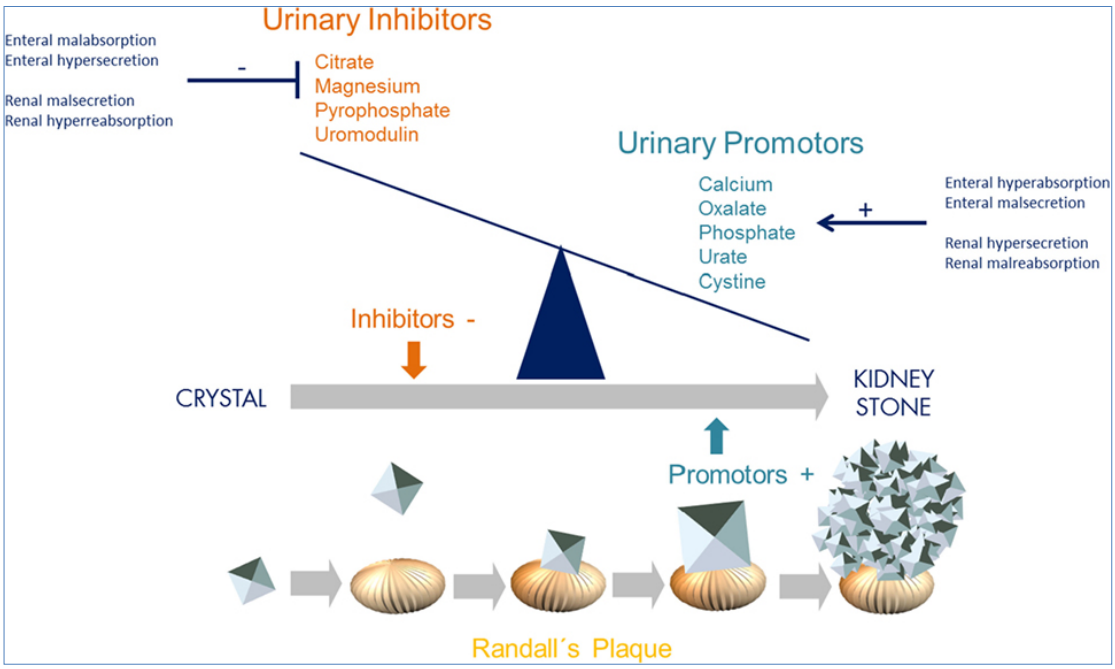
Kidney stones: Mechanism of formation, Pathogenesis & possible treatments

Abstract

- With a very high recurrence rate in both males and females, kidney stones also called as **urolithiasis (nephrolithiasis)** are affecting a remarkably significant population around the globe.
- As kidney stones formation **largely depends on urine's oxalate content** rather than the calcium concentration of the urine, kidney stones are predominantly made up of oxalate and also there are **multiple steps involved in the pathogenesis of calcium oxalate including**
    - **Nucleation,**
    - **Crystal growth,**
    - **Crystal aggregation and**
    - **Crystal retention.**
- Although there are several therapies such as thiazide like diuretic, allopurinol, painkillers, and dietary modifications or in severe conditions shock-wave treatment, ureter-endoscopic and percutaneous nephrolithotomy are being presently used for kidney stones treatment, however, **the side effects that these treatments possess and reoccurrence of the disease** have motivated researchers to search for better and safer options.
- **Herbal drugs** as well as several medicinal plants display antiurolithiatic activity and thus perform an important role in treatment of kidney stone disease.
- Studies in both humans and animal models of hyperoxaluria-associated calcium oxalate kidney stone disease indicated that **oxalate-degrading microorganisms**, in particular the more widely-studied **Oxalobacter formigenes** are both capable of and important in regulating urinary levels of oxalate.
- Such regulation of oxalate levels in the body have displayed prominent reductions in hyperoxaluria followed by diminished rate of recurrent stone formation.
- The present work discusses the mechanism of stone formation, several forms of kidney stones as well as the various therapeutic measures for treatment of urinary stones including many medicinal plants as herbal option as well as oxalate degrading enzyme.

Keywords

- Urolithiasis;
- Hypercalciurea;
- Hyperoxaluria;
- Nephrolithiasis;
- Calcium oxalate;
- Oxalate degrading bacteria



Introduction

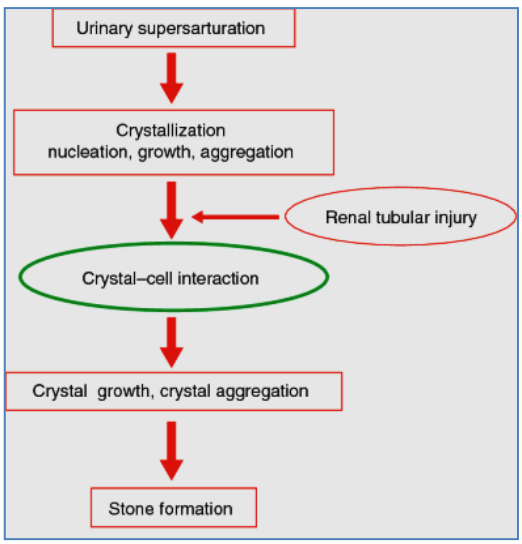
- Urolithiasis or **kidney-urinary tract stone disease** has emerged as a severe health concern throughout the World, affecting around 12% of the population globally.
- It does **cause severe pain when extruded through the ureter**, obstruction and destruction through infection and epithelial metaplasia.
- With a **high recurrence rate** in both, males and females & in certain parts of the world such as the Middle East countries the hazards of urolithiasis are there is much greater.
- Because of the **inhibiting ability of estrogen** in females, low capacity of estrogen and greater muscular mass kidney stones are **more prevalent in males rather than in females** and affects all age groups from less than 1 year old to more than 70 years.
- The prime cause of nephrolithiasis is ***the super saturation of urine with calcium and oxalate that leads to pathological mineralization in the kidneys***.
- **Calcium oxalate** accounts for the maximum percentage of kidney stones (approximately 75%)
- While **calcium hydroxyl phosphate** 50% (***brushite or calcium hydroxyapatite***) **magnesium ammonium phosphate** (10-20) %, (***struvite or triple phosphate***), 5%**urate and** (1-2) % **cysteine** of the kidney stones.
- Kidney or urinary stones **vary widely in their size from micrometers to several centimeters in diameter and so remain unnoticed most of the times for long**

