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A COMPREHENSIVE REVIEW ON TREATMENT OF UROLITHIASIS

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ABSTRACT

Renal stone formation is one of the oldest diseases known to human. Kidney stone disease is a crystallopathy characterized by the formation of a solid piece of material (kidney stone) in the urinary tract. It is also known as nephrolithiasis or urolithiasis. Nephrolithiasis is the third most common urological disease, accounting for about 15% of all cases. Urolithiasis affects 7–13% of people in North America, 5–9% of people in Europe, and 1–5% of people in Asia. Calcium stones, usually in the form of calcium oxalate are the most frequently reported stone type in India. Hyperparathyroidism, hyperthyroidism, sarcoidosis, gout, malabsorption (inflammatory bowel disease, ileal resection or bypass), cystic fibrosis, and renal abnormalities are all associated with an increased risk of kidney stone formation (medullary sponge kidney, distal renal tubular acidosis, and anatomical abnormalities). Small stones do not require much treatment; they are removed from the body by drinking plenty of water. The movement of stones causes pain, which can be treated with pain relievers while large stones are difficult to remove even with plenty of water because they get stuck in the renal tube. These stones can be harmful to the body because they can damage the kidneys and cause internal bleeding, UTIs, and kidney damage. Treatment like Synthetic drugs**,** surgical treatment, non-surgical treatment, herbal drugs, Ayurveda like Pashanbheda, and other herbs, are available. The present review, therefore, is intended to provide up-to-date information on the etiology, types of stone, signs and symptoms, risk factors, complications, mechanism of formation of stone, the composition of stone, diagnosis, and treatment.

Keywords: Ayurveda, Herbal drugs, Nephrolithiasis, Pashanbheda, Renal stone

1. INTRODUCTION

1.1. The Urinary System and kidney stone

Renal stone has been considered one of the most ancient diseases known to mankind. Kidney stone disease is a crystallopathy characterized by the formation of a solid piece of material (kidney stone) in the urinary tract. It is also known as nephrolithiasis or urolithiasis. Nephrolithiasis is the third most common urological disease; accounting for about 15% of all cases **[1]**. The kidney is a functional organ that is linked to urinary bladder and ureter, which is the lower part of the body. Prior to that, the kidney also regulates the volume of various body fluids, acid-base balance, and concentration of various electrolytes, fluid osmolality and removal of toxins. The glomerular filtrate flows into the tubules, where reabsorption and secretions change the volume and content. The proximal tubules are responsible for the majority of solute reabsorption, while the distal tubules and collecting ducts are responsible for fine adjustments to urine composition and acid-base balance. The Henle loop concentrates urine, which is 95% water, 2.5% urea and a mixture of minerals, salts, hormones, and enzymes that makes 2.5% **[2]**. Any imbalance in kidney function can result in diseases such as renal calculi, chronic kidney disease (CKD), polycystic kidney disease (PKD) and urinary tract infections (UTI)**[3]**. Renal stone disease is distinguished by insoluble deposits found in the urinary tract, known as stones, which obstruct normal urine flow. The location of stone might differ as shown in **Figure 1**.

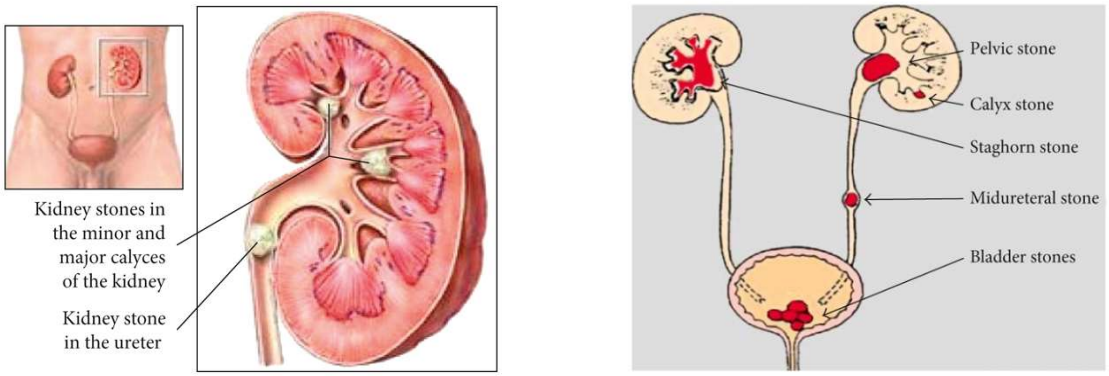

Figure 1: Location of kidney stone in urinary system. (a) Adopted from[4], (b) Adopted from[5]

