Antiurolithiatic Activity: An overview

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Abstract: Urolithiasis (nephrolithiasis) or kidney stone is formation of urinary calculi at any level of urinary tract. It is estimated that 12% of world population experiences renal stone disease with a recurrence rate of 70-80% in male and 47-60% in female. Urolithiasis is still a mysterious disease even after extensive research in Urology. Sophisticated instruments, investigations etc., have failed to trace out the exact cause and mechanism of urolithiasis. Urinary calculi are the third most common affliction of the urinary tract which are exceeded by the urinary tract infections and prostate diseases.

Keywords: Antiurolithiatic, urolithiasis, pathophysiology, calcium oxalate crystal

Introduction:
Urolithiasis, also known as nephrolithiasis, is a condition that affects the kidneys. Urolithiasis is a debilitating disease that has plagued humanity since the dawn of time. Renal stone disease affects approximately 12% of the world's population, with a recurrence rate of 70-80 percent in men and 47-60 percent in women. Urinary calculi are the third most common urinary tract ailment, trailing only urinary tract infections and prostate diseases.¹² The mechanism of calcium oxalate renal calculi formation has piqued the interest of medical researchers due to its common clinical occurrence and treatment difficulty. This affects ion transport across the cellular organelle by altering membrane fluidity and permeability. One of the main components of urinary tract deposits is calcium oxalate. Calcium oxalate crystallisation is of particular interest, both theoretically and biologically. The exact mechanism that leads to the formation of calcium oxalate stones is unknown. The presence of various foreign substances influences the nucleation, crystal growth, and aggregation of various calcium oxalate hydrates.¹² With a lifetime risk of 2-5 percent in Asia, 8-15 percent in Europe and America, and around 20% in the Middle East, it is the third most common urinary tract problem. It's linked to a high recurrence rate of 10-23 percent per year, 50% in 5-10 years, and 75% in 20 years. After being afflicted, the likelihood of relapse increases, and the time between recurrences decreases.

1. Reasons for stone formation diseases
Stone formation diseases are caused by a variety of factors. Insufficient urinary discharge, microbial infection in the urinary tract, a diet high in oxalates and calcium, vitamin deficiencies such as vitamin A deficiency and excess vitamin D, and metabolic diseases such as hyperthyroidism, cystinuria, gout, and intestinal dysfunction, among other things, are all factors that contribute to stone formation (Suman Kumar Mekap 2011).

Urolithiasis (kidney stone formation) is a complicated process that occurs when promoters and inhibitors in the kidneys are out of balance.
Urinary output is a factor that influences stone formation (hence the concentration).
The amount of a particular constituent in the urine, the pH of the urine, and infection or damage to the urinary tract are all factors to consider (Michell et al., 1989).

2. Urolithiasis:
A kidney stone is formed when urine becomes supersaturated with certain urinary salts, such as calcium oxalate. The most common component of kidney stones is calcium oxide, which is an important factor in crystallisation, along with nucleation, growth, and aggregation.

2.1 Types of Urolithiasis: The stone type is named after its mineral composition. The most common stones are struvite (magnesium ammonium phosphate), calcium oxalate, urate, cystine and silica.

a) Calcium oxalate stones: Calcium oxalate stones are the most common type of kidney stone in the world. They are made up of calcium phosphate in the form of apatite or brushite. Calcium oxalate stones are linked to factors that promote the precipitation of oxalate crystals in the urine, such as primary hyperoxaluria. Hyperparathyroidism and renal tubular acidosis are linked to the formation of calcium phosphate stones. Microscopically, calcium oxalate stones look like ‘envelopes.’ They can also be formed into ‘dumbbells.’ The most common constituent of human kidney stones is calcium oxalate crystals in the urine, and calcium oxalate crystal formation is also one of the toxic effects of ethylene glycol poisoning. Whewellite (monohydrate, found in some coal beds), weddelite (dihydrate), and ca oxalates (trihydrate) are three mineral species that contain hydrated forms of the compound. The majority of crystals resemble a sided prism, and they frequently resemble a pointed picket from a wooden fence. This morphology will be found in more than 90% of the crystals in urine sediment. These other shapes are less common than sided prisms, but they must be recognised quickly in the event of an emergency.

