

A Comprehensive Review on Urolithiasis

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ABSTRACT:

Urolithiasis, a multifactorial urinary disorder, is characterized by the formation of kidney or urinary tract stones, primarily composed of calcium oxalate. Its increasing global prevalence is influenced by factors such as age, sex, genetics, climate, and lifestyle, particularly modern dietary patterns and inadequate hydration. Stone formation arises chiefly from urinary supersaturating with calcium and oxalate, compounded by reduced levels of natural inhibitors like citrate, magnesium, potassium, phytate, and pyrophosphates, which typically prevent crystal aggregation. While no definitive curative therapy exists, several pharmacological agents—such as alpha-blockers (e.g., tamsulosin), calcium channel blockers (e.g., nifedipine), and PDE-5 inhibitors (e.g., tadalafil)—aid in stone expulsion by relaxing ureteral smooth muscles. Acute pain is managed using opioids and anti-inflammatory agents in emergency care. Comprehensive metabolic evaluation is essential for identifying patient-specific risk factors and guiding preventive strategies. Advancing research into molecular mechanisms and crystal growth inhibitors holds promise for more effective prophylactic and therapeutic interventions.

KEYWORDS: Calcium oxalate Urolithiasis, Urinary stone inhibitors, Pharmacological management

INTRODUCTION:

A major global health concern, nephrolithiasis, also referred to as kidney stone disease, affects about 12% of the world's population. It is linked to higher chances of end-stage renal failure and chronic kidney disease. Physicochemical processes include supersaturation, nucleation, crystal development, aggregation, and retention of urine components, which are the main causes of kidney stones. Calcium oxalate stones are the most common kind, making up between 75 to 90 percent of cases. Even if they work, conventional therapies like ureteroscopy, extracorporeal shock wave lithotripsy (ESWL), and percutaneous nephrolithotomy (PCNL) are

expensive, invasive, and have a high recurrence rate. As a result, alternative therapeutic approaches—especially those based on medicinal plants—have gained popularity. [1] A major global health concern, nephrolithiasis, also referred to as kidney stone disease, affects about 12% of the world's population. It is linked to higher chances of end-stage renal failure and chronic kidney disease. Physicochemical processes include supersaturation, nucleation, crystal development, aggregation, and retention of urine components, which are the main causes of kidney stones. Calcium oxalate stones are the most common kind, making up between 75 to 90 percent of cases. Even if they work, conventional therapies like ureteroscopy, extracorporeal shock wave lithotripsy (ESWL), and percutaneous nephrolithotomy (PCNL) are expensive, invasive, and have a high recurrence rate. As a result, alternative therapeutic approaches—especially those based on medicinal plants—have gained popularity. 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. **In this way, the point of our review is to summarize the foremost vital viewpoints of kidney stones, paying our consideration to the major and follow component composition of these stones. We also Briefly examine the most common strategies for kidney stone investigation at both the natural and atomic levels and incorporate those subtle elements of the types of kidney stones with their characteristics that can be valuable to the analysts. Our Essential accentuation is to investigate the part of major and follow components within the pathogenesis of kidney stones. [2]**