Urolithiasis affects 7–13% of people in North America, 5–9% of people in Europe, and 1–5% of people in Asia **[6-8]**. Men aged 40-50 and women aged 50-70 are most frequently affected by nephrolithiasis. Urinary supersaturation, crystal nucleation, crystal development, accumulation and retention of urinary stone constituents within tubular cells are all physicochemical events that occur during this process **[9]**. When urine becomes concentrated, minerals may crystallize, adhere, and solidify, resulting in kidney stones. Hypercalciuria is a significant risk factor for calcium urolithiasis. Urinary stones can be classified on the basis of their location, size, and composition, etiology of formation, X-ray properties and risk of recurrence. Calcium oxalate (75%-90%) is the most common component of calculi, followed by uric acid (5%-20%), calcium phosphate (6%-13%), struvite (2%-15%), apatite (1%), and cystine (0.5%-1%) **[10]**. Kidney stone formation is caused by an imbalance between crystallization promoters and inhibitors shown in **Table 1**.

In Ayurveda, the main cause of calculi formation is a lack of Panchakarma (five methods of body purification), an unhealthy diet, and bad lifestyle. In conventional medicine, urolithiasis is caused by three major factors: geographic location, heredity and dietary factorsshown in **Table 2**.

Table 1: Kidney stone promoters and inhibitors

Stone promoters	Stone inhibitors
Cell membrane lipids[11], parathyroid hormone stimulation[12], calcium, oxalate, low urine volume[13], sodium and cystine.	Small organic and inorganic anions like citrate and pyrophosphates, multivalent metallic cations like magnesium and macromolecules (osteopontin, glycosaminoglycans, glycoproteins, urinary prothrombin fragment-1 and Tamm–Horsfall proteins[14, 15].

Table 2: Conditions favoring the development of kidney stone

Sr. No.	Factors	Functions
1	Urinary pH	Acidic- cysteine, uric acid Alkaline- calcium phosphate
2	Increased urinary crystals	Form nucleus on the existing surface Supersaturated urine
3	Dehydration	Low urine volume, supersaturated urine
4	Diet	Hypercalciuria, uricosuria, oxaluria
5	Increased promoters	Uric acid
6	Decreased inhibitors	Magnesium, citrate, uropontin, nephrocalcin, tammhorsfall
7	Medication	Furosemide- decreases urinary volume Sodium bicarbonate- increases urinary calcium

Hyperparathyroidism, gout, sarcoidosis, cystic fibrosis, malabsorption and renal abnormalities are all linked with an increased risk of renal calculi (anatomical abnormalities, distal renal tubular acidosis and medullary sponge kidney). Symptoms of kidney stone include pain in lower abdomen or back, pain while peeing or blood in urine. Urinary stones as small as a few millimeters in diameter may pass easily through urine. The spontaneous passingrate of stones with diameters of less than 5 mm and 5-10 mm is 68% and 47%, respectively. Patients with large stones must be treated using modern interventional methods.

Treatment of kidney stones includes supportive care such as increased fluid intake, several medications such as NSAIDs, Ca^{+2} channel blockers, corticosteroids, potassium citrate, thiazide diuretics, allopurinol, pyridoxine, bicarbonate salts anti-bioticsand medical procedures such as Extracorporeal shock wave therapy, uteroscopic stone removal, and laser lithotripsy; however, these procedures are expensive, and recurrence of kidney stones and side effects cannot be avoided **[16]**.

In 2000, the total cost of healthcare for kidney stone patients in the United States was approximately $2.1 billion **[17]**. Surprisingly, the rising prevalence of diabetes and obesity is expected to increase by $1.24 billion per year by 2030 and thus the demand for polyherbal formulations in preventing lithiasis has increased **[18]**.

The term "mutrashmari" appears in Ayurvedic literature. Mutra refers to urine, while Ashmari refers to stones **[19]**. PittajAshmari is Uric acid urate, cysteine calculus, Vataj Ashmari is calcium oxalate, and KaphajaAshmari is phosphatic calculus. Furthermore, recurrence rates are close to 50% **[20]**.

Medicinal plants have been used for centuries due to their safety, efficacy, cultural acceptability, and lower side effects than synthetic medicines. The World Health Organization (WHO) is also interested in the use of herbal drugs due to their ease of availability, low cost, and lack of side effects **[21, 22]**. Cystone, a polyherbal formulation, was created based on a reference found in the ancient Ayurvedic system of medicine and has been widely used for a long time to treat urinary/renal calculi**[23]**.

