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Current scenario of urolithiasis and the use of medicinal plants as antiurolithiatic agents in Manipur (North East India): A Review

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ABSTRACT

Almost every family in Manipur has a member afflicted with urolithiasis. Standard pharmaceutical drugs used to prevent and cure urolithiasis are not effective in all cases, costly, quite common recurrences, risks of long term fertility, potential side effects and no guarantee. Despite the improvements in medical techniques such as extracorporeal shock wave lithotripsy and percutaneous nephrostolithotomy, the worldwide incidence of urolithiasis is quite high and there is no truly satisfactory drug for treatment of renal calculi. A large number of Indian medicinal plants have been used in the treatment of urolithiasis and they have been reported to be effective with fewer side effects. This paper deals with the current scenario of Urolithiasis in Manipur and reported the detail documentations of 107 plants from Manipur currently used by different ethnic communities as antiurolithiatic agents.

Keywords: Urolithiasis, Manipur, Biodiversity Hot spots, medicinal plants.

1. Introduction

Urolithiasis, which is referred to as the process of formation of calculi (singular calculus) in the urinary system includes Nephrolithiasis (Renal Calculi or Kidney Stones), Ureterolithiasis (Ureter Calculi) and Cystolithiasis (Bladder Calculi). Urinary stones are one of the major problems and an important cause of morbidity and end stage renal failure in India. Stone formation is one of the painful urologic disorders that occur in approximately 12% of the global population, and its recurrence rate in males is 70-81% in males and 47-60% in females^[1]. These calculi (stones) create problems by blocking the flow of urine and cause severe pain termed as renal colic when they move along the ureter. Urolithiasis can also be associated with morbidity and renal damage. The disease affects all age groups from less than 1 year old to more than 70 years^[2]. After their initial stone episode the recurrence rate of stone is approximately 10% within one year, 35% within five years, and 50% within 10 years^[3].

1.1 Prevalence of Urolithiasis

Primary stone formation and recurrence of stone formation is one of the biggest challenges faced by urologists today and remain a major source of morbidity in humans^[4]. The peak age for onset of stone formation is in the third decade, and prevalence increases with age until 70. During the past few decades, the prevalence of kidney stones in both males and females has markedly increased in industrialized countries. This is presumably due to changes in lifestyle and dietary habit of the people in these regions^[5]. The increased incidence of urinary stones in the industrialized world is associated with improved standards of living (mainly including the high dietary intake of proteins and minerals)^[6]. Kidney stone incidence varies in different parts of the world, high incidence areas are Scandinavian countries, Mediterranean countries, British Isles, northern Australia, central Europe, portions of the Malayan Peninsula, China, Pakistan and northern India whereas the incidence of kidney stone formation is lower in areas like Central and South America, some parts of Africa. In Asia stone-forming belt has been reported to stretch across Sudan, Saudi Arabia, the United Arab Emirates, the Islamic Republic of Iran, Pakistan, India, Myanmar, Thailand, Indonesia and Philippines. In India, the "stone belt" occupies some parts of Maharashtra, Gujarat, Punjab, Haryana, Delhi and Rajasthan^[7]. The effect of geography on the incidence of stone formation may be direct, through its effect on temperature; high temperatures increase perspiration, which may result in concentrated urine, which in turn promotes increased urinary crystallization.

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^[8]. 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^[9, 10]. 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^[11]. Also, the increase daily breakdown of the tissues in men could result in increased metabolic waste and a predisposition to stone formation^[12]. The other more significant cause may be because of the male urinary tract being more complicated than the female urinary tract^[13]. Estrogen may also help to prevent the formation of calcium stones by keeping urine alkaline and raising protective citrate levels^[14]. 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^[15]. Some reports have described that vegetarians are at lower risk for stone formation in contrast to non-vegetarians^[16].

1.2 Prevalence of urolithiasis in Manipur

In Manipur, the situation is not an exception as the incidence of urolithiasis is high. It is commonly believed that almost every family has a member afflicted with this disease. A study in Manipur on a sample of 875 individuals with urolithiasis revealed that the disease was observed to be significantly more common 109 (56.7%) in the age group of 25 to 44 years, and majority 820 (93.7%) of the people consumed fish daily and nearly two-third of the study population consumed only 2–4 glasses of water per day^[17]. From hospital records for a period of seven years and three months urolithiasis was found to be the case in 11.6% of all general surgery cases in General Hospital, Imphal^[18]. Also, males are more affected. Urolithiasis was also significantly more prevalent among those individuals with history of UTI (50.6%), and the condition was also observed to be more common among those who had a family history of urolithiasis 73 (67%) and among individuals who are more stressed. Among the affected cases the majority of them are Hindus, and few percentage of Tribals and Muslims. In Hindus of Manipur, the cereal food is introduced between five to 7 months of life after a ceremony called “anaprashan” or “chaumba”. The involvement of single cereal diet in the stone formation can be speculated^[20]. The occurrence of stones is very low in the affluent class, but very high in the low socioeconomic class.