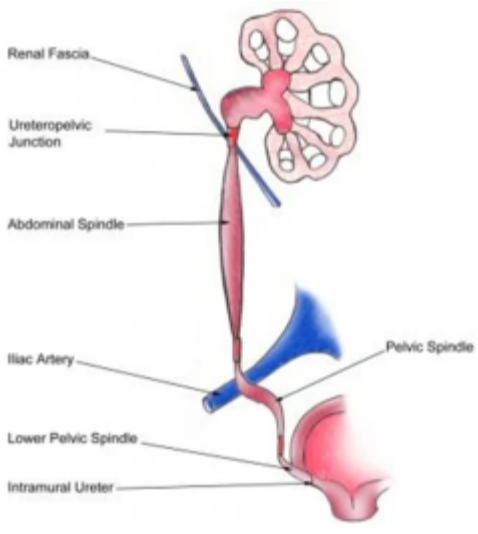
periods and are often discovered incidentally on radiography or ultrasound scanning or by **painful manifestations.**

- The study of **papillary biopsies** in patients with kidney stones have demonstrated that on the basis of the **type of stone and the urine chemistry**, the sequence of events leading to stone formation differ greatly.
- ***Hence involving a number of physicochemical events such as***
    - **Super-saturation,**
    - **Nucleation,**
    - **Growth,**
    - **Aggregation and**
    - **Retention within the kidneys**
- Development of kidney stone or urolithiasis **is a complex process**.

- In the urinary tract, stones are **located at different sites** such as the urinary bladder, ureters and the kidneys.
- **Staghorn** (filling numerous major and minor calices) and **non-staghorn** are the two classes into which the kidney stones have been grouped.
- Although the proximal, middle or distal are the various locations that have been reported for ureteral stones, the non-staghorn stones are mainly pelvic or calyceal in nature.
- Small kidney stones of:
    - **Less than 5 mm in diameter possess the largest possibility of being passed out easily** however associated with renal colic, followed by
    - **Stones of 5mm to 7 mm** that have about 50% possibility but
    - Stones **over 7 mm** do not pass out on their own and often require urological intervention.
- While only 10% of the stones in the kidneys have to be removed surgically, 90% of them move out of the urinary tract and as the stone moves down the urinary tract, **renal colic or flank pain begins to grow** [8].

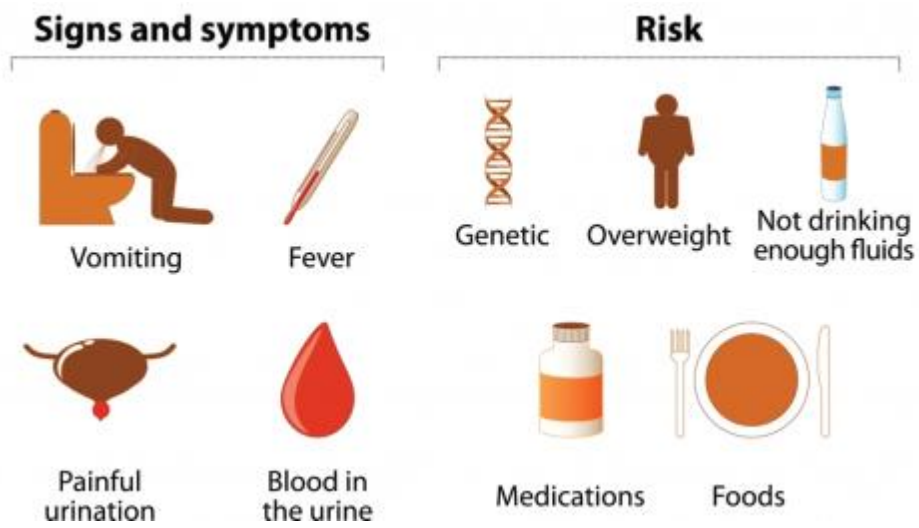
Mechanism of Kidney Stone Formation





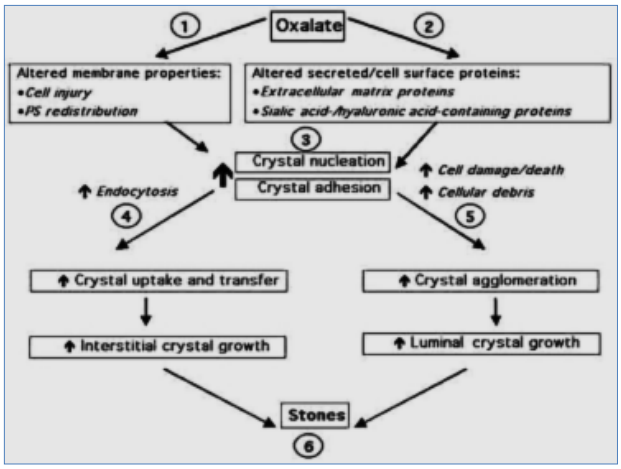
- The uneven proportion of **inhibitors and promoters** are responsible to the complex process of stone formation in kidneys or urolithiasis.