Pashanbheda represents a group of plants that have anti-urolithiatic and diuretic activity (Pashana=stone; Bheda=break) **[24]**. *Dolichus biflorus* **[25]**, Cystone **[23]**, Stonil **[26]**,

Phyllanthus niruri **[27]**, *Nigella sativa* **[28]**, *Pedalium murex*, *Crataeva nurvala*,

Boerhavia diffusa, *Bergenia ligulata* **[29]**, *Tribulus terrestris* and anti-lithiatic biomolecules such as epigallocatechin-3-gallate (EGCG), thymoquinone, lupeol, quercetin and bergenin are used to treat urolithiasis **[30]**.

1.2 History

The history of urolithiasis roughly begins and parallels the history of civilization. The origins of modern science and philosophy can be traced back to ancient Egypt, where the first signs of social and scientific development can be found. E. Smith, a British archaeologist, discovered a bladder stone from a 4,500-5,000 year old mummy in 1901, El Amrah, Egypt. Since 1500 BC, stone treatment has been mentioned in ancient Egyptian medical writings **[31, 32]**.

1.3 Epidemiology

Nephrolithiasis prevalence and recurrence rates are rising worldwide. Effective drugs have a limited potential. Approximately 12% of the world's population suffers from urolithiasis at some point in their lives **[33]**. It affects people of all age, gender and race, but men are affected more than women between the age of 20 and 49 **[34]**. The recurrence rate of secondary crystal formation in patients is estimated to be 10-23% per year if metaphylaxis is not used, 50% after 5-10 years, and 75% after 20 years **[35]**. Men had a higher lifetime recurrence rate than women even though kidney stones are more common in women **[36]**. According to recent research, the prevalence of urolithiasis has risen in both developing and developed countries over the last few decades. This rising trend is believed to be related to dietary and lifestyle changes, such as sedentary and dietary habits **[37]**.

1.4 Etiology

Urolithiasis results when urine solutes crystallize to form stones. Urolithiasis can be caused by a urinary tract obstruction, decreased urine output, insufficient fluid intake, dietary factors (such as high levels of oxalate or sodium), urinary tract infections, systemic acidosis, medications or abnormal genetic factors such as cystinuria. Hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia are the other four most common factors that contribute to urolith formation **[38]**. Drugs like atazanavir, indinavir, triamterene, guaifenesin, silicates and sulfonamide are medications that have been linked to kidney stone formation. Renal calculi appear to have a genetic link. There may be mutations that affect how calcium and other substrates are handled by the renal tubule in some families.

1.5 Types of Kidney Stone

Anomalies in the composition of various chemicals in urine determine the chemical

composition of kidney stones, shape and size. Alsochemical composition of stones differ (mineralogy) **[39]**. Based on differences in mineral composition and pathogenesis, stones are typically divided into five types, as shown in **Figure 2** and **Table 3 [40]**.