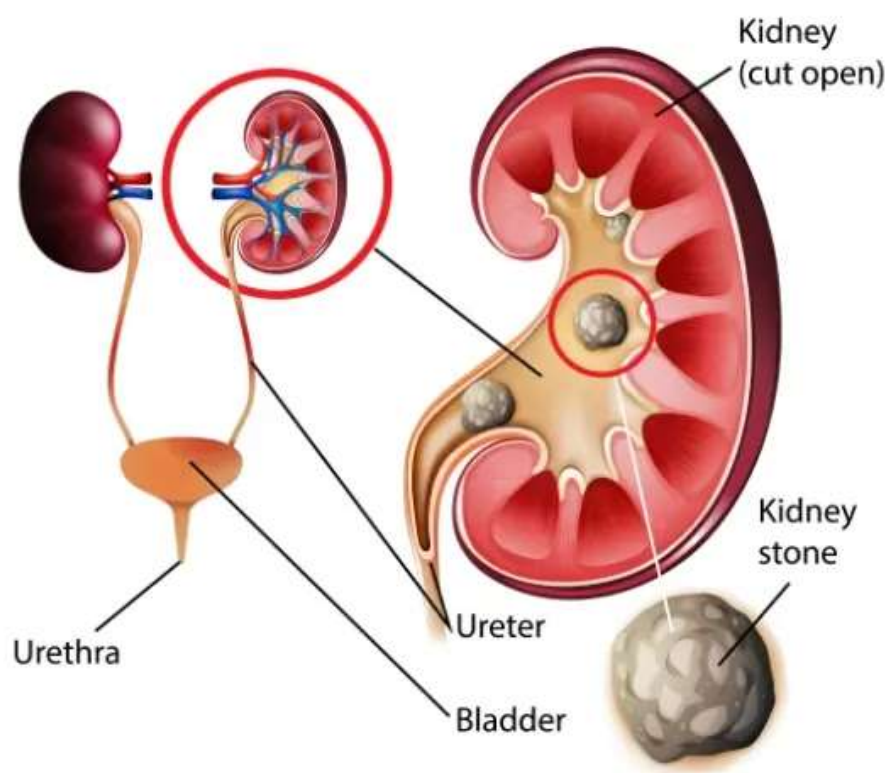


Figure No. :1

HISTORY OF UROLITHIASIS

The history of urolithiasis generally starts and parallels the history of civilization. The roots of advanced science and logic can be followed back to old Egypt, where the primary signs of social and logical improvement can be found. E. Smith, a British paleontologist, found a bladder stone from a 4,500-5,000-year ancient mummy in 1901, El Amrah, Egypt. Since 1500 BC, stone treatment has been specified in antiquated Egyptian restorative works [3].

Epidemiology of Urolithiasis

Nephrolithiasis predominance and repeat rates are rising around the world. Compelling drugs have a restricted potential. Roughly 12% of the world's populace endures from urolithiasis at a few points in their lives. It influences individuals of all age, sex and race, but men are influenced more than ladies between the age of 20 and 49. The repeat rate of secondary crystal arrangement in patients is assessed to be 10-23% per year in the event that metaphylaxis isn't utilized, 50ter 5-10 years, and 75ter 20 a long time. Men had the next lifetime repeat rate than ladies indeed in spite of the fact that kidney stones are more common in ladies. Concurring to later investigate, the predominance of urolithiasis has risen in both creating and created nations over the final few decades. This rising drift is accepted to be related to dietary and way of life changes, such as stationary and dietary propensities [4].

Etiology of Urolithiasis

Urolithiasis comes about when urine solutes crystallize to create stones. Urolithiasis can be caused by a urinary tract hindrance, diminished pee yield, deficiently liquid admissions, dietary components (such as high levels of oxalate or sodium), urinary tract diseases, systemic acidosis, medicines or anomalous hereditary components such as cystinuria. Hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia are the other four most common variables that contribute to urolith formation. Drugs like atazanavir, indinavir, triamterene, guaifenesin, silicates and sulfonamide are medicines that have been connected to kidney stone formation. Renal calculi show up to have a hereditary connection. There may be changes that influence how calcium and other substrates are taken care of by the renal tubule in a few families. [5]

TYPES OF UROLITHIASIS

Urinary stones are categorized into five major types:

1. Calcium oxalate stones

Calcium oxalate urolithiasis is the foremost predominant shape of urinary stone, bookkeeping for generally 50% of all cases. Hypercalciuria, a condition regularly related with calcium kidney stones, has an etiology that's still not completely caught on. In arrange to hinder the arrangement of CaOx stones, it is fitting to direct pee chemistry through controlled modification of sodium, citrate, oxalate, uric corrosive, calcium, and specific gravity levels. By following to a clear dietary arrange that targets five urinary parameters, patients with idiopathic CaOx stone arrangement may decrease their urinary supersaturation. Tis arrange places accentuation fundamentally on weaken pee concentration, reducing crystallization promoters (by means of bringing down oxalate), and lifting crystallization inhibitors (through expanded citrate). Retention of intestinal oxalate can be diminished through higher fluid admissions and calcium utilization amid dinners. Tere is prove that tall dietary calcium admissions can speed up kidney stone advancement, whereas expending low-calcium nourishments nearby oxalate-rich ones

may diminish this chance. Furthermore, the improvement of uric corrosive and CaOx stones is significantly related with weight, not at all like stones comprising calcium phosphate or cystine. The advancement of renal papillary calcifications appears pertinence in prognostic capacity in CaOx urolithiasis cases. Advance inquire about into these features is justified to educate effective preventative procedures against stone arrangement [6,7].

