Efficacy And Safety of Herbal Medicine For Urolithiasis- A Systemic Review

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Abstract- *Urolithiasis is the medical term for the development of kidney, bladder, and/or urethral (urinary tract) stones. WHO states that urolithiasis covered 12 percent of the total population, with a ratio of 2.4:1 and a male-to-female ratio of 70 to 81 percent and 47 to 60 percent, respectively. Traditional plants had a variety of chemical components that, through numerous molecular pathways, have positive benefits on lithiasis. Moringa oleifera, Crataeva Magna, Aerva javanica, Peperomia tetraphylla, Terminalia bellirica, Ipomoea eriocarpa, Punica granatum, Hibiscus rosa Sinensis, Costus spiralis, and Herniaria hirsuta are a few medicinal plants that have antiurolithiatic properties. The goal of the current review is to enlighten readers about the latest developments in the study of medicinal plants that have antiurolithiatic effects. This review may aid in identifying the primary substances or herbal remedies that cause urolithic activity.*

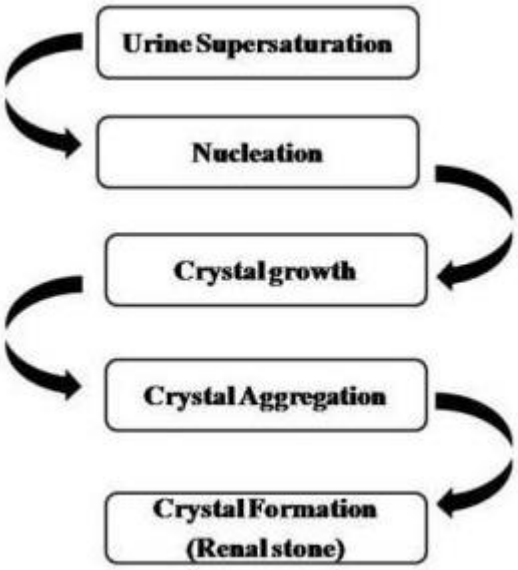
Keywords- Urolithiasis, Molecular mechanism, Traditional plants, Lead compound

I. INTRODUCTION

The development of stones in the kidney, bladder, and/or urethra (urinary tract) is known as urolithiasis [1]. Urolithiasis, from the Greek words ouron, "urine," and lithos, "stone," is the condition in which urinary stones form or are present in the urinary system. Nephrolithiasis (or "renal calculus") refers to kidney stones, ureterolithiasis (or "vesical calculi") refers to ureter stones, and cystolithiasis (or "vesical calculi") refers to stones that originate in or have entered the bladder [2].

Stones can be categorized depending on where they exist or based on the chemicals that make them up. In urinary stones, calcium oxalate is the main ingredient. According to a poll, men encounter their first episode of kidney stones between the ages of 20 and 30, whereas for women it happens later in life. Men also suffer their first episode more frequently than women. [3] \s. In their lifetime, 10% of people will get urinary stones, and the prevalence rises with age. Recurrence rates are 50% within 5–10 years and 75% within 20 years. Women's numbers have rapidly increased over the past 30 years and are now almost at men's levels. [4]

PATHOGENESIS [5]:



The presence of calcium, phosphate, oxalate, and sodium ions in urine contributes to the development of kidney stones. Low urine volume, a low pH, high ion concentrations, and low citrate concentrations all contribute to the development of urinary calculi. Stone creation involves a number of phase physicochemical processes. [6]

Nucleation

In an unstable zone of supersaturation, crystal nucleation takes place as the first step in the production of stone as a result of homogenous salt nucleation. Promoters stimulate heterogeneous nucleation, which results in the production of crystalluria and stones. The promoters supply the reduced energy needed for crystallisation. Due to the lowered energy of the solution, crystal components are formed and integrated into the crystal structure. The other crystalline particles can attach to one another as the crystal components assemble, forming either a directed or random growth pattern before expanding into a bigger particle [7].

crystal formation

When crystals are growing, they can do so epitaxially (overgrowing one crystalline substance on top of another or along a substrate crystalline lattice). Following more crystal growth, the Direct growth of one crystal results from monoepitaxial growth, which is the individual adsorption of molecules or ions from supersaturated urine on the crystal surface. A surface with a distinct composition, or the crystal or substrate surfaces. The components of molecule size and shape, the physical characteristics, pH, and potential structural flaws all play a role in how crystals grow. One of the key steps in the production of stones is crystal growth [8].