- **Supersaturation of the urine** with calcium and oxalate salts followed by crystalline particle formation is the major reason behind kidney stone formation with supersaturation being the driving force.
- The mechanism involved in the process of stone formation (**Figure 1**) include nucleation of crystals fractions, growth or gathering of these crystals to a size so that they can interact with some intra-renal structure(s), confinement of these crystals inside the kidney or **renal collecting system succeeded by further aggregation and/ or secondary nucleation ultimately forming the clinical stone** [10].
- **Calcium oxalate (CaOx)** forms the major proportion of the kidney stones that is around **80%**, while **calcium phosphate (CaP)** forms a small percentage (15%) of these stones.
- The crystals formed either in **renal tubular fluid or in the renal interstitial fluid** that is supersaturated with respect to these constituents, which in turn might be a consequence of
    - Reduced urine volume,
    - An alteration in urine pH,
- Mechanisms causing increased secretion of stone forming constituents such as
    - Hypercalciuria,
    - Hyperuricosuria,
    - Hyperoxaluria
    - Hypocitraturia, or
    - A combination of these factors [13].
- The urine and presumably, the tubular fluid of stone formers are often more highly supersaturated than that of normal healthy adults, which favors nucleation and growth of crystals.
- Long-term accumulation of additional elements, **crystalline** as well as **organic matrix** produces the clinical stone.



- The reciprocal actions between **genetic susceptibility** and **environmental factors** in different proportions promote both hypercalciuria and hyperoxaluria.
- A **few genetic disorder** which a
    - Rare autosomal recessive disorder,
    - Dietary routine including greater intake of oxalate and low calcium intake,
    - Potential abnormalities of anion transporters found in both gut and kidney,

- **Enhanced absorption of oxalate in the intestines other than mal absorptive diseases (enteric hyperoxaluria),** changes in the normal flora of the gut thereby **decreasing degradation of oxalate** in the colon may cause one form of hyperoxaluria called **primary hyperoxaluria types 1 and 2.**
- **Some rare genetic disorders such as**
    - **Adenine phosphoribosyl transferase (APRT) deficiency,**
    - **Cystinuria, and**
    - **Dent disease,**
    - **Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC) and**
    - **Primary hyperoxaluria (PH)**
- May lead to severe or chronic kidney stone diseases in children.
- The above mentioned processes in humans are influenced by several factors known as **promoters and inhibitors that either support or prevent the process of stone formation** thus affecting a person's ability to promote or prevent stone formation.
- Stone formation is facilitated by promoters while inhibitors prevent it (**Table 1**).
- **Among the promoters of calcium oxalate stones are**
    - High oxalate,
    - Sodium,
    - Calcium,
    - Urate,
    - Low urine pH and
    - Low urine volume
- **while the inhibitors** include
    - Organic substances such as nephrocalcin and
    - Urinary prothrombin fragment-1,
    - Osteopontin and
    - Various inorganic substances such as **citrate, magnesium** [5].



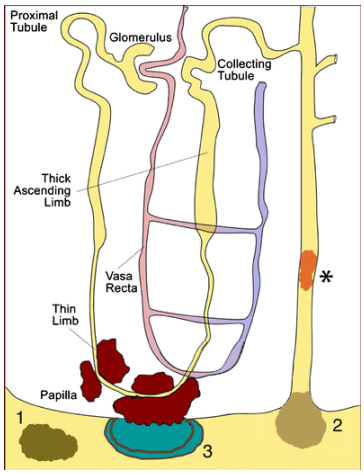
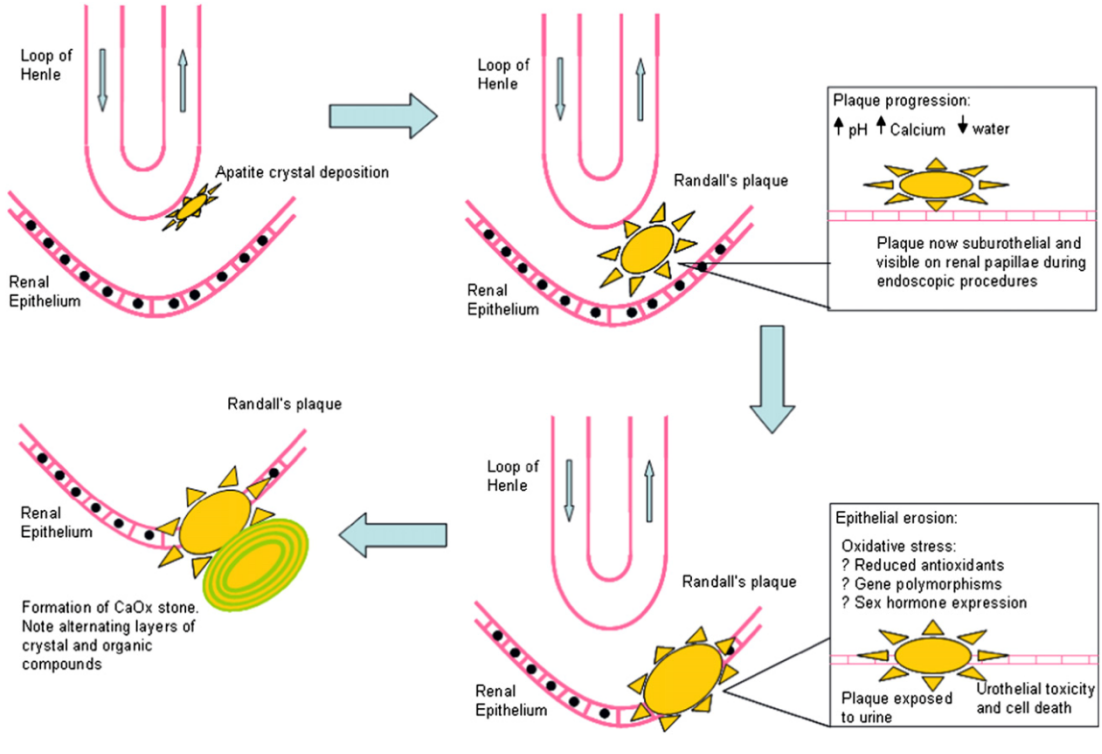