2. Calcium phosphate stones

Calcium phosphate stones, a sort of urolithiasis stone, constitute around 10–20% of all urinary stones, which is a significant worldwide urological concern. Later inquiries have illustrated that calcium urolithiasis frequently emerges due to renal phosphate spillage and concomitant phosphaturia. People with strangely hoisted levels of phosphate in their pee (known as hyperphosphaturia) are at an increased hazard for the repeat of these stones [8].

3. Uric acid stones

Uric acid stones, a specific sort of urolithiasis, include roughly 10% of all occurrences of urinary calculi. These radiolucent stones can be efficiently treated utilizing endoscopic and chemotherapeutic strategies, as well as surgical intercessions such as percutaneous nephrolithotomy and extracorporeal shock wave lithotripsy [9]. The etiology of uric corrosive urolithiasis has still not completely caught on in spite of serious examination. Hyperuricosuria, reliably high pH, and low urinary volume are hazard components for the improvement of these stones. Illnesses such as uncontrolled diabetes mellitus, gout, and leukemia, which cause hyperuricosuria, are known to incline people to uric acid urolithiasis [10]. Moreover, dietary modifications, counting decreased salt admissions and constrained utilization of creature protein, have been illustrated to be effective in avoiding uric acid stones [11].

4. Struvite (magnesium ammonium phosphate) stones

Urinary tract stones known as struvite or magnesium ammonium phosphate stones can be created within the urinary tract. These stones frequently happen in people with urinary tract contaminations caused by microbes that create urease, such as *Klebsiella* or *Proteus* [12]. In spite of the fact that not as common as CaOx stones, this sort of urinary stones constitutes roughly 10–15% of all cases. They are more predominant in females and people with a history of repetitive urinary tract contamination. Struvite stones, composed of ammonium, magnesium, and phosphate can form when urease created by bacteria breaks down urea within the pee, resulting in a rise in pH and the arrangement of struvite stones that can total and shape stones [13]. The avoidance of struvite stones includes treating and avoiding Urinary tract diseases (UTIs) caused by microbes that deliver urease through anti-microbial treatment and great cleanliness hones. Moreover, keeping up urinary tract well-being and satisfactory fluid admissions can also offer assistance avoid the arrangement of struvite stones [14,15]. Depending on their estimate and area, struvite stones require different medicines: little stones may pass suddenly, though bigger stones might require therapeutic intercession intervention intercession mediation Synonyms [16].

5. Cystine stones

Cystine stones, an unprecedented shape of kidney stone, shape due to an acquired metabolic clutter called cystinuria. This clutter leads to a lifted concentration of cystine within the pee, which can crystallize and frame stones within the kidneys, ureters, or bladder. Characterized

by their yellowish-brown color and hexagonal shape, they are ordinarily bigger and harder than other sorts of kidney stones. The predominance of cystinuria, the fundamental cause of cystine stones, is assessed to be around 1 in 7,000 to 1 in 20,000 people around the world. Be that as it may, it changes among different ethnic groups, with higher rates detailed in certain populaces such as Ashkenazi Jews, Libyans, and Cypriots. Cystine stones consist of cystine, an amino acid that contains sulfur. Due to its low solvency, cystine tends to precipitate and shape precious stones in the urine, coming about within the arrangement of cystine stones [17]. The essential avoidance of cystine stones includes overseeing cystinuria through dietary modifications and therapeutic intercessions, counting keeping up high fluid admission, following a low-sodium slim-down, and dodging over-the-top intake of creature protein. Restorative treatment for cystinuria includes the utilization of medicines such as alpha-mercaptopyropionylglycine (tiopronin) or D-penicillamine, which offer assistance to diminish cystine concentration within the urine by shaping solvent complexes with cystine. Preservationist administration, torment administration, and surgical mediation may moreover be fundamental for the treatment of cystine stones [18,19].