Aggregation

Aggregation, which comes after crystal development, is a process in which crystal nuclei join together to produce bigger particles. Rapid aggregation is caused by the attractive force that arises from the spacing between particles. The development of early nuclei is also aided by the addition of appropriate salts. Crystal aggregation, which is a more important stage than nucleation and growth in the production of stones, plays a key role. A narrow interparticle distance that favours particle aggregation as well as the balance of forces between aggregating and disaggregating processes determine which particles are in solution during aggregation [9].

Retention

The connection of crystals within the epithelial cells lining is what causes the crystal retention. The stages of urolithiasis include crystal nucleation, crystal development, crystal retention, and crystal accumulation in the kidney. One of the processes for the production of stones is crystal retention. The pathophysiology of urinary stone production includes crystal growth, crystallisation, and aggregation. The surface composition of the renal tubular epithelial cells may potentially affect the retention process.

II. CLASSIFICATION

1. Stones made of calcium

A significant amount of calcium is present in around 80% of urine calculi in renal stones [10]. Men between the ages of 20 and 30 are more likely than women to develop calcium stones. Stone forms when calcium is combined with oxalate, phosphate, or carbonate [11]. Foods like spinach have a high oxalate level, and vitamin C pills also include oxalate. [12] \s.

2. Cystine stones:

Cystinuria affects those with a high cystine stone burden. Both men and women might be impacted by these stones. There are fewer than 2% of all stone types. in a stone called cystine [13]. A hereditary disease and an excess of cystinuria in urine excretions are caused by the combination and transport of amino acids and cystine [14].

3. Struvite stones:

The prevalence of these stones increases by 10% to 15% and is particularly common in female patients with urinary tract infections. Struvite stones are associated with chronic urinary tract infections (UTI) caused by gram-negative, urease-positive organisms that break down urea into ammonia, which subsequently crystallises into a calculus when combined with magnesium and phosphate. Because struvite stones grow more quickly, they can block the kidney, ureter, or bladder. [15]

4. Uric acid stones:

Women are more likely than men to develop these. With gout or chemotherapy, uric acid stones can occasionally develop. Purines cause hyperuricosuria when consumed in large quantities, and low urine volume and urinary pH (pH 5.05) accelerate the development of uric acid stones[16].

5. Protease-related stones:

Due to the use of the protease inhibitor medication indinavir sulphate, stones of this sort are typically encountered in HIV positive patients [17].

6. Silica stones:

Certain drugs, such as Sulfa indinavir, acetazolamide, ciprofloxacin, triamterene, ephedrine, Zonisamide, guaifenesin, laxatives (when misused), loop diuretics, and topiramate, have the ability to cause silica stones [18].

III. SYMPTOMS AND SIGN

Patients with urinary calculi describe hematuria, discomfort, or infection. Symptoms are typical and easily managed for those with small, non-obstructing stones or staghorn calculi. Additional signs include the following:

Some symptoms include frequent, dysuric urination, suprapubic discomfort, urine urgency and frequency, stranguria, and gastrointestinal problems.