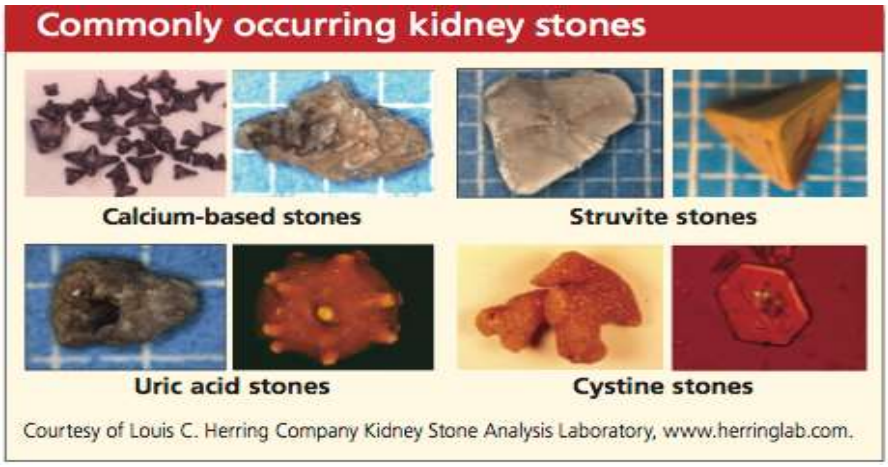

Figure 2: Types of kidney stone

Table 3: Types of kidney stone

Sr. No.	Name of Stone	Approximate Incidence	Constituents	Comments
1	Calcium oxalate	70% of all stones	Calcium, oxalate	It may be caused due to high levels of calcium as in hyperparathyroidism & also due to high level of oxalates, renal calcium leak, hypomagnesaemia and hypocitraturia
2	Calcium phosphate	10% of all stones	Calcium, phosphate	
3	Uric acid	5-10% of all stones	Uric acid	Formed due to low urine output, excessive intake of protein, gout, inflammatory bowel disease, and in acidic urine
4	Struvite	10% of all stones	Calcium, ammonia, phosphate	Associated with urinary infection and form staghorn calculus and may cause chronic kidney disease and permanent damage to the kidney
5	Cystine	Less than 1% of all stones	Cystine	Occur due to inherited defect in amino acid transport, manifests as recurrence stone in young patients
6	Medication-induced stones	Less than 1% of all stones	Composition varies depending on the drug or herbal product	Guaifenesin, indinavir, triamterene, silicate (antacids), and sulpha medication produce kidney stones

1.6 Signs and Symptoms

When kidney stones are small, they may pass on their own without causing any symptoms. Larger stones obstruct urine flow, resulting in painful symptoms such as **[41]**, a back and side pain that is sharp and wavy and may extend to the lower abdomen or genitalia. Some female patients believe that the agony is worse than

labour contractions during childbirth. It results in a state of intermittent pain and discomfort, urge to urinate suddenly **[42]**; a burning sensation during urination, the presence of RBC blood particles will make the urine dark or red in colour. Blood can occasionally be so light in colour that it cannot be seen with the naked eye, Male patients experience discomfort at the tip of their penis, Fever and chills if there is an infection, nausea and vomiting, urinary retention, and pus in the urine, cloudy or foul-smelling urine shown in **Table 4**.

Table 4: Relationship of the stone location to symptoms [43]

Sr. No.	Stone location	Common symptoms
1	Proximal ureter	Flank pain, upper abdominal pain, renal colic
2	Middle section of the ureter	Flank pain, renal colic, anterior abdominal pain
3	Distal ureter	Urinary frequency, renal colic, dysuria and anterior
4	Kidney	Hematuria, vague flank pain abdominal pain

1.7 Risk Factors

Obesity **[44]**, family history, dehydration, individuals who frequently perspires due to living in hot, dry climates are also more susceptible to stone disease, dietary factors- protein, sodium (salt), fat, sugar, and oxalate-rich diets may increase the risk of kidney stones, digestive diseases and surgery- certain surgeries, such as gastric bypass surgery, Crohn's disease, and chronic diarrhoea, interfere with calcium absorption and increase the risk of stone formation **[45]**. As compared to others, people who have urinary tract infections (UTIs) or other kidney related infections especially in women are more prone to acquire struvite stones, Other medical issues that can increase the likelihood of stone formation include renal tubular acidosis (RTA), diabetes, gout, obesity, urinary tract infections, metabolic syndrome, hyperparathyroidism, sarcoidosis, cystinuria, and some cancer **[46]**.

1.8 Complications

Complications may arise not only from the stones themselves but also from the treatment procedures, Recurrence (the most common complication is the recurrence of kidney stones), Xanthogranulomatous pyelonephritis-cell carcinoma of renal pelvis, Urinary tract obstruction and infection- urinary tract obstruction can cause kidney damage and make the urinary tract susceptible to infection, Urine extravasation- leakage of urine due to injury in renal parenchymal cells or collecting systems, hydronephrosis (excess accumulation of urine in kidney), ureteral stricture- narrowing of urethra, impaction, infection, sepsis, and perinephric abscess-

collection of pus resulting from bacterial infections.

1.9 Mechanism of Stone Formation

Randall's plaque, which is formed at the junction of the nephron collecting duct and the papilla renal pelvis, is the origin of the majority of urinary calculi. These plaques form beneath the urinary tract and spread gradually until they reach the renal pelvis. With continued urine contact, a layer of calcium oxalate usually forms over calcium phosphate lesions (all Randall's spots are calcium phosphate). When the urine pH falls below 7.2, calcium oxalate stones form, whereas calcium phosphate stones form in alkaline urine. Similarly, metabolic disorders such as hyperparathyroidism and renal tubular acidosis typically result in calcium phosphate stones. All kidney stone patients have urinary saturation. Occasionally, calcium oxalate stones can form in the renal papillae. Calcium phosphate stones typically erode into the stroma after falling into the basement membrane of the thin loop of Henle. Colic is typically caused by ureter dilation and spasm **[47, 48]** Shown in **Figure 3**.