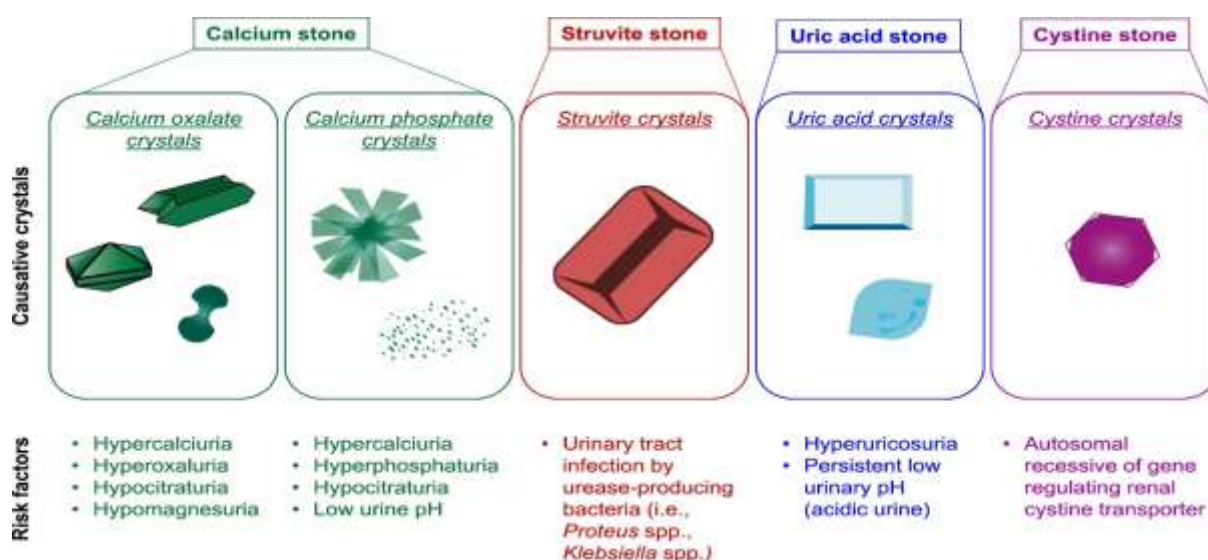


Figure No.: 2

TABLE NO.1: 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.

Promoters of increasing urolithiasis

Urolithiasis can develop due to various factors, including genetic, environmental, and lifestyle influences. Several examples of these variables, along with their respective components contributing to the development of urolithiasis, are presented in Table 1.

Urolithiasis formation inhibitors

Significant advances have recently been made in the creation of inhibitors that target the arrangement of CaOx crystals, such as small molecules, peptides, and proteins [21]. These inhibitors play a crucial role in preventing the pathological crystallization of CaOx crystals. Notably, growth-inhibiting compounds with acidic moieties, including carboxylates, phosphates, and sulfates, have demonstrated remarkable inhibition of calcium oxalate monohydrate (COM) crystal growth, attributed to their specific interaction with Ca²⁺ ions at the crystalline interface. [22] Additionally, synthetic peptides, polymers, and proteins have also shown significant restraint on COM crystal formation. However, it is important to note that the combination of these effective inhibitors heavily relies on synthetic strategies, leading to high costs and potential regulatory approval challenges [23].

Table No: 2 Represent kidney stone inhibitors and their mechanism

Name of the Inhibitor	Mechanism
Citrate	Citrate ties with calcium in urine, decreasing free calcium levels and avoiding crystal arrangement. It stops crystals from clumping by bringing down their capacity to stay together and improves the action of inhibitors like Tamm-Horsfall protein and osteopontin. This makes it a key operator in avoiding kidney stone arrangement.
Magnesium	Magnesium decreases the assimilation of calcium within the stomach related framework and improves its excretion. This brings down the calcium concentration in urine, subsequently diminishing the chance of stone formation. It moreover competes with calcium for oxalate authoritative, lessening calcium oxalate crystallization.
Inter-alpha-trypsin inhibitor family	This protein family makes a difference to avoid calcium oxalate crystal development by halting their connection to kidney tubule dividers. These glycoproteins, such as bikunin, are found in pee and can minimize stone arrangement by lessening precious stone conglomeration and stabilizing their development.