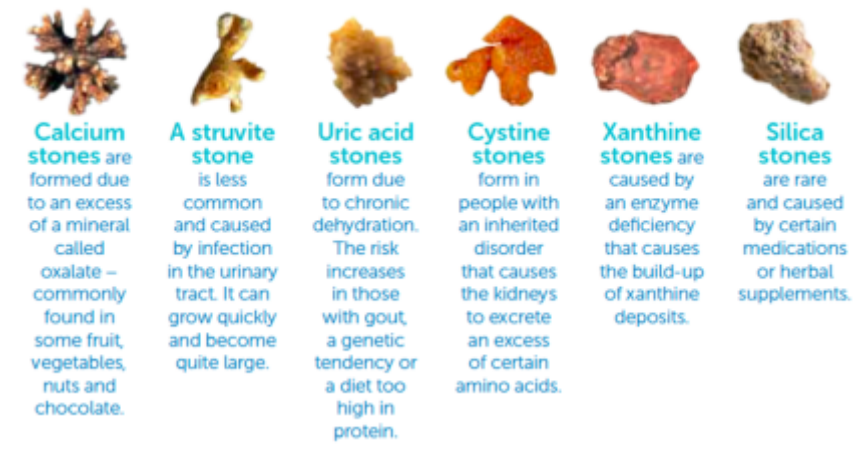
Figure 1: Mechanism of kidney stone formation.

Components	Pathophysiological mechanism
Promoters:	
Uric acid or urate	Has an Antagonistic effect on substances in the urine. Promotes heterogeneous nucleation by uric acid or monosodium urate. Binding of calcium oxalate to cells is increased.
Urine pH	Highly acidic pH enhances calcium oxalate crystallization. Formation of uric acid crystals is enhanced. Promotes secondary nucleation of calcium oxalate by formation of calcium phosphate precipitates.
Urine volume	Promotes crystallization
Hypercalciuria	Increased intestinal calcium absorption which may be 1, 25-dihydroxyvitamin D [1, 25(OH) 2D] dependent or independent. Decreased renal calcium reabsorption. Increases movement of calcium from bones. Enhances urine supersaturation and hence crystallization of calcium.
Hyperoxaluria	Because of an innate error in metabolism oxalate overproduction occurs. Increased dietary intake and bioavailability Increased intestinal oxalate absorption. Urinary supersaturation and formation of calcium oxalate crystals.
Inhibitors:	
Alkaline pH	Inhibits cystine and uric acid stone formation
Citrate	Forms complexes with calcium and therefore lower calcium oxalate supersaturation, inhibits aggregation of preformed crystals and attachment of crystals to urinary epithelium.
Pyrophosphate	Formation of both calcium oxalate and calcium phosphate crystals is inhibited.
Phytate	Inhibits calcium crystallization both in the intra-papillary tissue and urine.
Magnesium	Inhibits of growth (and presumably nucleation) of crystals as well as aggregation. While for the attachment of calcium oxalate crystals its supra-physiologic concentrations are required.
Glycoproteins	Inhibits spontaneous nucleation from metastable solutions as well as the growth of preformed crystals.



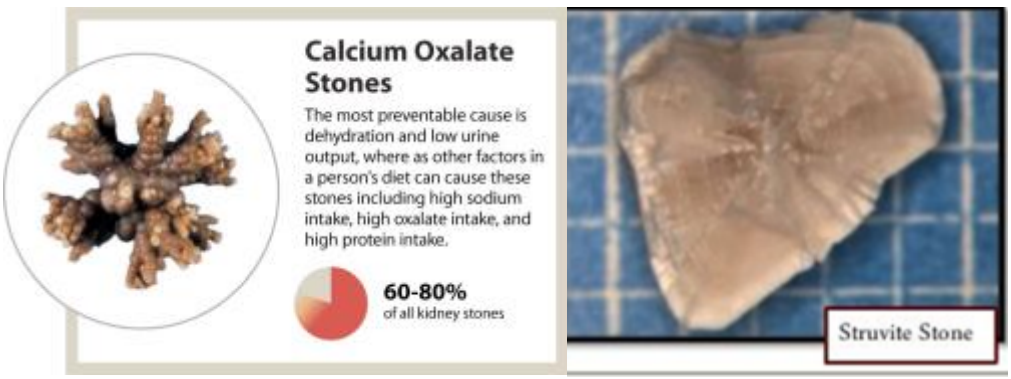
Major Types of Kidney Stones

- There are several locations for the tones along the urinary tract such as the kidneys, ureters and urinary bladder.
- Kidney stones are categorized as either
  - ***Staghorn (filling numerous major and minor calices) or***
  - ***Non-staghorn***.
- Non-staghorn stones are described as calyceal or pelvic in location, while ureteral stones are defined as proximal, middle or distal.
- With differences in their pathogenesis and composition kidney stones have been categorized into several types.