2. Types of Calculi

Kidney stones are mainly of four types^[20]. The stone types are named after its mineral composition. The most common stones are calcium oxalate, struvite, uric acid and cystine stones. These chemicals are part of a person’s normal diet and make up important parts of the body, such as bones and muscles. In Manipur, oxalate and calcium were present in all the stones, followed by few percentages of stone of phosphate and uric acid. Uric acid was present in all renal stones. Calculi can occur in various sites in the urinary tract in the following order of frequency i.e. vesical < renal < ureteral < urethral. In general, the occurrence of calculus is

higher in the lower part of the urinary tract in all age groups. Globally, calcium oxalate is considered as the main constituent in the renal calculi. Calcium containing stones, especially calcium oxalate monohydrate (COM), also known as whewellite, calcium oxalate dehydrate (COD), also known as weddellite, and basic calcium phosphate (apatite) are the most commonly occurring stones to an extent of 75-90% followed by magnesium ammonium phosphate (struvite) to an extent of 10-15%, uric acid 3-10% and cystine 0.5-1%^[21]. Silicate stones or drug induced stones are very rarely seen, and can be a result of taking certain medications or herbal products and the subsequent build-up of chemicals from those products in the urine^[22]. Some of these drugs are loop diuretics, acetazolamide, topiramate, zonisamide, laxatives (when abused), ciprofloxacin, sulfa medications, triamterene, indinavir, ephedrine, guaifenesin, and products containing silica. A less common type of stone is caused by infection in the urinary tract. This type of stone is called struvite or infection stone. Another type of stone namely uric acid stones are a bit less common, and cystine stones are very rare.

3. Current management and treatment of Urolithiasis

The first step in the prevention and treatment of recurrent urolithiasis is to increase the daily fluid intake to at least 2.5 L to 3 L per day^[23] along with pain controlling drugs and medications to monitor salts that may increase or reduce formation of stones. Many allopathic agents like thiazide diuretics (hydrochlorothiazide), alkali (potassium citrate), allopurinol, sodium cellulose phosphate (SCP), penicillamine (cuprimine), analgesic (diclofenac sodium), bisphosphonates, potassium phosphate and probiotics (*Oxalobacter formigenes*) are used in treating stones. Thiazide diuretics (e.g., hydrochlorothiazide, chlorthalidone and indapamide) produce an increase in tubular reabsorption of calcium, which diminishes calciuria, and hence are effective in reducing calciuria and stone recurrence. These drugs also induce positive calcium balance and thereby increase bone mineral density. Alkalis are used to increase the urinary citrate excretion in patients with hypocitriuria. Allopurinols are used to reduce uric acid synthesis and urinary excretion in patients with hyperuricaemia and hyperuricosuria. Sodium cellulose phosphates (SCP) are used to restore normal calcium excretion by reducing intestinal calcium absorption. SCP may also induce hypermagnesiuria leading to increase saturation of CaOx by reducing the complexation of urinary oxalate. Penicillamines are often recommended if drinking more fluids does not control cystine formations. Analgesics are recommended for less painful passage of ureteral stones which are expected to pass spontaneously. They are also useful in controlling recurrent pains associated with urolithiasis. Bisphosphonates are used to decrease calciuria. Potassium phosphates help in increasing serum phosphate, increase urine phosphate and possible increase in urine pyrophosphates. *Oxalobacter formigenes* and other probiotics help in decreasing oxalate excretion. However, most of these standard pharmaceutical drugs used to prevent and cure urolithiasis are not effective in all cases, costly, quite common reoccurrences, risks of long term fertility, potential side effects and no guarantee^[24].

Small stones are more likely to pass spontaneously than large ones, and distal stones are more likely to pass spontaneously than stones more proximal in the urinary tract. Ureteral stones of less than 4 mm in diameter have a chance of over 80% to pass spontaneously^[25]. Most ureteral stones smaller than 5 mm in diameter pass

spontaneously within 4 weeks of the onset of symptoms [26, 27]. The spontaneous passage rate depending on their location are 25% for the proximal ureter stones, 45% for the mid ureter stones and 70% for the distal ureter stones, provided the mean diameter does not exceed 7 mm, and the stones are expelled out between 5 days (for smaller distal stones) to 59 days (for larger proximal stones) [28, 29]. High oral fluid intake of at least 2 to 3 L of fluids per 24 hours is recommended for enhance spontaneous stone expulsion. Recently, a number of studies have investigated the effect of various drugs on spontaneous stone expulsion of distal ureteral stones. These drugs include analgesics, anti-inflammatory drugs, and calcium antagonists such as nifedipine and alfablockers such as tamsulosin. Of the above mentioned agents tamsulosin seems to be especially promising in preliminary studies [30].

On the contrary, most stones with a diameter >8 mm will ultimately necessitate intervention. Before the advent of lithotripsy and ureteroscopy, most patients with symptomatic upper tract calculi underwent open surgical lithotomy. However, lithotripsy and ureteroscopic extraction have dramatically reduced the role of open stone surgery [31, 32]. Despite these advancements, techniques such as extracorporeal shock wave lithotripsy and percutaneous nephrostolithotomy do not assure the prevention of recurrence of the stone. They cause side effect such as haemorrhage, hypertension, tubular necrosis, and subsequent fibrosis of the kidney leading to cell injury, and ultimately recurrence of renal stone formation [33]. Also these methods are costly, non-affordable by the poor section and the re-occurrence rate is also high (50-80%) [34]. Thus, even with the improved understanding of the mechanisms of stone formation and treatment, the worldwide incidence of urolithiasis is quite high and there is no truly satisfactory drug for treatment of renal calculi [35].