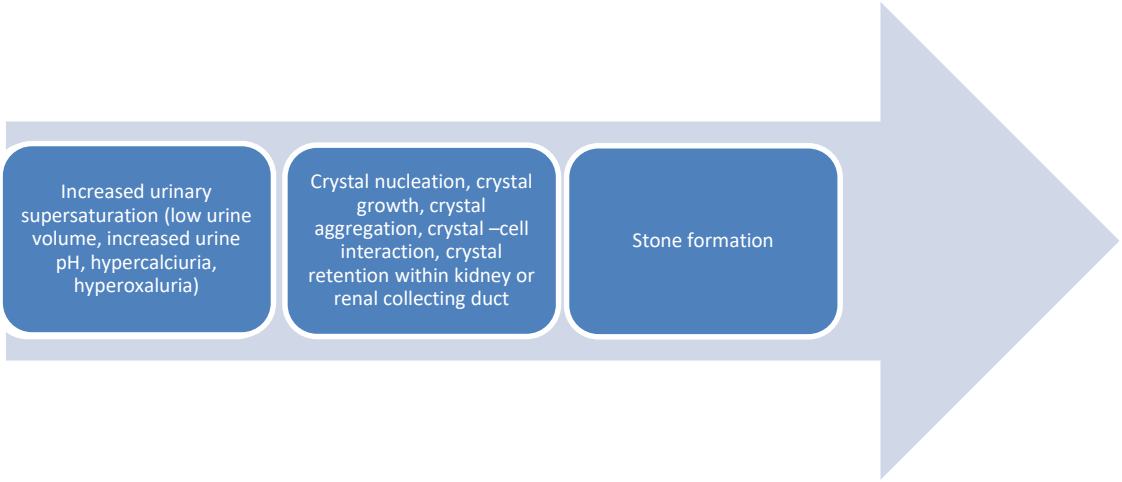

Figure 3: Mechanism of stone formation

1.10 Composition of Kidney Stone

Crystalline and non-crystalline phases make up the chemical composition of kidney stones. Glycosaminoglycans (GAGs), carbohydrates, protein, and lipids formsthe organic matrix of kidney stones. These molecules play a vital role in the formation of kidney stones. Proteins (64%), hexosamine as glucosamine (5%), non-amino sugars (9.6%), water (10%), and inorganic ash (10.4%) are the essential elements of the stone matrix. Phospholipids (8.6% of total lipid) comprise the matrix of all stones, accounting for approximately 10.3% of the stone matrix. Cell membrane

phospholipids contribute to the formation of calcium stones as a component of the organic matrix **[14]**. The most abundant component of all stone matrices is albumin **[11]**.

2. DIAGNOSIS

Diagnosis is done on the basis of patient history, physical examination, laboratory findings, imaging tests, and stone analysis.

a) **Patient history:** A medical practitioner will inquire if you have a medical history of any disorders that increase your risk of kidney stones.

b) **Physical examination:** The physician asks patients about the symptoms like nausea, vomiting, abdominal discomfort, pain while urinating, and fever.

c) **Lab tests:**

- **Blood tests:** These are performed to assess kidney function, calcium, phosphorus, electrolytes, uric acid, and other substances that may have contributed to the formation of stone.
- **Urine tests:**A 24-hour urine sample collected and analyzed for urine pH, volume, uric acid, calcium, oxalate, and other substances. Microscopic analysis of the urine may also reveal crystals, casts, germs, leukocytes, and red blood cells**[49]**.

d) **Imaging test:** Imaging studies are critical in the treatment of patients with urolithiasis. Plain X-ray of abdomen, ultrasound scans, magnetic resonance imaging, intravenous urograms and computed tomography (CT) are among the techniques available **[50]**.

- **CT scans:** It is a type of imaging test that combines X-rays with computer technology that create images of urinary tract. A CT scan can produce significantly more radiation than an X-ray. These scans have more sensitivity than X-rays and can identify smaller kidney stones. CT scans are frequently used by emergency room personnel because they provide faster and more detailed images, allowing for faster diagnosis. They also provide more detailed images, showing the stones' exact size and location.
- **Ultrasound:** Although CT scans are the most accurate and are frequently used in emergencies, ultrasounds are also acceptable. A doctor may advise you to start with an ultrasound because it is quick, safe, and simple. It does not use radiation, unlike an X-ray or CT scan. Although CT scans have higher sensitivity, using ultrasound first is a common practice that has been shown to perform similarly in emergencies. If the

ultrasound image is unclear, you may still require a CT scan.