Phytate	Found in plant-based nourishments, phytate anticipates calcium from authoritative to oxalate by connecting to calcium within the gastrointestinal tract. This diminishes calcium's availability for stone arrangement conjointly limits calcium assimilation into the circulatory system, decreasing urinary calcium levels.
Potassium	Potassium makes a difference in decreasing calcium levels in urine, subsequently diminishing the potential for calcium crystal formation. It accomplishes this by moving forward calcium adjust within the body and decreasing urinary calcium excretion, minimizing the chances of kidney stone advancement.
Pyrophosphates	These substances square the formation of calcium phosphate crystals and diminish calcium assimilation. Pyrophosphates work by restraining the nucleation and development of crystals, and their activity is regularly bolstered by vitamin D control, making them valuable in overseeing stone arrangement.
Osteopontin (Uropontin)	Osteopontin ties to precious stone surfaces and pieces their connection to kidney cells. It moreover diminishes the clumping of crystals, constraining their development. This protein anticipates calcium oxalate precious stones from shaping huge totals, bringing down the chance of stone formation.
Urinary prothrombin fragment 1	This protein part, determined from blood clotting variables, is discharged into the urine and makes a difference halt crystal development and attachment. It anticipates calcium oxalate crystals from joining to kidney cells, lessening their collection and making a difference to anticipate stone formation.
Tamm-Horsfall protein (THP)	Moreover called uromodulin, this urinary protein anticipates crystal clumping by blocking the interaction between precious stones and kidney cells. THP's ability to avoid stone formation is affected by components like pH and particle concentration, making it fundamental essential fundamental basic Synonyms for keeping up urinary health.
Glycosaminoglycans	These huge sugar-based particles in urine, such as chondroitin sulfate and hyaluronic corrosive, avoid crystal formation and development. They act as common inhibitors by blocking the conglomeration and connection of crystals, playing a imperative part in stone avoidance.
Renal lithostathine	Lithostathine, a pancreatic protein found in pee, anticipates the development of calcium carbonate gems. It restrains crystal formation by blocking their accumulation and makes a difference

control nucleation, avoiding conditions that advance kidney stone improvement.

[24]

Diagnosis of Urolithiasis

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

1. Patient history: A therapeutic professional will ask in case you have a therapeutic history of any disarranges that increment your chance of kidney stones.

2. Physical examination: The doctor inquiries about patients approximately the side effects like queasiness, spewing, stomach inconvenience, pain while urinating, and fever.

3. Lab tests

a. Blood tests: These are performed to survey kidney work, calcium, phosphorus, electrolytes, uric corrosive, and other substances that will have contributed to the formation of stones.

b. Urine tests: A 24-hour pee test was collected and analyzed for pee pH, volume, uric corrosive, calcium, oxalate, and other substances. Tiny examination of the urine may moreover uncover crystals, casts, germs, leukocytes, and red blood cells [25].

c. CT scans: It could be a sort of imaging test that combines X-rays with computer innovation that makes pictures of the urinary tract. A CT check can deliver altogether more radiation than an X-ray. These checks have more affectability than X-rays and can recognize smaller kidney stones. CT filters are as often as possible utilized by crisis room staff since they give quicker and more point-by-point pictures, permitting quicker decision-making. They moreover give more point-by-point pictures, showing the stones' correct estimate size measure estimate Synonyms and area.

d. Ultrasound: In spite of the fact that CT filters are the foremost exact and are regularly utilized in crises, ultrasounds are moreover worthy. A specialist may prompt you to begin with an ultrasound since it is fast, secure, and basic. It does not utilize radiation, not at all like an X-ray or CT scan. In spite of the fact that CT looks to have higher sensitivity, using ultrasound, to begin with, may be a common approach that has appeared to perform essentially in crises. In case the ultrasound picture is hazy, you will still require a CT filter. [26]

Treatment of Urolithiasis

1. Small stones: Small stones can be expelled effectively from the body by drinking a bounty of water. Pain relievers can be utilized to treat the pain caused by the separation of the stones. Alpha-blockers are commonly endorsed by specialists as they cause muscle unwinding in the ureters, permitting the stone to pass more rapidly. Diuretics can also offer assistance with stone evacuation by expanding urine flow [27].

2. Large stones: Huge stones get caught within the renal tube, making it troublesome to evacuate them indeed with a bounty of water. Due to their potential for kidney harm and inside death these stones pose a danger to well-being [28]

3. Synthetic drugs used for urolithiasis treatment:

The synthetic drugs widely used for kidney stone are listed with their class and mechanism of action in Table 3

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

4. Surgical treatment

- Within the United States, negligibly obtrusive intercessions for stone infection are essentially based on three surgical strategies:

Extracorporeal stun wave lithotripsy (ESWL), Ureteroscopic lithotripsy, and Percutaneous nephrolithotomy (PCNL)

- The characteristics of the stone and the quiet will decide the course of treatment for that quiet.
- Each negligibly obtrusive method utilizes ultrasound or fluoroscopy as an imaging source to discover the stone and a vitality source to break it up.
- ESWL fragments the stone employing a stun wave vitality source made exterior of the body.
- PCNL involves the expansion of a tract through the back into the renal pelvis in arrange for the disobedient to embed a device specifically onto the stone to part or pulverize it.[29]