Calcium stones:

- Calcium in **combination with oxalate, phosphate** and also **with uric acid** constitutes the major proportion of kidney stones.
- Oxalate being a naturally occurring substance is found in various food sources such as some **fruits, vegetables, nuts, and chocolate** which exhibit high oxalate levels.
- It is also **produced metabolically by the liver**.
- Normal oxalate level in a healthy adult is **around 20-40 mg/d**.
- **A number of dietary components such as**
    - **Elevated vitamin D doses,**
    - **Oxalate rich diet,**
    - **Various metabolic disorders and**
    - **Intestinal bypass surgery**
- Lead to increased concentrations of oxalate and calcium in the urine.
- Calcium oxalate and calcium phosphate stones are **white, grey or black** colored therefore demonstrating **radio-opaque appearance**, being roughly of 1 cm in diameter and in the radiographs these stones appear as dense and sharply circumscribed structures.
- Medical conditions such as **renal tubular acidosis** and **hyperparathyroidism** demonstrate an association with calcium phosphate stones.



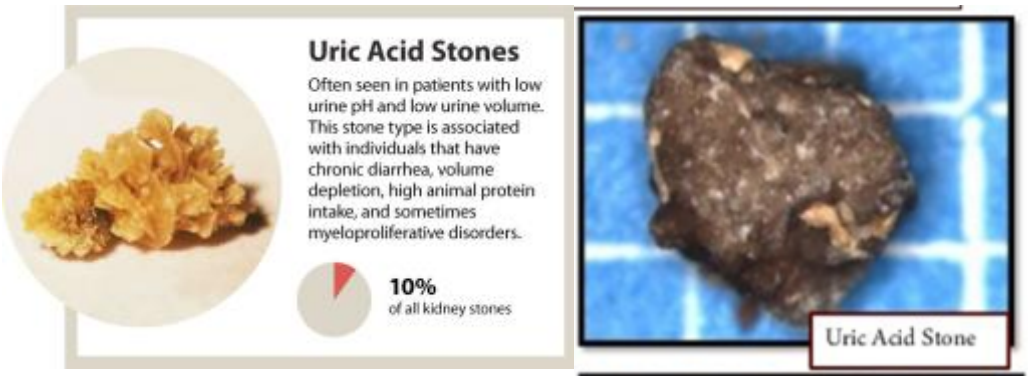
Struvite stones:

- A second type comprising about 10-15% of kidney stones are **triple phosphate or struvite stones** which are formed in presence of **bacterial infection** and is a crystalline substance made up of **magnesium ammonium phosphate**.
- The development of struvite stones is favored by the bacterial enzyme urease that splits the **urea into ammonia and carbon dioxide** thereby making the urine alkaline.
- **Mostly found in humans with certain metabolic diseases including**

    - **Gout,**
    - **Idiopathic hypercalciuria and**
    - **Hyperparathyroidism,**
- the struvite stones are large, glared and laminated [2].

Uric acid stones:

- **Yellow-orange**, round and smooth stones made up of uric acid constitute around 5-10% of the kidney stones which in the radiographs **appear nearly transparent** unless they have been mixed with calcium crystals or struvite.
- These stones are usually square, diamond or rod shaped, pleomorphic crystals which are polarizable.
- **People with abnormalities such as**
    - Gout syndrome,
    - Obesity or
    - Those taking a diet rich in proteins,
    - Purines especially ones eating meat and fish possess uric acid kidney stones.



Protease-related stones:

- This type of stone is usually observed in HIV positive patients **using protease inhibitor indinavir sulphate drug**.
- The use of this drug may lead to the formation of such stones in 4-12% of the patients under treatment

Cysteine stones:

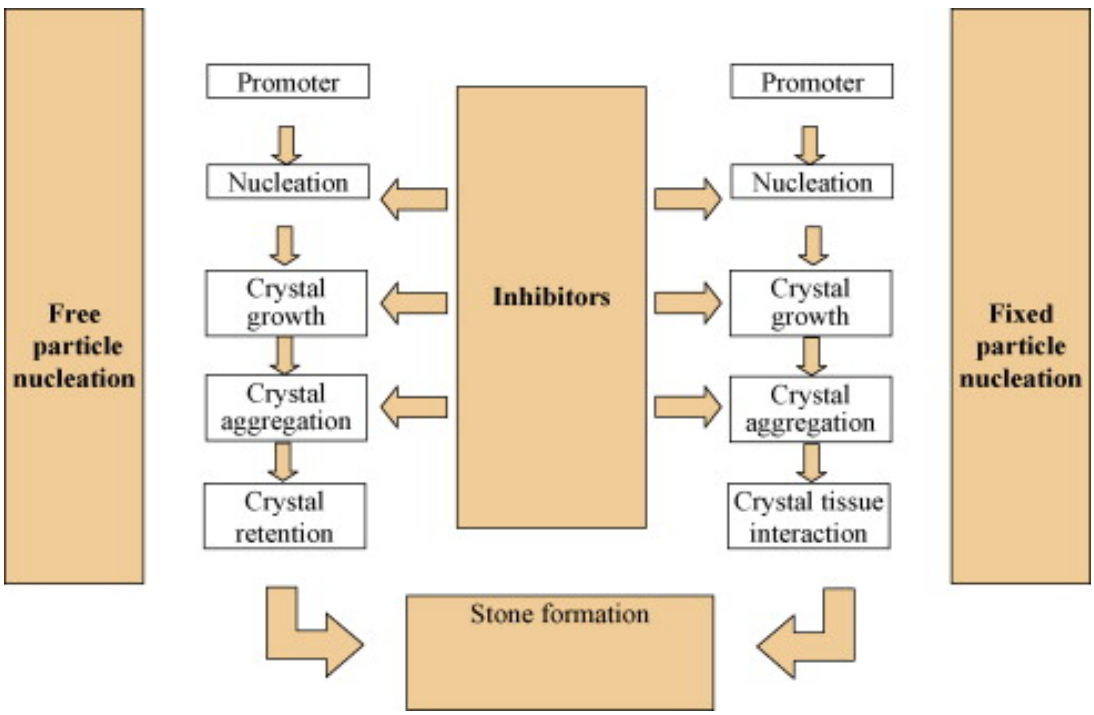
- These stones are caused due to hereditary disorders which cause the kidneys to secrete excessive amino acids (cystinuria) and are rare.
- With a moderate radio-opaque and rounded appearance these stones are marked with shiny **crystallites and are greenish-yellow in color**.