4. Role of medicinal plants as antiurolithiatic agents

Of late, there has been a growing resurgence and revival of interest in indigenous systems of medicine and traditional herbal remedies, which are regarded as quite safe with minimal or no side effects, cost effective, readily available and easily affordable [36-39]. Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for prevention of diseases and ailments [40]. Interest in herbal drugs is growing due to their efficiency, low toxicity and absence of side effects [41]. People living in the interiors and inaccessible remote rural areas have excellent knowledge about medicinal utility of the local flora. People in such areas have been traditionally using indigenous folk remedies to cure various diseases for generations and passing on this knowledge orally. Because of prompt and positive effect of herbal treatment they have strong faith in their own folk medicinal preparations or crude formulations [38, 41].

4.1 Antiurolithiatic plants of Manipur

The North-East India is a treasure house of vast variety of plant resources being a part of the Indo-Burma Biodiversity Hotspot. Manipur, which is one of the states in North-East India, is located between 23.83° N and 25.68° N latitude and 93.03° E and 94.78° E longitudes. It covers a geographical area of 22,327 sq. km of which 90% are hilly regions largely characterised by dense forests and inaccessible terrains, and is a home to 4000 angiospermic plants. The state is rich in flora and fauna and falls under the Indo-Myanmar biodiversity hotspot, one of the 25 global biodiversity hotspots acknowledged currently [42]. It is believed that this part of

India was used as crucial corridor for human migrations including, perhaps, the first migrations from Africa towards East Asia and Australia more than 40,000 years ago [43]. The use of medicinal plants plays a very vital role in the health care of tribal people. These primitive people have used plants to cure a variety of ailments, but they keep no records and the information is mainly passed on verbally from generation to generation [44].

Based on various documentations of medicinal plants used in treatment of kidney stones and ailments related to urinary system in Manipur by researchers working on this biodiversity rich region from 2005 till 2014, it is found that 107 plants, of which one is an alga, belonging to 51 different families are used by different ethnic communities of Manipur like Meeties, Muslims and tribals for treatment of kidney stones and related ailments such as urinary infections and urinary problems. The plants which are used as antiurolithiatic agents are reported along with uses and mode of uses [17, 45-61]. The complete documented lists of 107 antiurolithiatic plant agents are given in Table 1. These plants are traditionally used to dissolve kidney stones or to prevent formation of stone. From these documentations it is observed that plants belonging to Asteraceae, Rosaceae, Euphorbiaceae, Malvaceae and Cucurbitaceae are mostly used in treatment of kidney stones and ailments related to urinary stone and urinary problems. However, plants belonging to family Oxalidaceae, Nelumbonaceae, Mimosaceae, Magnoliaceae, Myrtaceae, Menispermaceae, Linderniaceae, Clusiaceae, Caesalpinaceae, Cyperaceae, Caricaceae, Bromeliaceae, Boraginaceae, Alliaceae, Amaryllidaceae, Amaranthaceae, Asclepiadaceae, Urticaceae, Plantaginaceae, Santalaceae, Solanaceae, Theaceae, Umbelliferae, Ulmaceae, and Pedaliaceae are less reported in the documentations for their use as antiurolithiatic agents.

Each tribe in Manipur has their own unique knowledge of using plants as medicines, also they have their unique traditional medicinal knowledge, which in many cases are different from other tribes, and are handed down orally from one generation to another since its civilization. The living population of this region has been using various medicinal plants for the treatment of stone cases. It was also found that different ethnic communities use different plants for treatment related to urolithiasis, which indicates the fact that their traditional knowledge are unique to themselves. For instance, the plant *Anneslea fragrans* was found to be used only by the Khoibu community [52], the Thadou tribe on the other hand uses *Saccharum officinarum* for kidney infections [54] asserting the fact that these traditional practices were unique to the communities that hold these knowledge, and are passed down from one generation to another orally. On the other hand, most of the plants used by the Muslims and the Meeitei communities of Manipur are common, with minor differences in the mode of use, which may be due to these communities having a common language as well as more closeness in their settlements as compared to the tribals who occupied most of the hills with more scattered pattern of settlements, and the differences in languages and cultures among the different tribes.

The documented works reported in this review on antiurolithiatic medicinal plants from Manipur beginning from 2005 till date is less than that of just 10 tribes of Manipur along with that of the Meeteis and the Muslims, whereas Manipur is comprised of about 34 tribes. It is, thus probable that the lists of the plants use as antiurolithiatic will add up in the following years, since the