5. Herbal drugs Treatment

Herbs and herbal drugs can be utilized to treat kidney stones. For the treatment of human maladies, normal herbs are utilized for their restorative potential and natural properties because of their deductively demonstrated benefits such as anti-oxidant, anti-microbial, anti-

inflammatory, nephroprotective, and diuretic activity. Too, the abuse of engineered pharmaceuticals leads to an expanded rate of antagonistic sedate responses which incited people to turn back to characteristic treatments. [30]

6. Ayurveda Treatment:

- Ayurveda gives a synergistic restorative approach that addresses different variables that cause and compound sickness within the body. Ayurvedic medications are based on the essential structure of the body and help with the fulfillment of ideal wellbeing.
- Urolithiasis is respected as one of the eight most troublesome infections in Ayurveda. A few plants and their definitions were said in old therapeutic writings as having antiurolithiatic properties. It is alluded to as Mutrashmari in Ayurvedic writing, where Mutra stands for pee and Ashmari for stone.[31]

Table 4: List of plants used in the treatment of urolithiasis

S.No	Scientific name	Common name	Family	Plant part used
1	<i>Apium graveolens</i>	Lavender	Apiaceae	Flowers
2	<i>Kalanchoe pinnata pers.</i>	Patharchatta	Crassulaceae	Leaves
3	<i>Carica papaya</i>	Papaya	Caricaceae	Root, Fruit
4	<i>Curculigo orchoides</i>	Kali musli, Golden eye grass	Amaryllidaceae	Root
5	<i>Bryophyllum pinnatum</i>	Patharchatta, Ajubu, Ghavapatta, Parnbeeja	Crassulaceae	Fresh leaf juice
6	<i>Cucumis trigonus R.</i>	Kattutumatti	Cucurbitaceae	Fruit
7	<i>Dolichops biflorus</i>	Kulatha, Horsegram, Ulavalu	Fabaceae (Papillionaceae)	Seeds
8	<i>Lagenaria siceraria</i>	Bottle gourd, Calabash, Lauki, Dudhi	Cucurbitaceae	Fruit
9	<i>Macrotyloma uniflorum lam</i>	Madras bean	Fabaceae	Seeds
10	<i>Momordica charantia</i>	Bitter gourd, Carilla, Blasam peer	Cucurbitaceae	Fruits
11	<i>Musa paradisiaca</i>	Banana	Musaceae	Stem juice
12	<i>Moringa oleifera</i>	Drum stick tree, Horse Radish tree	Moringaceae	Pods, Bark, Root, Wood
13	<i>Nigella sativa</i>	Black cumin, Small fennel	Ranunculaceae	Seeds
14	<i>Terminalia arjuna Roxb</i>	Arjuna, Arjun tree	Combrataceae	Bark
15	<i>Rosmarinus officinalis</i>	Rosemary	Lamiaceae	Leaves
16	<i>Nigella sativa</i>	Black cumin, Small fennel	Ranunculaceae	Seeds
17	<i>Tinospora cordifolia</i>	Guduchi, Giloy	Menispermaceae	Stems

18	Mimusops elengi	Spanish cherry, Bullet wood	Sapotaceae	Bark
19	Rubia cordifolia	Madder, Indian Madder	Rubiaceae	Root
20	Grewia flavescens	Kali-siali	Tiliaceae	Root

[32]

Conclusion

Urolithiasis remains a significant global public health concern due to its rising prevalence, recurrence rates, and associated healthcare costs. Despite advancements in diagnostic tools and treatment options—both surgical and non-surgical—recurrence highlights the limitations of conventional therapies. This review has explored the multifaceted nature of the disease, including its epidemiology, etiology, and treatment strategies. Calcium oxalate stones are the most prevalent, influenced by genetics, diet, dehydration, and metabolic disturbances. Understanding the underlying pathophysiology, particularly supersaturation and crystal aggregation, is key to effective management. Endogenous inhibitors such as citrate, magnesium, and phytate, along with plant-based and herbal remedies, have demonstrated promising protective effects. Current treatment spans pharmacological agents (e.g., alpha-blockers, diuretics) and surgical procedures like ESWL, PCNL, and ureteroscopy. Holistic approaches, including Ayurveda and lifestyle modifications, offer complementary benefits. Moving forward, personalized care, metabolic evaluation, and ongoing research into stone inhibitors are essential for developing targeted, sustainable therapies to prevent recurrence and improve patient outcomes.

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