Silica stones:

Medicines as well as herbal products including

- Zonisamide,
- Sulfa medications,
- Indinavir,
- Guaifene sin,
- Laxatives (when abused),
- Acetazolamide,
- Ciprofloxacin,
- Triamterene,
- Ephedrine,
- Loop diuretics,
- Topiramate, and
- Products containing silica

promote the formation of such stones which are also known as drug-induced stones.



Therapeutic Options and Methods of Prohibition of Kidney Stones

- Spontaneous passage of the urinary stones is the only objective of conventional management, the most persistent option for treatment of renal colic.
- Kidney stones can be prevented and treated by
    - **Drinking plenty of water,**
    - **Eating vegetarian diet and**
    - **A diet heavy on herbs.**
- The dreadful nature of kidney stones urges for improved treatment options although dietary restrictions with reduced calcium and oxalate intake and greater fluid intake has been one of the most usual method for the inhibition of kidney stones.
- Several investigations reveal that kidney stones can be prevented by intake of diet **rich in vegetables and fruits.**
    - **Green tea,**
    - **Pomegranate,**
    - **Oregano,**
    - **Parsley,**
    - **Common madder,**
    - **Raspberry,**
    - **Yellow-fruit nightshade,**
    - **Khela,**
    - **Black cumin etc.**
- Those are the some of the dietary plants that have been observed to be significantly effective in preventing the formation of kidney stones and treating hyperoxaluria.
    - **Narcotic analgesic,**
    - **Thiazide like diuretic,**
    - **Allopurinol and**
    - **Potassium citrate**
- Those are the main drugs which are prescribed as treatment strategy for preventing kidney stones.
- Treatment of kidney stones with diuretics and analgesics although is a common approach but their excessive consumption leads to intense side effects while shock waves cause traumatic side effects as well as may lead to infections and formation of residue stone fragments and hence have inspired researchers to move towards natural and safer remedies like **oxalate degrading enzymes and herbal medications**.
- Management of the initial processes of stone formation such as the crystallization events is the ideal method for treatment and prevention of urolithiasis.
- Medicinal plants such as
    - ***Amaranthus spinosus,***
    - ***Bambusa nutans,***
    - ***Abutilon indicum,***
    - ***Phyllanthus emblica,***
    - ***Cinnamomum bejolghota*** **and**
    - ***Amaranthus viridis***
- Play important part in the prevention of kidney stones and exhibit good antiurolithiatic property and therefore due to their clinically manifested antimutagenic, immunomodulatory as well as adaptogenic effects, **herbal drugs have generated great curiosity among the people.**

Oxalate-Degrading Bacteria as new Therapeutic Tools for Preventing Kidney Stones

- The discovery of oxalate-degrading bacteria in the human gastrointestinal tract has opened the way to explore several investigations regarding their potential role in reducing the urinary excretion of oxalic acid.
- By selectively enhancing the natural **oxalate degrading microflora of the gut,** i.e.,
  - ***Bifidobacterium* sp.,**
  - ***Bacillus* sp.,**
  - ***Oxalobacter formigenes* and**
  - ***Porphyromonas gingivalis*,**
- An oxalate degrading bacterial enzyme namely **oxalate decarboxylase** from *Bacillus subtilis* proved to be a possible therapeutic option for treating calcium oxalate stone disease in human.
- Oxalate decarboxylase breaks down oxalate thereby producing formate and carbon dioxide.
- Oral therapy of a cross-linked formulation of oxalate decarboxylase has proved to be an effective therapeutic option for hyperoxaluria as it strongly reduced the oxalate content in urine in hyperoxaluria model of mice.
- Previously, the heterologous expression of this enzyme in *Lactobacillus plantarum* (*L. plantarum*) was developed and utilized as a **potential probiotic for depletion of intestinal dietary oxalate**.
- For herbivores, transgenic plants expressing fungal oxalate decarboxylase may significantly reduce nutritional stress due to diminished oxalate content in the feed.

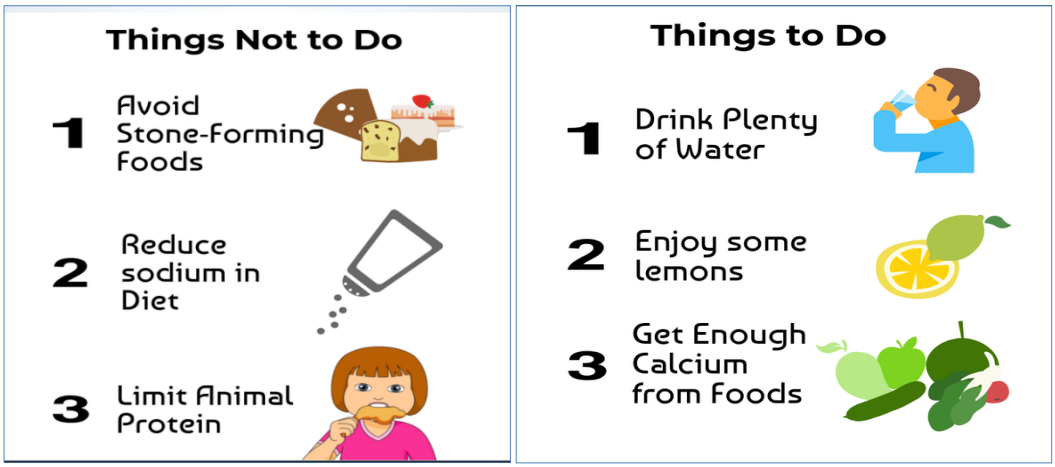
Conclusion

- **Attributed to a number of factors such as**
  - Nutritional disorders,
  - Genetic disorders and
  - Physiological disorders
- Renal urolithiasis or kidney stones are a common pathological condition.