ethnomedicinal knowledge of majority of the tribes have not been available in the documented form till now. Moreover, most of these medicinally claimed plants are yet to be subjected to phytochemical analysis for their efficacy except a few of them. In India, many medicinal plants are reported for use in urolithiasis, however their usefulness has not been scientifically assessed except in few cases. The simple extracts (infusions) from medicinal plants which have diuretic effect seem to be the most available for preparation and usage. Most of all, they are used only with purpose to increase diuresis. Meanwhile, they have ability to change other urine parameters. Out of seventeen medicinal plants from Manipur analysed *Cissus adnata*, *Cuminum cyminu.*, *Eupatorium birmanicum*, *Hibiscus sabdariffa*, *Oxalis corniculata*, *Piper longum* and *Tamarindus indica* significantly prevented crystal formation in urine and exhibit strong antibacterial activity against four urolithiasis inducing microbes. It was also reported that ethanol extracts of *Hibiscus sabdariffa*, *Tamarindus indica* and *Piper longum* showed comparatively the highest efficacies in dissolving the stone. Thus, *C. adnata*, *C. cyminum*, *E. birmanicum*, *H. sabdariffa*, *O. corniculata*, *P. longum* and *T. indica* showed promising role in prevention and control of urolithiasis^[62]. Investigation of the role of 'varuna' (*Crataeva nurvala*) in urinary disorders showed that it has a potent antiseptic property, changes the urine chemistry which would check the growth of the stone and tones up the bladder muscle, thereby facilitating the expulsion of stones^[63]. Medicinal plants such as *Cuminum cyminum* and *Eupatorium birmanicum* controls urolithiasis even though they render the urine alkaline. Herbal drugs such as Cystone are made from indigenous plants *Didymocarpus pedicellata*, *Saxifraga ligulata*, *Rubia cordifolia*, *Cyperus scariosus*, *Achyranthes aspera*, *Onosma bracteatum*, *Vernonia cinerea*, *Shilajeet purified* and *Hajrul yahood bhasma*. Cystone is reported to have a key role in controlling kidney stone formation as the antibacterial activities. 'Chandraprabha Vati' is an Ayurvedic formulation used for the treatment of Diabetes and urinary diseases. It is formulated from *Commipora wightii*, *Gomutra silajith*^[64]. Herbal formulation 'Trinapanchamool' consists of five herbal drugs namely *Desmostachya bipinnata*, *Saccharum officinarum*, *Saccharum nunja*, *Saccharum spontaneum* and *Imperata cylindrical* and is effective both as a prophylactic in preventing the formation and as a curative in dissolving the pre-formed stones in albino rats^[65]. Similarly, other ayurvedic medicine formulated from medicinal plants which are used in the treatment of urolithiasis are Calcuri, Rencare Capsul, Patherina tablet, Ber Patthar Bhasma.

Formulations of these herbal drugs are possible when the uses of such plants are available in documented forms.

5. Conclusion

At present, the traditional health care system which was once used to be the lifeline of the people seems to be in the verge of extinction. The wealth of information preserved as an unwritten medicinal knowledge amongst the ethnic communities seems to be slowly fading and the oral tradition of passing on knowledge from generation to generation is declining. Also, there are many other cases in which the knowledge still remains a secret amongst the tribes. In addition, the general trend towards more dependency on the modern way of living leads to diminishing in the age old practice of handling down the traditional medicinal knowledge orally from one generation to another among the tribals and remote people. Moreover, the extensive felling of trees for timber, fuel, practices of shifting cultivation for which vast vegetations have to be cleared, preparation of land for terrace cultivation and uncontrolled human settlement have also threatened the valuable medicinal plants. Further, the ever increasing demand of herbal medicines both in the domestic and international market leads to unauthorized collection, indiscriminate destruction and overexploitation of these resources from wild state. Also, the exploitation of the traditional knowledge by various pharmaceutical companies in the form of patenting, by selling the drugs obtain from indigenous medicinal plants with high price tags, for which the ultimate effects are visible to the poor and remote tribes who actually owns the medicinal knowledge is another issue. Thus documentation and preservation of the traditional knowledge are the great challenges of the hour, so that the vast knowledge of the ethnic communities residing in this biodiversity hot spot region of the country can still be preserved for future research in pharmaceuticals and drug discovery, without compromising the contributions and prospects of benefit sharing to the ethnic communities who have played a tremendous role in shaping modern drug formulations. The present review on documentations of the complete information of plants used as antiurolithiasis agents in Manipur will help in guiding the researcher to identify new source of drugs for this ever prevailing human ailment. These ethnomedicinal knowledge if properly safeguarded, will serve as a novel irreplaceable resource for isolation and synthesis of the most reliable drugs for urolithiasis which is still a long overdue.

Table 1: Complete list of plants used as antiurolithiatic agents in Manipur.

S. No	Scientific Name	Family	Common Name	Part Used	Uses	Reference
1.	<i>Abrus precatorius</i> Linn.	Malvaceae	Chaning angouba (M)	Leaves	Aqueous extract is used for treatment of kidney stones.	[51]
2.	<i>Abutilon indicum</i> Linn.	Malvaceae	Kanghi (H)	Whole plant	Herb is employed in urinary troubles.	[51]
3.	<i>Actinodaphne angustifolia</i> (Blume) Nees.	Lauraceae	Takara (M)	Leaves	The decoction of the plant is used in kidney diseases due to stone.	[51]
4.	<i>Aeschynomene indica</i> Linn.	Papilionaceae	Chigonglei (M)	Young tender leaves	Taken as salad, cures stone in urinary tract infection. Boiled extract of the leaves with black pepper is prescribed in painful urination.	[51]