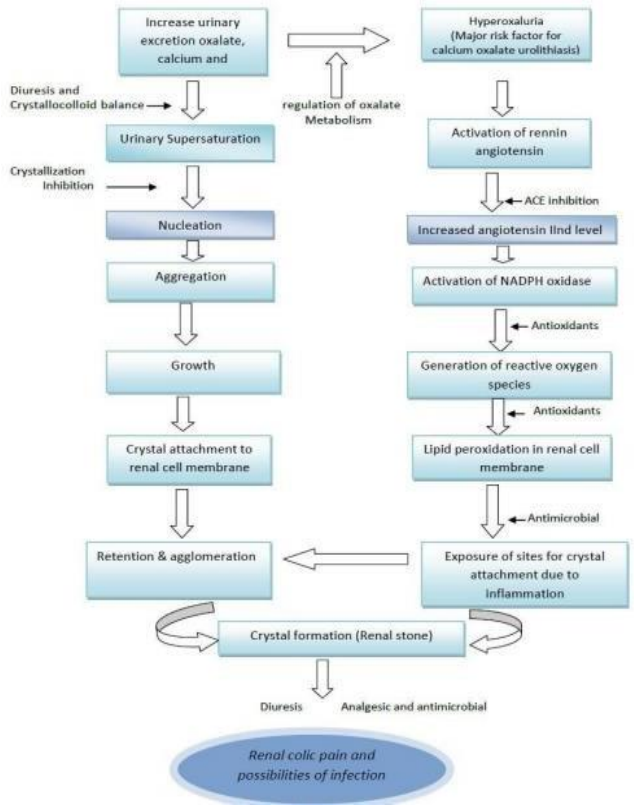
Severe lower abdominal discomfort that spreads to the testicles or the vulvar region, along with nausea and/or vomiting.

The lumbar and flank areas are where discomfort radiates. Both anteriorly and caudally, there is pain.

Even so, there may be groin, testicular, or labia majora pain (women).

stones that entered the bladder: Positional urine retention is sporadic and largely asymptomatic [19,20].

IV. MECHANISM OF ACTION



Urine tract infections, nutrition, impaired urinary outflow and urinary stasis, changed urinary solutes and colloids, Randall's plaque, extended immobility, and microliths, among other factors, are all associated with the multifactorial process that leads to the formation of uroliths [22].

STONE DISEASE CAUSED BY DRUGS

The following medications [23,24,25] can precipitate in urine and cause stone formation. Atazanavir, Indinavir, Guaifenesin, and Triamterene

Overuse of antacids containing magnesium silicate (silicate)

Sulfa medications, such as acetyl sulfamethoxazole, acetylsulfasoxazole, and acetylsulfaguanidine, as well as sulfasalazine, sulfadiazine, and others Ceftriaxone (rarely) [26]

MANAGEMENT

Stones are treated with reassuring care and management, which may include the use of the following substances [27]:

Hydration IV

A. The NSAIDs (eg, ketorolac, ketorolac intranasal, ibuprofen)
B. Non-addictive painkillers, such as acetaminophen [APAP]
C. Beta blockers (eg, tamsulosin, terazosin)
D. Narcotic analgesics administered orally or intravenously, such as morphine sulphate, codeine, hydrocodone/APAP, dilaudid, and fentanyl.
E. Antiemetic drugs (eg, metoclopramide, ondansetron)
F. Antibiotics (such as ofloxacin, ciprofloxacin, levofloxacin, ampicillin, gentamicin, trimethoprim-sulfamethoxazole)
G. Stone prevention/chemolysis uses the following medication groups [28]:
H. Uricosuric substances (eg, allopurinol)
I. Alkalinizing substances (such as sodium bicarbonate and potassium citrate)
J. Thiazide diuretics Can aid in the treatment of hypercalciuria.

Surgical options:

Stones that are 7 mm and larger and unable to pass naturally result in significant conditions that call for surgery, such as the following:

Insertion of a stent

Shockwave lithotripsy outside the body (ESWL)

Open nephrostomy, which has been mainly replaced by less invasive methods, ureteroscopy, percutaneous nephrostolithotomy (PCNL) or small PNCL, and percutaneous nephrostomy

Large-scale anatrophic nephrolithotomy. Complex staghorn calculi that can't be removed with enough PCNLs are usually removed with a laparoscopic or robotic procedure. [29]
Knowing that synthetic medications have a variety of adverse effects, traditional/herbal/higher plant-based drugs continue to play a significant role in modern medicine, leading to the development of novel therapeutic agents. [30] Moringa oleifera, Crataeva magna, Aerva javanica, Peperomia tetraphylla, Terminalia bellirica, Ipomoea eriocarpa, Punica granatum, Hibiscus rosa-sinensis, Costus spiralis, and Herniaria hirsuta are among the therapeutic plants that have antiurolithiatic effects. The antiurolithiatic properties of medicinal plants with negligible or nonexistent side effects were examined in this review.

