucedanum grande</i> C. B. Clarke [89]	Fruits (Umbelliferae)	Hydroalcoholic extract (50% distilled water and 50% ethanol) for	0.75% EG and 1% AC	21	56 97	Flavonoids and saponin The free radical scavenging, ant inflammatory and anti-microbial activity
82.	<i>Phlogacanthus thyriformis</i> Hardow [90]	Flower (Acanthaceae)	Aqueous silver nanoparticles	0.75% EG	28	200 10	Flavonoids
83.	<i>Phoenix dactylifera</i> L [91]	Fruits (Arecaceae)	n-butanol Aqueous	0.75% EG	28	200	
84.	<i>Phyllanthus niruri</i> ^[92]	Whole plant (Phyllanthaceae)	Aqueous	Introducing a CaOx disk	50		
85.	<i>Piper cubeba</i> L. [93]	Fruits (Piperaceae)	hydroalcoholic	0.75% EG and 1% AC	22	35 60	Flavonoid and alkaloids are responsible
86.	<i>Pleurotus ostreatus</i> (Oyster mushroom) [11]	Fruiting bodies (Pleurotaceae)	Aqueous	0.75% EG	28	100 mg (infused in 5 mL boiling distilled water)/kg b.w.	via affecting NF-kB activation, extrinsic apoptosis and intrinsic apoptosis pathways.
87.	<i>Polygonum Aviculare</i> L. [94]	Leaves (Polygonaceae)	Aqueous	1% EG and .25% AC	28	100 400	Saponins and phenolic and flavonoid substances, and has

							fat-reducing, anti-oxidant, antibacterial and diuretic effects,
88.	<i>Pomegranate Juice</i> [95]			0.75% EG	45	50 µL PJ/d 100 µL PJ/d	
89.	<i>Punica granatum</i> [96]	Fruits (Lythraceae)	Chloroform and Methanol	0.75% EG	28	100, 200 400	Antioxidant, Anti-inflammatory
90.	<i>Radix Paeoniae Alba</i> [97]	Root (Ranunculaceae)	Aqueous	1% EG	28	220 260	
91.	<i>Raphanus sativus</i> [98]	Tubercles (Brassicaceae)	Aqueous	Insertion of zinc disc		40 70 140	
92.	<i>Ricinus communis</i> [99]	Leaves (Euphorbiaceae)	Petroleum Extract Chloroform Benzene Extract Ethanollic	0.75% EG	28	2000 200	Diuretic, antioxidant effect and lowering of the stone forming constituents
93.	<i>Rosa canina L.</i> ¹ [100]	Fruit (Rosaceae)	Hydroalcohol (Methanol and water 1:1)	1% EG	30	250 500	
94.	<i>Rotula aquatica Lour</i> [101]	Roots (Boraginaceae)	Alcoholic	1% EG	28	200	Diuresis and lowering of urinary concentrations of stone forming constituents.
95.	<i>R. cordifolia Linn</i> [102]	Roots (Rubiaceae)	Hydro-alcoholic	0.75% EG with 1% w/v AC	28	286 667	Antioxidant, nephroprotective property and lowering the concentration of urinary stone-forming constituents.
96.	<i>Rubia tinctorum L.</i> [103]	Rubiaceae	Ethanollic Ethyl acetate	0.75% EG with 2% AC	10	1 g/kg and 2 g/kg	More potent antioxidant effect, due to its high content in polyphenols
97.	<i>Rubus idaeus</i> (Raspberry) [104]	Roots (Rosaceae)	Aqueous	Intra-abdominal injection of glyoxylate (80 mg/Kg).	12	100 200	Vitamin E content might provide protection against the deposition of CaOx stones in the kidney
98.	<i>Rutin and Curcumin</i> [105]	<i>Rutin</i>	-----	EG 0.75% and AC 1%	28	20	Lowering of urinary concentration of stone forming constituents, anti-inflammatory and antioxidant effects
		<i>Curcumin</i>	-----				
99.	<i>Saccharum spontaneum L.</i> [106]	Roots (Poaceae)	Alcoholic	Calculi-producing diet	28	200 300	To reduce the super saturation of urine with calculogenic ions, diuretic property and anti-oxidant potential
100.	<i>Salix taxifolia</i> [107]	Leaves (Salicaceae)	Aqueous	Implantation of a zinc disc	60	10, 20, 40	
101.	<i>Salvia hispanica L. seeds</i> [108]	Seeds (Lamiaceae)	Methanol	0.75% EG and 1% AC	21	100, 300 700	
102.	<i>Scoparia dulcis</i> [109]	Leaves (Plantaginaceae)	Ethanollic	0.75%EG	30	250	