5.	<i>Allium odorosum</i> Linn.	Alliaceae	Yenam nakuppi (M)	Leaves	Boil extract of leaves is given in painful urination especially urinary tract infections due to stone.	[51]
6.	<i>Ananas comosus</i> Linn.	Bromeliaceae	Kihom (M)	Ripe fruit	Extract of the ripe fruit is prescribed against bronchitis, asthma and urinary trouble due to stone.	[51]
7.	<i>Andrographis paniculata</i> Nees.	Acanthaceae	Kalmegh (H)	Leaves	Boiled leaf extract used against fever, cold, cough and urinary disorder.	[60]
8.	<i>Anneslea fragrans</i> Wall.	Theaceae	Thingphunchuo (Kh.)	Dried leaves	Boil 10 g in 1 litre water. Drink Three times a day for kidney stone.	[52]
9.	<i>Asparagus racemes</i> Wild.	Liliaceae	Nunggarei angouba (M)	Root	Boiled decoction of the root with sugar is prescribed in urinary troubles due to stone.	[51]
10.	<i>Averrhoa carambola</i> Linn.	Averrhoaceae	Heinou-Jom (M)	Fruit	The extract of the fruit mixed in asthma, bronchitis, and urinary trouble due to stone.	[51]
11.	<i>Averrhoa carambola</i> Linn.	Averrhoaceae	Heinoujom (M)	Fruit	Put 2.8 g silver element into 300 ml fruit juice. Drink half tea glass daily for five days for kidney stone.	[53]
12.	<i>Bambusa nutans</i> Wall.	Poaceae	Ootang (M)	Shoots	Sliced 250 gm of shoots and boiled in 1 litre water. Drink half tea glass daily for seven days, for kidney stone.	[53]
13.	<i>Bauhinia acuminata</i> Linn.	Caesalpiniaceae	Chingthao (M)	Bark or leaves	Decoction of bark or leaves is given to cure stone in bladder.	[51]
14.	<i>Benincasa hispida</i> (Thund.) Cogn.	Cucurbitaceae	Torobot (M)	Fruit	Boiled decoction of the plant with sugar is prescribed in urinary troubles due to stone and urinary tract infections, kidney stones.	[51] [55] [59]
15.	<i>Berberis aristata</i> DC.	Berberidaceae	Pambi napu (M)	Leaves	The boiled decoction of the leaves is prescribed in urinary tract infection and kidney troubles.	[51]
16.	<i>Blumea balsamifera</i> Linn.	Asteraceae	Nagal Camphor (M)	Leaves	Two teaspoon of such crushed leaves juice is added to a glass of water with a little "Meitei thum" (local salt), for treatment of stone formation.	[56]
17.	<i>Bonnaya brachiata</i> Link & Otto.	Scrophulariaceae	Kihommaan (M)	Whole plant	Urinary stone case.	[46]
18.	<i>Bonnaya reptans</i> (Roxb.) Spreng.	Scrophulariaceae	Lamkihohm (M)	Whole plant	The boiled decoction is prescribed for the kidney and urinary complaints due to stone.	[51]
19.	<i>Capsella bursa-pastoris</i> (Linn.) Medik.	Brassicaceae	Chantruk (M)	Whole plant	Freshly taken in Urinary problems.	[61]
20.	<i>Cardamine hirsuta</i> Linn.	Brassicaceae	Chantruk Maan (M)	Whole plant except root	Diuretic.	[57]
21.	<i>Carica papaya</i> Linn.	Caricaceae	Awathabi (M)	Young Fruit	Diuretic and Digestive.	[57]
22.	<i>Celosia argentea</i> Linn.	Amaranthaceae	Haorei-angouba	Roots	Boiled extract of the root	[51]