b) Struvite stones: Struvite stones, also known as “infection stones,” urease or triple-phosphate stones, form most commonly when urea-splitting bacteria infect the body. These organisms convert urea to ammonia and carbon dioxide by using the enzyme urease. This alkalinizes the urine, allowing struvite stones to form. The most common organisms isolated are Proteus mirabilis, Proteus
vulgaris, and Morganella morganii; fewer common organisms include Ureaplasma urealyticum, Providencia species, Klebsiella, Serratia, and Enterobacter species. People with spinal cord injury and other forms of neurogenic bladder, ileal conduit urinary diversion, vesicoureteral reflux, and obstructive uropathies are more likely to develop infection stones. They're also common in people who have underlying metabolic conditions like idioopathic hypercalciuria, hyperparathyroidism, or gout. Infection stones can grow quickly, forming large calyceal staghorn (antler-shaped) calculi that require invasive surgery such as percutaneous nephrolithotomy.

c) **Uric acid stones**: Uric acid is responsible for approximately 5–10% of all stones. Uric acid stones can be formed in people who have metabolic abnormalities, such as obesity. They can also develop in the presence or absence of hyperuricemia (excess uric acid in the urine) (an excessive amount of uric acid in the serum). They can also form as a result of acid/base metabolism disorders, such as when the urine is too acidic (low pH), causing uric acid crystals to form. The presence of a radiolucent stone in the presence of persistent urine acidity, as well as the discovery of uric acid crystals in fresh urine samples, support the diagnosis of uric acid urolithiasis. Urate stones are also a common occurrence in these patients. Following a colon resection, uric stones are especially common. Pleomorphic crystals of uric acid, typically diamond-shaped, form the stones. They could also resemble polarizable squares or rods. Allopurinol, a urate-lowering medication, can be used to treat hyperuricosuria. In this situation, urine alkalinization could be beneficial. Allopurinol, a urate-lowering medication, can be used to treat hyperuricosuria. In this situation, urine alkalinization could be beneficial.

d) **Cystine stone**: Cystine kidney stones are caused by cystinuria, an inherited (genetic) disorder of cystine transport that results in an excess of cystine in the urine (cystinuria) and cystine stones. The most common problem with amino acid transport is cystinuria. Although cysteine is not the only amino acid excreted excessively in cystinuria, it is the least soluble of all amino acids found naturally. In the urinary tract, cysteine tends to precipitate out of urine and form stones (calculi). In the urine, small stones pass. In the urine, small stones pass. Large stones, however, remain in the kidney, obstructing urine outflow, while medium-sized stones pass through the kidney and lodge in the ureter, further obstructing urine flow (urinary obstruction). The ureter and kidneys are under pressure when the urinary tract is obstructed. The ureter widens (dilates), putting pressure on the kidney. Obstruction also causes stagnant (stagnant) urine, which invites recurrent urinary tract infections. Kidney damage occurs as a result of pressure on the kidneys and urinary infections. Renal insufficiency and end-stage kidney disease can develop as a result of the damage, necessitating dialysis or a kidney transplant.

All of the signs and symptoms of cystinuria are caused by the stone, including:
- Haematuria — blood in the urine
- Flank pain — side pain caused by kidney pain
- Renal colic — intense, cramping pain caused by stones in the urinary tract
- Obstructive uropathy — urinary tract disease caused by obstruction Drug-induced stones or silicate stones Stones can form in the urine as a result of taking certain medications or herbal products and the build-up of chemicals from those products. Loop diuretics, Acetazolamide, Topiramate, Zonisamide, Laxatives (when abused), Ciprofloxacin, Sulpha medications, Triamterene, Indinavir, Ephedrine, Guaiifenesin, and silica-containing products are just a few examples.

### 2.2 Urolithiasic causes:

Urolithiasis causes Low fluid intake and a high dietary intake of animal protein, sodium, refined sugars, fructose and high fructose corn syrup, oxalate, grapefruit juice, apple juice, and cola drinks all increase the risk of stone formation. Inadequate urinary drainage, foreign bodies in the urinary tract, microbial infections, a diet high in oxalates and calcium, vitamin abnormalities such as vitamin A deficiency and excess vitamin D, and metabolic diseases such as hyperthyroidism, cystinuria, gout, and intestinal dysfunction are all common causes of stone formation. The main component in renal calculi is calcium oxalate.

a) Calcium is a component of calcium oxalate, which is the most common type of human kidney stone. High dietary calcium intake, unlike supplemental calcium, do not appear to cause kidney stones and may even help prevent them. This could be linked to calcium's role in binding ingested oxalate in the GI tract. As calcium intake decreases, the amount of oxalate available for absorption into the bloodstream rises, and the kidneys excrete more oxalate in the urine. Oxalate is about ten times more powerful than calcium in promoting calcium oxalate precipitation in the urine.

b) Vitamins, for example The evidence for a causal relationship between vitamin C supplements and kidney stones is inconclusive, despite widespread belief in the medical community. Although an excess of vitamin C in the diet may increase the risk of calcium oxalate stone formation, this is a rare occurrence in practise. There is also a shaky link between vitamin D and kidney stones.

c) Additional There is no conclusive evidence linking alcohol consumption to kidney stones. Some experts believe that certain behaviours associated with frequent and binge drinking can cause systemic dehydration, which can lead to kidney stones.