- **Kidney-Ureter-Bladder X-ray**: If your doctor suspects you have kidney stones, he or she may request a KUB (kidney-ureter-bladder) X-ray. It is an imaging test that produces images of abdomen using low levels of radiation. It helps to figure out the size and location of kidney stone in urinary tract.
- **Intravenous urography**: It is one of the imaging tests used to detect kidney, ureter, and urinary bladder problems. To examine the urinary tract organs, a contrast material is injected into the body through the veins. The X-ray images obtained following the procedure are referred to as an intravenous urograms or an intravenous pyelogram.

e) Stone Analysis: Analysis of kidney stone is an essential component of nephrolithiasis research in order to comprehend the role of trace constituents in stone formation and to come up with further approaches for both prevention and treatment of stone formation and recurrence **[51, 52]**.

3. TREATMENT

- **Small stones**: small stones can be removed easily from the body by drinking plenty of water. Pain relievers can be used to treat the pain caused by dislocation of the stones. Alpha blockers are commonly prescribed by doctors as they cause muscle relaxation in ureters, allowing the stone to pass more quickly. Diuretics can also help with stone removal by increasing urine flow **[53]**.
- **Large stones:** Large stones get trapped in the renal tube, making it difficult to remove them even with plenty of water. Due to their potential for kidney damage and internal bleeding these stones pose a threat to health **[54]**.

3.1 Synthetic drugs used for kidney stone treatment

The synthetic drugs widely used for kidney stone are listed with their class and mechanism of action in **Table 5**.

Table 5: Synthetic drugs used in the treatment of Kidney Stone

Sr. No.	Drug	Class	Mechanism of action
1	Allopurinol (Lupurin, Zyloprim)	Analogue of hypoxanthine	Prevents the synthesis of urate by inhibiting xanthine oxidase
3	Cholic acid	Bile acid derivatives	Enhances bile flow and maintains bile acid homeostasis
4	Cholestyramine (Questran)	Bile acid sequesterats	Increases LDL receptor activity
5	Digoxin (Lanoxin)	Cardiac glycoside	Inhibition of Na^+, K^+ ATPase
6	Etidronate disodium	Bisphosphonates	Prevents hydroxyl apatite dissolution
7	Fluvastatin (Lescol)	Statin	Reduction of LDL levels
8	Gemfibrozil	Fibric acid derivatives	It reduces triglycerides through PPAR-α moderated stimulation of fatty acid oxidation
9	Indinavir	Peptidomimetic hydroxy ethylene	Protease Inhibitor
10	Zonisamide	Sulphonamide Derivatives	Blocks sodium and T-type calcium channels and suppress neuronal hyper-synchronization

3.2 Surgical treatment

- In the United States, minimally invasive interventions for stone disease are primarily based on three surgical procedures: Extracorporeal shock wave lithotripsy (ESWL), Ureteroscopic lithotripsy and Percutaneous nephrolithotomy (PCNL)**[55]**.
- The characteristics of the stone and the patient will determine the course of treatment for that patient.
- Each minimally invasive procedure employs ultrasound or fluoroscopy as an imaging source to find the stone and an energy source to break it up.
- ESWL fragments the stone using a shock wave energy source created outside the body.
- PCNL entails dilation of a tract through the back into the renal pelvis in order for instruments to be inserted directly onto the stone to fragment or pulverize it.
- Ureteroscopy involves the use of a ureteroscope to direct laser energy directly on the stone.

3.3 Non-Surgical treatment

- Non-surgical therapies for kidney stone includes: Fluid intake therapy, probiotic therapy, diuretics, expulsive therapy and herbal therapy **[56]**.

3.4 Herbal drugs

- Herbs and herbal medicines can be used to treat kidney stones. For the treatment of human diseases, natural herbs are used for their therapeutic potential and biological properties because of their scientifically proven benefits such as anti-oxidant, anti-microbial, anti-inflammatory, nephro-protective, diuretic action. Also, the overuse of synthetic pharmaceuticals leads to an increased rate of adverse drug reactions which prompted humans to turn back to natural therapies.

- Quercetin, thymoquinone, lupeol, epigallocatechin-3-gallate (EGCG), bergenin are significant antilithiatic biomolecules that have the potential to reduce the size and count of renal calculi. The biological activity of each of the individual active ingredients determines how effective a herbal extract is. By combining these biomolecules with standard medical care and dietary changes, the physician could possibly be able to improve the likelihood of restoring kidney function.
- *Mentha piperita* (family-Labiatae), *Elettaria cardamom* (zingiberaceae), and *Syzygiumcumini* (family-Myrtaceae) leaves are reported to be useful in the treatment of urinary stones in indigenous medicine **[57]**.
- *Nigella sativa* (black cumin seed), *Crataeva nurvala* (varuna bark), *Dolichos biflorus* (horse gram) and *Tribulus terrestris* (Gokshura) have the supporting pre-clinical data and the best clinical trials showing effectiveness in reducing kidney stone formation and recurrence. For safety and effectiveness, some of these medicinal plants have been compared to tamsulosin (Flomax®) and potassium citrate. These plants have anti-oxidant and anti-microbial properties **[58]**.