103.	<i>Seenakara Parpam (Siddha formulation)</i> [110]	-----	-----	Zinc Disc Implantation	7	200 400	Diuretic, antioxidant and anti-inflammatory effects of the drug
104.	<i>Sesbania grandiflora</i> [111]	Leaves (Leguminosae)	fresh leaf juice	calculi-producing diet (CPD)	14	1 ml 2 ml	Disintegration of mucoproteins by saponins and the complexation of tannins with calcium. And antioxidant
105.	<i>6-Shogaol</i> [112]	Flavanone type flavonoid	-----	0.75% EG and 1% AC		50 100	
106.	<i>Solanum nigrum</i> [113]	Fruit (Solanaceae)	Hydroalcoholic extract	0.75% EG and 1% AC	28	200 400	Downregulation of TNF- α and upregulation of adiponectin expression
107.	<i>Solanum xanthocarpum</i> Schrad. & Wendl. (Solanaceae) [114]	Fruit (Solanaceae)	Saponin rich fraction	0.75 % EG	28	800 40 20 10	Through inhibition of CaOx crystal formation and its effect on the urinary concentration of stone-forming constituents and nephrolithiasis inducing factors
108.	<i>Stevia rebaudiana</i> [115]	Leaves (Asteraceae)	Ethanollic	0.75 % EG	28	2000 100 200	Phenolic compounds present in <i>S. rebaudiana</i> may prevent the lipid peroxidation induced renal damage caused by calcium oxalate crystal deposition in the kidney.
109.	Taraxasterol (<i>Taraxacum officinale</i> L.) [116]	(Compositae)	-----	1% EG 0.75% AC	33	2, 4, 8	
110.	<i>Taxillus tomentosus</i> [117]	Plant powdered material (Loranthaceae)	Ethanollic	0.75% EG and 2% AC	28	2000 200 400	Diuresis and lowering of urinary concentration of stone forming constituents.
111.	<i>Tephrosia purpurea</i> roots [118]	Roots (Fabaceae)	Ethanol Aqueous	0.75 % EG	21	300	Synergistic property of flavonoids and other components present in roots
112.	<i>Thymoquinone</i> [119]	-----	-----	1% EG	28	5 10	Antioxidant effect, scavenges free radicals and superoxide anions, and inhibits cyclooxygenase and 5-lipoxygenase pathways
113.	<i>Trachyspermum ammi</i> [120]	Seeds (Umbelliferae)	Trachyspermum ammi anticalcifying protein (TAP)	0.4% EG and 1.0% AC	9	2	
114.	<i>Tragia involucrate</i> [121]	Leaves (Euphorbiaceae)	Aqueous silver nanoparticles	1% EG along with 0.75% AC	28	2000 200 10	Rich content of bioactive phenol, flavonoid and terpenoid contents of the TIA.

115.	<i>Trianthema portulacastrum</i> Linn. [51]	Leaves (Aizoaceae)	Ethanollic	0.75% EG and 1% AC	28	4000 200 400	Diuretic property and presence of phytochemicals like alkaloids, phenols, flavonoids, saponins, tannins
116.	<i>Triclisia gillettii</i> (moonseed vine) [122]	Leaves (Menispermaceae)	Aqueous Methanolic	1% ethane-1,2-diol ad	28	50, 100, 200	Inhibition of crystal growth, modulation of electrolyte imbalance, and antioxidant and anti-inflammatory ability
117.	<i>Trigonella foenum graecum</i> L. [123]	Seeds (Leguminosae)	Aqueous	0.75% EG with 2% AC		100 200	Increased diuresis, antioxidant activity and lowering of urinary concentrations of stone forming constituents.
118.	<i>Vernonia cinerea</i> Less. [124]	whole plant (compositae)	Hydro-alcoholic (30:70) extract	0.75% EG	28	2000/ 100, 200, 400	Decreasing the concentration of stone-forming components, diuretic property
119.	<i>Viburnum opulus</i> [125]	Fruits (Adoxaceae)	n-hexane, Ethyl acetate, Methanol	NaOx, 70 mg/kg, i.p	7	100	Inhibition of oxalate levels and free radical production as well as diuretic activity which probably due to its phenolic contents.
120.	vitamin E and sodium selenite [126]	-----	-----	Feeding calculi producing diet	30	400 0.2	Prevent the tissue of lipid peroxidation, inhibit oxalate synthesis and enhance enzymatic and non-enzymatic antioxidant status in liver and kidney under lithogenic environment.
121.	<i>Xanthium strumarium</i> (L.) [127]	Bur (Asteraceae)	Hydo-ethanolic (1:1)	0.75% EG along with 1% AC	28	500	Inhibition of various pathways involved in renal calcium oxalate formation, antioxidant property and down regulation of matrix glycoprotein, OPN.

Table 2 Number of studies based on the methods used for urolithiasis

Sr. No	Animal model	No of Studies
1.	0.75% EG	39
2.	0.75 %EG + 1% AC	28
3.	0.75 %EG + 2% AC	10
4.	Feeding calculi producing diet	4
5.	NaOx,	5
6.	Implantation of a zinc disc	6
7.	Introducing a CaOx disk	2
8.	other	13

Table 3 Number of studies based on the part of the plant used

Sr. No	Part of plant	No of Studies
1.	Leaves	28
2.	Seeds	13
3.	Roots	19
4.	Fruits	14
5.	Aerial Parts	5
6.	Whole plants	6
7.	Barks	5
8.	Flowers	4
9.	Others	26

Table 4 Number of studies based on the type of solvent used

Sr. No	Type of solvent	No of Studies
1.	Aqueous	42
2.	Ethanol	24
3.	Methanol	16
4.	Hydroalcoholic	22
5.	Alcoholic	7
6.	Ethyl acetate	7
7.	Chloroform	6
8.	Petroleum ether	4
9.	Others	17

CONCLUSION

As there is no proper medicine in allopathy for the management of urolithiasis and also the surgical treatment has the more chances of recurrence, these two factors particularly diverted the large population towards the use of herbal medicines. Medicinal plants have wide acceptance due to a large no. of advantages such as lesser toxic effects, safe, effective, cheap (cost effective), less chances of recurrence of disease, easily available in rural areas. The present paper provides information regarding extract, screening models, dose and mechanism of the potential medicinal plants and active constituents used in the management of urolithiasis and develop a new drug for the urolithiasis to overcome the various disadvantages faced by the wide range of population now-a-days and get relieve from

the disease. Let us hope for the development of safe and effective drug for the management of urolithiasis.

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Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this review article.

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