### 2.3 Urolithiasis disease pathophysiology:

In the pathogenesis of kidney stones, there are two main aspects to consider:

a) Stone formation increases urinary flow Calcium, phosphorus, and other mineral constituents cysteine, uric acid, and oxalate

b) Stone-influencing physico-chemical changes pH of urine, stone matrix, and other factors all play a role in the formation of these stones. Urine containing a protective substance Urine must be present in the urinary tract in order for a stone to form. Precipitation requires supersaturation component made of crystals Agents capable of Nucleation, crystallisation, and other processes can be altered. The pH of the urine, as well as aggregation, are crucial. In the formation of stones (Malhotra et al., 2008)

### 2.4 Urolithiasis diseases' signs and symptoms

Colicky pain, nausea/vomiting are some of the symptoms of kidney stones. Hematuria, Pyuria, Dysuria, Oliguria, and other disorders of the urinary system.

### 2.5 Diagnosis of urolithiasis diseases

Following the use of technologies such as x-ray and computed tomography, ultrasound is used to confirm the diagnosis, and a variety of other tests can be performed to help determine both the cause and consequences of the stone.
2.6 Urolithiasis disease treatment and prevention
For the treatment of urolithiasis, a variety of procedures are used.
(a) shock wave therapy, which is the only non-invasive treatment for stone disease, and
(b) endoscopic, ureterorenoscopic, and percutaneous nephrolithotomy, which are all effective at treating stones. Because of the severity of renal colic, a lower threshold for prescribing narcotic analgesics, thiazide-like diuretics, and potassium citrate has been established (Orson et al., 2006).

2.7 The foods listed below increase the risk of calculi formation:
1. Fruit juices such as grapefruit, cranberry, and apple juice, as well as dark colas
2. Foods high in organic acids (oxalates), such as spinach, rhubarb, nuts, and wheat bran.
3. Meat, eggs, and fish are high in animal protein.
4. Other vitamins, such as C and D
5. Alcoholic beverages, Purines can be found in beer and wine to some extent. Excessive salt consumption.

2.8 Foods that help prevent the formation of calculi are listed below:
1. Coffee, tea, and lemon and citrus fruit juices soft drinks with a lot of citrates
2. Radish, beet root, and horse gramme are some examples of healthy foods.
3. Low-protein, high-fiber foods
4. Vitamin E, B6, and magnesium are some of the others.
5. Diets low in sodium.

2.9 Treatment options
2.9.1 Medicine Treatment
Thiazide diuretics (e.g. Hydrochlorothiazide), Alkali (e.g. Potassium citrate), Allopurinol, Sodium cellulose phosphate (SCP), Penicillamine (Cuprimine), Analgesic (Diclophenac sodium), Bisphosphonates, Potassium phosphate, Oxalobacter Formigenes, and other probiotics, among others.

2.9.2 Surgical Therapy:
Like as Extracorporal Shock Wave Lithotripsy, Percutaneous Nephrolithotomy, Ureteroscopic stone removal etc.

2.9.3 Herbal Treatment
Cystone, Calcuri, Chandraprabha bati, Trinapanchamool, Rencare Capsule, Patherina tablet, Ber Patthar Bhasma, Chander Prabha vati, and others are some examples.

Herbal folk drugs have the following effects:
1. Diuretic activity (helps to increase urinary volume, making it easier for small calculi to pass through the body in urine).
2. Crystallization inhibition activity (aids in inhibiting the various stages of stone formation by balancing inhibitors and promoters of stone formation)
3. Lithotriptic activity (avoids binding mucin of calculi to prevent crystal aggregation and formation of large stones), analgesic, and anti-inflammatory activities (assists in avoiding stone formation symptoms)
4. Antioxidant (prevents renal tissue injury) and antimicrobial (prevents infection) activity (Charde et al., 2011)
5. Herbs improve renal function and regulate oxalate metabolism, which helps to prevent renal calculi from recurring (Pareta et al., 2011).

3. Conclusion
The current review provides information on the various types of urolithiasis as well as the causes of urolithiasis.
The main cause of urolithiasis is the deposition of calcium oxalate, which is found in all minerals. Men have a threefold higher rate of occurrence than women. When compared to other parts of the country, the southern part has a lower incidence of urolithiasis. Urolithiasis is more common in people who eat a high-protein diet or don’t drink enough water or calcium.

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