- **The process of stone formation encompasses a number of steps such as**
  - Crystal nucleation,
  - Aggregation,
  - Binding to the kidney,
  - More aggregation and
  - Secondary nucleation.
- **Although kidney stone formation can be prevented by**
  - Controlling the dietary intake of oxalate,
  - Adequate nutrient intake, also
  - Suitable medication and
  - Various therapies are available for treating renal stones
- But re-occurrence of kidney stones as well as the side effects posed by these treatments has become a great issue that has attracted the people to use
- **Better and safer medications such as**
  - Herbal drugs and
  - Medicinal plants
- Which play vital roles in kidney stone diseases treatment.
- Treatment with oxalate-degrading bacteria or purified oxalate-degrading enzymes (isolated from bacterial and fungal sources) could be promising new therapeutic options for patients with hyperoxaluria.

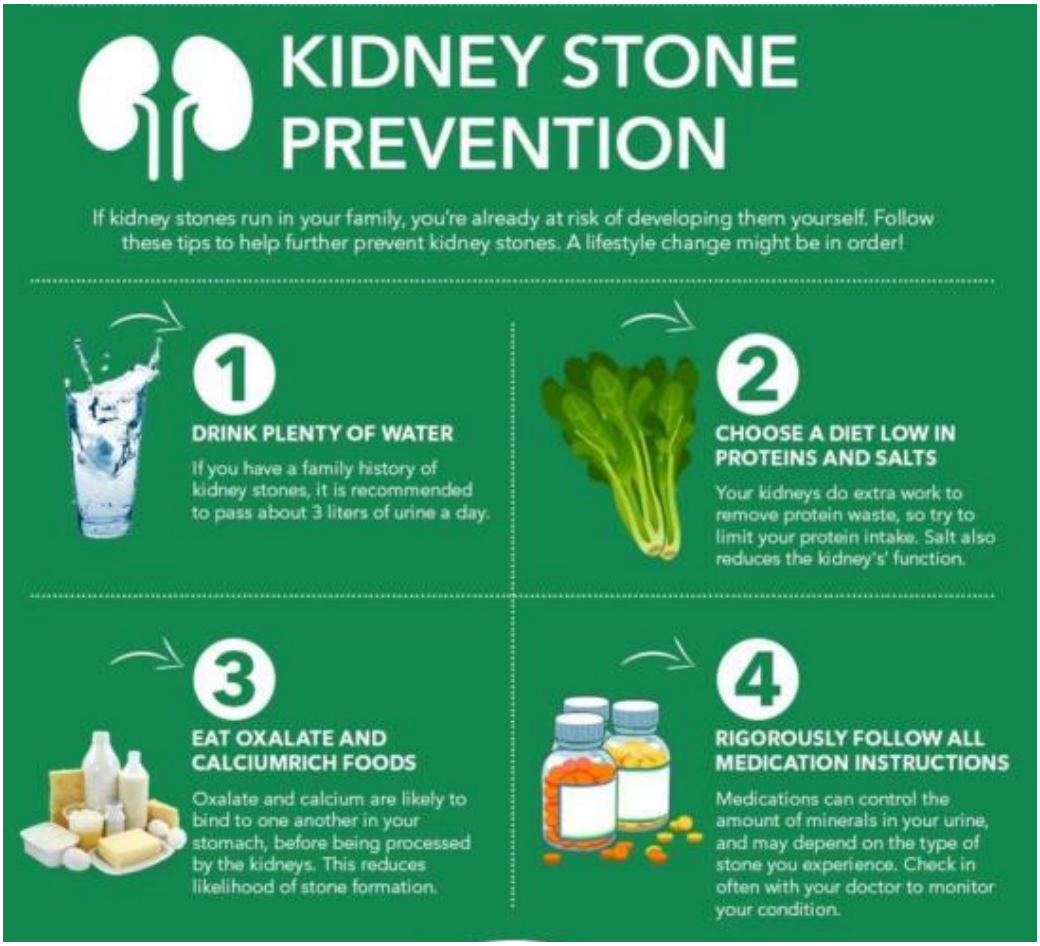
- Novel and practical techniques can be developed in the near future that can easily analyze the physicochemical process involved in stone formation that will surely be a boon for this field.
-
- The above document thereby contributes towards a better understanding of the basis of calcium and non-calcium kidney stones formation, both molecular as well as genetic basis.
- It will prove to be helpful in giving greater insight in the development of better treatment of kidney stone.
- Based on the elemental pathophysiological mechanisms of nephrolithiasis, targeted therapy using microbial oxalate degrading enzymes **for prevention and treatment of nuclei formation** or **salt crystallization** may prove to be highly successful with or without using herbal formulations.