			(M)		with sugar is given in urinary tract and kidney stone.	
23.	<i>Celtis australis</i> Linn.	Urticaceae	Heikreng (M)	Leaves	Boiled decoction of the leaves is given against stone in the urinary tract, and in stone cases.	[51]
24.	<i>Celtis timorensis</i> Span.	Ulmaceae	Heikreng (M)	Aerial parts	Boiled 10 g with 2 litres water by putting 2 spoonful of sugar. Drink 1 tea glass twice daily for 10 days for kidney stone.	[53]
25.	<i>Centella asiatica</i> (Linn.) Urban.	Apiaceae	Nungjreng peruk (M)	Whole plant	Plant Juice with sugarcane molasses are taken in urinary calculus.	[48]
26.	<i>Cinnamomum bejolghota</i> (Buch.-Ham.) Sweet.	Lauraceae	Tezpat (M)	Bark	Bark is useful for treatment in urinary stone troubles.	[51]
27.	<i>Cinnamomum glaucescens</i>	Lauraceae	Vahmin (K)	Bark	The powder of the bark is used in kidney trouble.	[51]
28.	<i>Cinnamomum tamala</i> Linn.	Lauraceae	Tezpat (M)	Leaves	Boiled with <i>Celtis timorensis</i> and drink in kidney stone .	[53]
29.	<i>Cissus adnata</i> Roxb.	Vitaceae	Kongouyen (M)	Leaves	Boil decoction of the leaves and roots is given in kidney problem due to stone.	[51]
30.	<i>Cissus discolor</i> Blume.	Vitaceae	Kongyouyenlaba (M)	Leaves	Skin diseases, poxes, & urinary disorder.	[45]
31.	<i>Cissus javana</i> DC.	Vitaceae	Kongouyen Laba (M)	Leaves	Boiled extract of leaves is considered tonic for curing urinary trouble due to stone and to cure the burning sensation during urination.	[51]
32.	<i>Cissus javanica</i> D.C.	Vitaceae	Kongyouyen laba (M)	Leaf	Boiled extract of leaves is taken for Urinary disorder	[61]
33.	<i>Citrus latipes</i> (Swingle) Tanaka.	Rutaceae	Heiribob (M)	Fruit	The fruit extract mixed with that of <i>Averrhoa carambola</i> and a pinch of salt and honey is prescribed in urinary tract and kidney stone.	[51]
34.	<i>Coix lacryma-jobi</i> Linn.	Poaceae	Chang-ning (M)	Leaves	Stone Case.	[50]
35.	<i>Coriandrum sativum</i> Linn.	Apiaceae	Phadigom (M)	Leave and Young Stalks	Diuretic, stomachic, aphrodisiac, to correct foul smell.	[57]
37.	<i>Cordia grandis</i> Roxb.	Boragineae	Lamuk (M)	Fruits	Fruits are considered medicine for urinary trouble due to stone.	[51]
38.	<i>Costus speciosus</i> (Koenig) Smith.	Zingiberaceae	Khongban takhelei (M)	Roots	Decoction of roots is prescribed in urinary complaints.	[51]
39.	<i>Crinum asiaticum</i> Linn.	Amaryllidaceae	Kanwal (H)	Bulb	Bulb is used in urinary complaints.	[51]
40.	<i>Curcuma angustifolia</i> Roxb.	Cucurbitaceae	Lamthabi (M)	Whole plant	Juandice, Kidney infection, Stone Case.	[50]
41.	<i>Cuminum cyminum</i> Linn.	Umbelliferae	Jeera (M)	Fruits	The boiled decoction of the fruits is used in urinary trouble	[51]
42.	<i>Cymbopogon citratus</i> Stapf.	Poaceae	Hoana (M)	Whole plant	The dried plant is boiled in water and decoction is taken orally for Stone case.	[61]

43..	<i>Cyperus rotundus</i> Linn.	Cyperaceae	Shembang Kaothum (M)	Whole plant	The decoction of the plant is prescribed in urinary trouble.	[51]
44.	<i>Desmodium microphyllum</i> (Thunb.) DC	Papilionaceae	Nuggai Yensil (M)	Whole plant	The decoction of the plant is prescribed for urinary complaints due to stone.	[51]
45.	<i>Docynia indica</i> (Colebr.) Decne.	Rosaceae	Heitoop (M)	Fruit	Infusion with sugar kept for two week and orally taken for Urinary troubles	[61]
46.	<i>Duchesnea indica</i> (Andr.) Focke.	Rosaceae	Heirongkak-laba (M)	Whole plant	Decoction of plants with sugar is used for treatment of stone case and other urinary infection.	[51]
47.	<i>Emblica officinalis</i> Gaertn.	Euphorbiaceae	Heigru (M)	Fruit	Juice extraction is prescribed in kidney stone.	[53]
48.	<i>Enhydra fluctuans</i> Lour.	Asteraceae	Komprek-tujombi (M)	Aerial parts	Boiled with sugar and prescribed in kidney stone.	[53]
49.	<i>Eupatorium birmanicum</i> DC.	Asteraceae	Langthrei (M)	Leaves.	Boiled decoction of the leaves with a pinch of indigenous Manipuri salt helps in exiting and eliminating calculi/stones.	[51]
50.	<i>Euphorbia hirta</i> Linn.	Euphorbiaceae	Pakhangleiton (M)	Whole	Boiled with <i>Cuminum cyminum</i> Linn. Seeds in water and is taken orally for stone case.	[61]
51.	<i>Fragaria indica</i> F.	Rosaceae	Heirongkaklaba (M)	Vegetative part.	The vegetative part of this plant is boiled with sugar and used in problems of urinary tract & stone case.	[56]
52.	<i>Fragaria nilgerensis</i> Schlttdl. Ex. J. Gay.	Rosaceae	Samu hongpak laba (M)	Vegetative part.	Boiled with water by putting a little sugar candy and drink to cure kidney stone.	[53]
53.	<i>Hedychium aurantiacum</i> Rosc.	Zingiberaceae	Takhellei Angangba (M)	Rhizome	Boiled with water and drink in kidney stone problem.	[53]
54.	<i>Hedychium coronarium</i> Koening.	Zingiberaceae	Takhellei-anganganba (M)	Rhizome	Boiled extract of rhizome is given in urinary tract.	[51]
55.	<i>Helianthus annuus</i> Linn.	Asteraceae	Numitlei (M)	Fresh Leaves	The juice of the fresh leaves is used in urinary trouble and diseases of kidney.	[51]
56.	<i>Hemidesmus indicus</i> (Linn.) Schult.	Asclepiadaceae	Kwa-manbi (M)	Root	Used as medicine Rheumatism, urinary diseases and skin troubles.	[45]
57.	<i>Hibiscus sabdariffa</i> Linn.	Malvaceae	Silot sougri (M)	Leaves	Decoction of leaves in used in urinary troubles, especially due to stone in kidney.	[51]
58.	<i>Homonoia riparia</i> Lour.	Euphorbiacea	Tuipui-sulhla (A)	Root	The decoction of the root is given in piles, stone in the urinary bladder.	[51]
59.	<i>Hydrocotyle javanica</i> Thunb.	Apiaceae	Awa-peruk (M)	Whole plant	Used as medicine Stomach ulcer, urinary troubles, digestive complaints, dysentery and skin diseases.	[45]
60.	<i>Indigofera tinctoria</i> Linn.	Papilionaceae	Neem (M)	Roots	Roots are used in urinary complaints.	[51]