PLANTS HAVING ANTI-UROLITHIC ACTIVITY ACCORDING TO SIDDHA MEDICINE SYSTEM:

No	Medicinal Plant	Botanical Name
1	Kandangattiri	Solanum xanthocarpum
2	Uttamani	Pergularia daemia
3	Nerunjil	Tribulus terrestris
4	Kattumurungai	Moringaoleifera
5	Pavakka chedi	Momordia charantia
6	Kollu	Dolichosbiflorus
7	Mullangi	Raphanus sativus
8	Kadukkai	Terminalia chebula
9	Venthayam	Trigonella foenumgraecum
10	Pushanikai	Benincasa hispida
11	Yelakkai	Elettaria cardomomum
12	Shimai Shadavari	Asparagus racemosus
13	Arugampullu	Cynodondactylon
14	Barliyarisi	Hordeum vulgare
15	Sirupoolai	Aerva lanata
16	Karunjiragam	Nigella sativa

MORINGA OLÉFERA

The drumstick tree or horse-radish tree, Moringa oleifera Lam., is a member of the family Moringaceae and is utilised as a phytotherapeutic agent. Rats are given root- wood aqueous and alcoholic extracts along with ethylene glycol, and this causes lithiasis. The plant extract has antiurolithiatic activity and reduces the size and prevents the growth of urinary stones. Although the exact mechanism of urolithiasis is yet unknown, it reduces urine concentrations of the substances that contribute to stone formation and increases diuresis. [31].

Crataeva magna

The Crataeva magna Lour extract in ethanol. Baruna bark, a member of the Capparaceae family, was studied in vitro and in vivo as a potential treatment for urinary stones. When compared to the hazardous group, the maximum dose of plant extract considerably reduced calcium, serum creatinine, urine oxalate, and kidney weight while also significantly increasing urine volume output and final body weight. The standard polyherbal drug-treated group was compared to the group that received plant extracts and has strong antiurolithiatic activity.[32]

Aerva javanica

It commonly known as Tella burga, is a plant that some believe can help treat renal calculi. Alkaloids, flavonoids, phenol, tannin, proteins, amino acids, steroids, saponins, and carbohydrates are among the chemical components of the plant. inquiry of the possible effectiveness of different Aerva javanica extracts against rats' artificially-induced renal calculi.

Ethylene glycol caused hyperoxaluria, whereas groups treated with ethyl acetate, aqueous, and methanol extract of Tella burga significantly decreased the elevated urine oxalate. Additionally, there was a striking reduction in the increased accumulation of substances that cause stones in the urine and serum of calculogenic rats. [33]

Peperomia tetraphylla

It popularly known as Ala ala wai nu Kani, belongs to the Piperaceae family and has the Tamil name vanabhrami. When compared to positive control rats, the animals given ethanolic extracts had significantly less kidney calcification and lower calcium levels in the renal tissue.

Rats with urolithiasis respond to the ethanolic extract of Peperomia tetraphylla in both an inhibitory and therapeutic manner.[34]

Poppy granatum

Pomegranates, often known as pomegranates, are members of the Punicaceae family and control urine flow and soothe burning. In ethylene glycol-induced rats, treatment of Punica granatum chloroform extract and Punica granatum methanolic extract at doses of 100, 200, and 400 mg/kg resulted in a decrease in urine oxalate, phosphate, calcium serum creatinine, urea, uric acid, and renal tissue oxalates. Punica granatum chloroform extract and Punica granatum methanolic extract have been shown to have more capacity to eliminate renal stones and to diminish renal tissue regeneration in male rats when administered at doses of 400 mg/kg each. [35]

Hibiscus rosa-sinensis

It also known as China Rose, this barren shrub from the Malvaceae family is primarily found in tropical regions as an ornamental plant. It has a wide range of bloom colours.