3.5 Ayurveda

- Ayurveda provides a synergistic therapeutic approach that addresses multiple factors that cause and exacerbate illness in the body. Ayurvedic medications are based on the basic constitution of the body and aid in the attainment of optimal health.
- Urolithiasis is regarded as one of the eight most troublesome diseases in Ayurveda. Several plants and their formulations were mentioned in ancient medical texts as having anti-urolithiatic properties. It is referred to as Mutrashmari in Ayurvedic literature, where Mutra stands for urine and Ashmari for stone.
- There are four different kinds of Ashmari, Vatika, Paitika, Shlaishmika, and Shukraja. Pittaj Ashmari is Uric acid urate, cysteine calculus, and KaphajaAshmari is phosphatic calculus. And Vataj Ashmari is calcium oxalate.
- For the treatment of Ashmari roga, three types of drugs have been mentioned in Ayurvedic texts: Mutravirechaniya (diuretic), Ashmarighna Dravya (lithotriptic),

and Kshara Karma (alkali therapy) (Urolithiasis). Mutravirechaniya (diuretic) and Ashmarighna Dravya (lithotriptic) have been mentioned in Ayurvedic texts as being very beneficial for urolithiasis. Varuna (*Crataeva nurvala*), Gokshura (*Tribulus terrestris*), Pashanbheda (*Bergenia ligulata*), Shilajit (*Asphaltam Panjabinum*), YavaKshara (alkali preparation of *Hordeum vulgare L.*), and other drugs are frequently mentioned in our texts **[59]** Shown in **Table 6**.

Table 6: Adapted from Ayurvedic Pharmacopoeia, Volume I –VI

S.No.	Plant name	Family	Sanskrit Name	Part used	Constituent	Dose
1.	*Abutilon indicum*	Malvaceae	Kankatika Risyaprakta	Root	Aspargin	3-6 gm, powder
2.	*Aerva lanata*	Amaranthaceae	Goraksaganja Bhadra	Whole plant	α & β-Sitosterol Chrysin Flavonoid Glycoside	50-100 ml, decoction
3.	*Apium graveolens*	Apiaceae	Bonjamani Bonajain Yamani Ajowan	Root	α and β- pinene Limonene Beta-selinen	5-7 gm, powder
4.	*Boerhavia diffusa*	Nyctaginaceae	Kathilla Sophagnhni Sothaghni	Dried whole plant	Alkaloid (punarnanine)	20-30 gm, decoction
5.	*Curcuma longa*	Zingiberaceae	Rajani Nisa Nisi Ratri Ksanada	–	Essential oil&coloring matter (curcumin)	1-3 gm, powder
6.	*Celosia argental*	Amaranthaceae	Sushunimaak Shushunishak	Seed	Non-peptide Celogenamide Celosian	3-6 gm, powder
7.	*Crataeva nurvala*	Capparaceae	Varana	Dried stem bark	Saponins Tannin	20-30 gm, decoction
8.	*Citrus media*	Rutaceae	Matulunga	Fresh fruit	Volatile oil	10-20 ml, juice
9.	*Hordeum vulgare*	Poaceae	Dhanya Raja Tiksnasuka Hayesta	Dried fruit	Starch Sugars Protein Glycosides Flavonoids	100-200 gm
10.	*Mimosa pudica*	Fabaceae	Samanga Varakranta Namaskari	Dried whole plant	Alkaloid	10-20 gm, decoction
11.	*Melia azedarach*	Meliaceae	Ramyaka Dreka	Dried stem bark	Tannins Alkaloid	5-10 gm
12.	*Moringa oleifera*	Moringaceae	Sobhanjana Bahala Tiksnagandha Aksiva	Dried root bark	Fixed oil	5-10 gm, powder
13.	*Nigella sativa*	Ranunculaceae	Sthulajiraka Vpakumci Susavi	Seed	Essential oil Fixed oil Resin Saponins Tannin	1-3 gm, powder
14.	*Ocimum sanctum*	Lamiaceae	Surasa Bhutaghni	Seed	Fixed oil mucilage	1-2 gm, powder
15.	*Raphanus sativus*	Brassicaceae	Salamarkataka Visra Saleya Marvsambhava	Root	Glucoside Methyl-mercaptan Volatile oil	5-30 ml, juice