61.	<i>Ixora sub-sessilis</i> Wall.ex G.Don	Rubiaceae	Shenglong (R)	Fruits and seeds	Fruits and seeds are useful in urinary complaints.	[51]
62.	<i>Knoxia roxburghii</i> (Spreng) M.A.Rau.	Rubiaceae	Hurim (R)	Leaves	Leaf- juice is given for urinary troubles.	[51]
63.	<i>Lindernia ruellioides</i> (Colsm) Pennell.	Linderniaceae	Kihomman (M)	Whole plant	Boiled with water by putting a little sugar candy and drink in kidney stone.	[53]
64.	<i>Lemanea fluviatilis</i> Linn.	Lemaneaceae	Nungsam (M)	Whole Thallus	Used in urinary trouble due to kidney stones.	[54]
65.	<i>Magnolia grandifolia</i> Linn.	Magnoliaceae	Uthambal (M)	Leaves	Stone case.	[50]
66.	<i>Mallotus philippensis</i> (Lan) Muell. Arg.	Euphorbiaceae	Ureirom laba (M)	Bark	Boil decoction of the bark with sugar is given in urinary tract stone problem.	[51]
67.	<i>Melothria purpusilla</i> (Blume) Cong.	Cucurbitaceae	Lamthabi (M)	Whole parts of plant	Vegetative parts of this plant is boiled with sugar candy in water and given in patient of Jaundice, Kidney infection.	[56]
68.	<i>Mentha arvensis</i> Linn.	Lamiaceae	Podina/Nungshi hidak (M)	Leaves	Crush 250 g leaves with 50 ml water by using mortar and pestle Drink half tea glass daily for 3-7 days.	[53]
69.	<i>Meriandra benghalensis</i> Benth.	Lamiaceae	Kanghuman (M)	Leaves	Expectorants against dyspepsia, dizziness and urinary problem.	[57]
70.	<i>Mesua ferrea</i> Linn.	Clusiaceae	Nageshor (M)	Flower	Asthma, Urine with blood.	[47]
71.	<i>Mimosa pudica</i> Linn.	Mimosaceae	Kangphal-ikaithabi (M)	Roots	Root decoction with the rhizome of <i>Cyperus rotundus</i> and Flintstone is administered to remove stone.	[59]
72.	<i>Momordica cochinchinensis</i> (Lour.) Spreng.	Cucurbitaceae	Karot (M)	Fruits	Kidney stone treatment.	[55]
73.	<i>Momordica dioica</i> Roxb.ex Willd.	Cucurbitaceae	Kaksa (H)	Fruits	Roots are used in urinary complaints.	[53]
74.	<i>Myriogyne minuta</i> Less.	Asteraceae	Hakthi khanbi (M)	Aerial parts	Extract of the plants mixed in equal proportion with the juice of sugarcane is given against stone in the urinary tract.	[51]
75.	<i>Nelumbo nucifera</i> Gaertn.	Nelumbonaceae	Thambal (M)	Young leaves, flower and rhizomes	Diuretic, against dizziness and stomachic.	[57]
76.	<i>Orthosiphon spiralis</i> (Lour) Merr.	Lamiaceae	Warak leikham (M)	Leaves	Boiled extract of leaves is prescribed in urinary complaints.	[51]
77.	<i>Oxalis corniculata</i> Linn.	Oxalidaceae	Yensil (M)	Leaves	Boiled decoction of the leaves with a pinch of indigenous Manipuri salt helps in exiting and eliminating calculi/stones.	[51]
78.	<i>Pavetta indica</i> Linn.	Rubiaceae	Kukurchura (M)	Roots	Roots are used for urinary diseases.	[51]
79.	<i>Piper nigrum</i> Linn.	Piperaceae	Gul (M)	Seeds	Boiled with water and prescribed in kidney stone.	[53]