According to the in vitro tests conducted for the study, the flower extract shown a very good inhibitory impact on the several stages of stone formation, such as nucleation, growth, aggregation, and retention, at different doses. It is abundantly clear that the elements in the floral extract may be to blame for its ability to inhibit kidney stone formation. As a result, the extract's ingredients could very well be included in pharmaceutical formulations for the treatment of lithiasis. [36]

Spiral costus

In Brazilian traditional medicine, it has been used to get rid of kidney stones and stop urinary infections. It is a member of the ginger family, Zingiberaceae. Aqueous extract of Costus spiralis Roscoe prevented the production of urinary stones in rats, which are either caused by calcium oxalate crystal or zinc disc implants. At various doses, the plant extract showed potential activity in male and female rats and inhibited the development of urinary stones. The aqueous extract was also examined for toxicity; up to 4 weeks after aqueous extract administration, neither it nor any indicators of toxicity changed the spontaneous motor activity.[37]

Bellirica terminalis:

The compounds from the combretaceae family, commonly referred to as Baheda, may have an impact on urolithiasis brought on by ethylene glycol. By stifling hyperoxaluria, the deposition of CaOx crystal on the surface of the renal tubular membrane is avoided. Fruits from Terminalia bellirica stop different stones in their early stages of development.

In other investigations, these fruits were also discovered to contain saponin and flavonoids, which are thought to be responsible for the antiurolithiatic activity of herbal medicines. T. bellirica is therapeutically beneficial for the treatment of CaOx stones and may potentially have additional effects due to its high antioxidant, anti-inflammatory, and anti-microbial activity, which is one of the anti-urolithiasis- urolithiatic action. [38]

Eriocarp Ipomoea

Morning glory is a member of the Convolvulaceae family. The location of calcium oxalate crystals and the structure of the kidneys are revealed by a histopathological examination under a light microscope. Ipomoea eriocarpa plant extract is essential for restoring blood, urine, and kidney homogenate measurements to their normal levels. Ipomoea eriocarpa extract administration reversed the formation of calcium oxalate crystals in the renal tubules as well as the enlargement and congestation of parenchymal blood vessels, as shown by histological analyses. I. eriocarpa leaf extract has antiurolithiatic efficacy by preventing and slowing the development of kidney stones. [39]

Hirsute herniaria

An instance of Hairy Rupturewort, a member of the Caryophyllaceae family. Three weeks were spent doing the study on rats with nephrolithiasis caused by calcium oxalate and normal rats. examination of water consumption, pH, volume of urine produced, crystalluria, and urinary chemistry. Rats treated with plant extract excrete a little amount of CaOx dihydrate crystals, compared to the large amount of CaOx monohydrate and few dihydrate crystals excreted by untreated rats. Herniaria hirsuta plant extract has an antiurolithiatic effect and acts as a preventive agent for calcium oxalate

crystals in the formation of urinary stones, according to the final report following kidney examination [40].

NIGELLA SATIVA:

Annual herb Nigella sativa L., a member of the Ranunculaceae family, is grown over the world, particularly in the East Mediterranean region 1. Nigella sativa seeds have been used for a very long time in traditional folk medicine in the ancient medicinal systems of Unani, Ayurveda, Chinese, and Arabic to cure a variety of ailments. Seed extracts have been shown to have anti-inflammatory and antioxidant properties, as well as the ability to treat polio, disintegrate renal calculi, quiet coughs, and delay the development of cancer.

V. CONCLUSION

Many therapeutic plants had antiurolithiatic properties. In order to pave the way for their clinical applications due to efficacy and safety, this study emphasises the aetiology, risk factors, epidemiology, symptoms, forms of kidney stones, pathogenesis, certain medications with mechanism, and the antiurolithiatic properties of medicinal plants.

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