16.	***Rubia cordifolia***	**Rubiaceae**	**Yojnavalli Rakta Vastrarajini**	**Dried stem**	**Glycosides**	**2-4 gm**
17.	***Ricinus communis linn***	**Euphorbiaceae**	**Gandharvahasta Vatari Pancangula Rubu**	**Root**	**Alkaloid (ricinine)**	**20-30 ml, decoction**
18.	***Terminalia arjuna***	**Combretaceae**	**Kakubha Partha Svetavaha**	**Stem bark**	**Tannins**	**3-6 gm, powder**
19.	***Tribulus terrestris linn***	**Zygophyllaceae**	**Goksuraka Trikanta Svadamstra Traikantaka**	**Fruit**	**Potassium nitrate Sterols Sapogenin with pyroketone**	**20-30 gm, decoction 3-6 gm, powder**
20.	***Trigonella foenum-graecum***	**Fabaceae**	**Methini**	**Seed**	**Alkaloid Sapogenin Mucilage**	**3-6 gm, powder**

3.6 Pashanbheda

- Pashanbheda is a drug used in Ayurveda for various urinary disorders, primarily as lithotriptic and diuretic. Many diuretic and other plants, including *Didymocarpus pedicellata*, *Rotula aquatica*, *Bryophyllum spp.*, *Ocimum basilicum*, *Coleus spp.*, *celosia argental*, *Bauhinia racemosa* and others, have been called Pashanbheda. *Bergenia ligulata* syn.. *Saxifrega ligulata* is now commonly known by this name.
- *Bergenia ligulata:* This name is widely accepted as a synonym for *Saxifrega ligulata*. It is a succulent perennial herb found in the Himalayas, as well as in Central and East Asia and Pakistan. Pashanbheda contains Bergenin, 1, 8-cineole, Isovaleric acid, Pashanolactone, Stigmesterol, Parasorbic acid, Gallic acid Tannic acid which has diuretic, anti-inflammatory, and anti-lithiatic activity. The use of the various names attributed to *Bergenia ligulata* fully justifies their chemical efficacy in removing kidney stones, including Ashmabhed, Ashmabhid, Nagabhid, Asmaribheda, Pashana, Pashana, Pashanbheda, Shilabhed (dissolving or piercing stones or slabs), Parwatbhed and Upalbhedak among others **[60]**.
- *Tribulus terrestris:* It is well-known for its immune-modulatory, diuretic, and anti-urolithic properties **[61]**. *Tribulus terrestris* aqueous extract (Zygophyllaceae family) has anti-urolithic, antioxidant, anti-inflammatory, and diuretic properties **[62, 63]**.

- *Aerva javanica:* It belongs to the Amaranthaceae family and has nephroprotective activity **[64]**.
- *Aerva lanata:* It have anti-urolithiatic and mild diuretic properties, reduce the size of kidney stone and increase excretion of calcium, phosphate, and oxalate while maintain magnesium levels **[65]**.
- *Bryophyllum pinnatum*: Leaf extract inhibited the formation of renal calculi caused by ethylene glycol. Extracts have an antilithiatic effect by dissolving preformed stones and/or preventing the formation of Calcium oxalate crystals as well as antioxidant activity **[66]**.

3.7 Researcher reported for stone dissolving activity

- *Melia azedarach Linn* leaves exhibit strong anti-urolithiatic action in both aqueous and ethanol extracts **[67]**.
- Anti-oxidant and anti-urolithiaticproperty of *trigonellafoenum-graecum* exerts beneficial effect in kidney stone **[68]**.
- Urolithiasis can be treated with methanolic extracts of *Launaea procumbens* leaves **[69]**.
- *Berberis vulgaris* a homoeopathic preparation acts as a reno-protective remedy, alleviating renal calculi-associated damage by increasing anti-oxidant status **[70]**.
- *Didymocarpus pedicellata* showed no crystals and reduced damage to kidney, protecting against urolithiasis and nephrotoxicity and is useful in the treatment of urolithiasis **[71]**.
- An ethanolic extract of *Ocimum sanctum* leaves prevented the formation of calcium oxalate crystals in vitro **[72]**.

4. CONCLUSION

The effects of various available treatments with proposed uses for the treatment of urolithiasis are critically reviewed in this article. Currently, in the treatment of urinary stones, synthetic drugs and surgical methods like extracorporeal shock wave lithotripsy are widely applied. The main limitation of these procedures is recurrence of stones. Herbal drugs and their formulations may not replace these processes, but can certainly help to reduce kidney stone recurrence rates. The multifactorial nature of urolithiasis, the biochemical disturbances that cause urolithiasis and the various chemical forms of kidney stones could be the primary obstacles for the development of a standard drug.

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