80.	<i>Piper longum</i> Linn.	Piperaceae	Taboppi (M)	Leaves	Boiled decoction of the leaves with sugar is given in urinary tract and kidney stone.	[51]
81.	<i>Plantago major</i> Linn.	Plantaginaceae	Yempat (M)	Whole plant	Slightly warmed leaf applied on boils; boiled plants used against urinary disorder.	[60]
82.	<i>Polygonatum multiflorum</i> Allioni.	Liliaceae	Kundalei Agouba Thondaba (M)	Root	The decoction of root is prescribed by local medicine man in kidney and urinary troubles.	[51]
83.	<i>Potentilla anserina</i> Linn.	Rosaceae	Samu khongpak (M)	Whole plant	Boiled decoction of the plant with sugar is prescribed in urinary troubles due to stone.	[51]
84.	<i>Pratia nummularia</i> Kurz.	Companulaceae	Nungai peruk (M)	Whole plant.	Boiled extract of whole plant is administered in kidney stone.	[51]
85.	<i>Prunus persica</i> (Linn.) Batsch.	Rutaceae	Heikha (M)	Fruit	Infusion with sugar kept for two week and is orally for Urinary troubles.	[61]
86.	<i>Phyllanthus urinaria</i> Linn.	Euphorbiaceae	Chakpaheikru (M)	Whole plant	Urinary disorder, Jaundice.	[47]
87.	<i>Ranunculus sceleratus</i> Linn.	Ranunculaceae	Kakyel-khujil (M)	Whole plant	Urinary disorder, blisters & skin diseases	[46]
88.	<i>Rhus semialata</i> Murr.	Anacardiaceae	Heimang (M)	Shoots, leaves and fruit	Used as medicine in intestinal worms, diarrhoea, kidney and urinary complaints, dyspepsia, stomach ulcer and hair lotion.	[45]
89.	<i>Rhus succedanea</i> Linn.	Anacardiaceae	Heimang (M)	The powders of the fruits	The powders of the fruits mixed with egg are given in kidney trouble, urinary complaint due to the stone.	[51]
90.	<i>Rotala baccifera</i> Linn.	Lythraceae	Ishingkundo (M)	Whole plant	The plant is prescribed in urinary trouble by the people in the valley.	[51]
91.	<i>Rotala rotundifolia</i> Roxb. Koehne.	Lythraceae	Labook Leiri (M)	Whole plant	Urinary Troubles.	[50]
92.	<i>Rubus niveus</i> Thumb.	Rosaceae	Heijompat (M)	Leaves	The decoction of the leaves is useful in urinary complaints, for relaxing uterus muscles.	[51]
93.	<i>Saccharum officinarum</i> Linn.	Poaceae	Chu (M)	Stem	Extract purify blood, cures liver and kidney infections.	[59]
94.	<i>Santalum album</i> Linn.	Santalaceae	Cha-chandan (M)	Oil and powder of the wood	Urinary troubles and skin diseases.	[55]
95.	<i>Sesamum indicum</i> Linn.	Pedaliaceae	Thoiding amuba (M)	Seeds	Seed oil is given in urinary complaints.	[51]
96.	<i>Sida acuta</i> Burm.	Malvaceae	Uhal (M)	Roots	Roots are used in urinary complaints.	[51]
97.	<i>Sida rhombifolia</i> Linn.	Malvaceae	Uhal (M)	Whole plant	Urinary disorder, rheumatism, tuberculosis & snake bite.	[45]
98.	<i>Smilax lanceaefolia</i> Roxb.	Liliaceae	Kukur (S)	Rhizome	The rhizome of is used for curing urinary calculi.	[49]

99.	<i>Smilax ovalifolia</i> Roxb.	Liliaceae	Jangli-aushbah (H) Kaitha (Mz)	Roots	Roots are used in urinary complaints.	[51]
100.	<i>Solanum nigrum</i> Linn.	Solanaceae	Leipungkhanga (M)	Seeds	The seed is also used in urinary stones.	[51]
101.	<i>Stephania hernandifolia</i> Walf.	Menispermaceae	Thangga Uriangagangba (M)	Leaves	The juice of the leaves is given in urinary trouble.	[51]
102.	<i>Syzygium aromaticum</i> (Linn.) Merr. and Perry.	Myrtaceae	Long (M)	Flower bud	Boiled with water and administered in kidney stone.	[53]
103.	<i>Tagetes erecta</i> Linn.	Asteraceae	Sanalei (M)	Leaves	The extract of leaves is prescribed in kidney troubles.	[51]
104.	<i>Tamarindus indica</i> Linn.	Caesalpinaceae	Mange hei (M)	Leaves	Boiled decoction of the leaves with sugar helps in exiting and eliminating calculi/stones.	[51]
105.	<i>Thunbergia alata</i> Boj. Ex Sims.	Acanthaceae	Lilha (M)	Leaves	Boiled extract of the leaves is prescribed in urinary tract stones.	[51]
106.	<i>Wedelia chinensis</i> (Osborn) Merril.	Asteraceae	Chinlengbi (M)	Whole plant	The decoction of the plant is used as a medicine for curing urinary trouble due to stone.	[51]
107.	<i>Xanthium strumarium</i> Linn.	Asteraceae	Hameng Sampakpi (M)	Roots	The root decoction is also useful in cancer, urinary stone and purple pains.	[51]

For each plant species listed, scientific name, family name, vernacular names in Assamese (A), Bengali (B), Hindi (H), Khoibu (Kh.), Manipuri (M), Mizo (Mz.), Rongmei (R) and Sikkimese (S) or local dialects used by the tribe, if available are given.

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7. Conflict of Interest

There is no conflict of interests amongst the authors while conducting and compilation of the review. We the authors have share equal contribution to bring out the review in its best form

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