Do & Not to do during kidney stones treatment



Urinary Risk Factors For Calcium Stone Formation

Risk Factor	Causes	Treatment	Level of Evidence
Low urine volume	Exercise, sweating, low fluid intake, heat, bowel disease	Increase fluid intake to 2.5-3.0 L/d	RCT (Borghi et al. *J Urol* 1996; 155:839-43)
Hypercalciuria	Idiopathic, Vitamin D Intoxication	Reduce sodium intake; begin thiazide diuretic therapy; do not reduce calcium intake except in extreme cases; increase dietary calcium intake to 1000 mg	RCT (Borghi et al. *N Engl J Med* 2002; 346:77-84)
Hyperoxaluria	Dietary ingestion and endogenous metabolism; inflammatory bowel disease	Restrict oxalate intake; increase dairy intake accompanyin oxalate-containing foods	No RCT (Holmes et al. *Urol Res* 2004; 32:311-6)
Hypocitraturia	Renal tubular acidosis; other metabolic acidoses; chronic bowel disease; often idiopathic	Begin potassium citrate supplementation	RCT (Barcelo et al. *J Urol* 1993; 150:1761-4)
Hyperuricosuria	Excessive purine ingestion as animal protein	Reduce purine ingestion; begin allopurinol therapy	RCT (Ettinger et al. *N Engl J Med* 1986; 315:1386-9)
Increased sodium excretion	Excessive dietary sodium intake	Restrict sodium intake	No RCT of sodium restriction alone (Borghi et al. *N Engl J Med* 2002; 346:77-84)



6 Easy Ways to Prevent Kidney Stones

Did you know that one in ten people will have a kidney stone over the course of a lifetime?
Recent studies have shown that kidney stone rates are on the rise across the country. Those in the know believe that some major misconceptions may be the culprit.

The National Kidney Foundation has teamed up with Dr. Allan Jhagroo, a kidney stone specialist at the University of Wisconsin School of Medicine and Public Health, **to help you stay stone-free by debunking some of the major kidney stone myths and misconceptions.**

Here are the top 6 kidney stone prevention tips:

1. **Don't Underestimate Your Sweat.**

- **Saunas,**
- **Hot yoga and**
- **Heavy exercise** may be good for your health, but they also may lead to kidney stones.
- **Why?** Loss of water through sweating - whether due to these activities or just the heat of summer—leads **to less urine production**.
- The more you sweat, the less you urinate, **which allows for stone-causing minerals to settle and bond in the kidneys and urinary tract.**

Instead:

- **Hydrate with H2O.**
- One of the best measures you can take to avoid kidney stones is to drink plenty of water, leading you to urinate a lot.
- So, be sure to keep well hydrated, especially when engaging in exercise or activities that cause a lot of sweating.

2. **It's Not Just the Oxalate.**

- **Oxa-what?**
- Oxalate is naturally found in many foods,
- Including:
    1. **Fruits and vegetables,**
    2. **Nuts and seeds,**
    3. **Grains,**
    4. **Legumes, and even**
    5. **Chocolate and tea.**
- ***Some examples of foods that contain high levels of oxalate include:***
    - **Peanuts,**
    - **Rhubarb,**
    - **Spinach,**
    - **Beets,**
    - **Chocolate and**
    - **Sweet potatoes.**
- **Moderating intake of these foods may be beneficial for people who form calcium oxalate stones, the leading type of kidney stones**.
- ***A common misconception is that cutting the oxalate-rich foods in your diet alone will reduce the likelihood of forming calcium oxalate kidney stones.***
- Most kidney stones are formed when oxalate binds to calcium while urine is produced by the kidneys.

Instead:

- Eat and drink calcium and oxalate-rich foods together during a meal.
- ***In doing so, oxalate and calcium are more likely to bind to one another in the stomach and intestines before the kidneys begin processing, reducing renal formation of stones.***

3. **Calcium is Not the Enemy.**
   - But it tends to get a bad rap!
   - Most likely due to its name and composition, many are under the impression that calcium is the main culprit in calcium-oxalate stones.
   - A diet low in calcium actually increases one's risk of developing kidney stones.

     Instead:
   - Don't reduce the calcium.
   - **Work to cut back on the sodium in your diet and to pair calcium-rich foods with oxalate-rich foods.**

4. **It's Not One and Done.**
   - Passing a kidney stone is often described as one of the **most painful experiences a person can have**, but unfortunately, it's not always a one-time event.
   - Studies have shown that having even one stone greatly increases your chances of having another.
   - "Most people will want to do anything they can to ensure it doesn't happen again," said Dr. Jhagroo.
   - About 15% of kidney stone patients didn't take prescribed medications and 41% did not follow the nutritional advice that would keep stones from recurring.

     Instead:
   - Take action!
   - **Without the right medications and diet adjustments, stones can come back,** and recurring kidney stones also could be an indicator of other problems, including kidney disease.

5. **When Life Hands You Kidney Stones…** don't agonize.
   - And as the saying goes, **"make lemonade."**
   - **I**t's important to consider dietary remedies alongside prescription medications.
   - While it may seem easier to just take a pill to fix a medical problem, **consider what lifestyle changes will also make a big impact on your health.**

     Instead:
   - Next time you drive past a lemonade (or limeade) stand, consider your kidneys.
   - Chronic kidney stones are often treated with **potassium citrate,** but studies have shown that limeade, lemonade and other fruits and juices **high in natural citrate offers the same stone-preventing benefits.**
   - **Beware of the sugar, though, because it can increase kidney stone risk**.
   - **Instead**, buy sugar-free lemonade, or make your own by mixing lime or lemon juice with water and using a sugar substitute if needed.
   - "We believe that ***citrate in the urine may prevent the calcium from binding with other constituents that lead to stones***," said Dr. Jhagroo.
   - "Also, some evidence suggests that **citrate may prevent crystals that are already present from binding with each other**, thus preventing them from getting bigger."

6. **Not All Stones are Created Equal.**
   - In addition to calcium oxalate stones, another common type of kidney stones is uric acid stones.
     - Red meat,
     - Organ meats, and
     - Shellfish
   - Have high concentrations of a natural chemical compound known as purines.
   - "High purine intake leads to a higher production of uric acid and produces a larger acid load for the kidneys to excrete.
   - Higher uric acid excretion leads to **lower overall urine pH, which means the urine is more acidic**.
   - The high acid concentration of the urine makes it easier for uric acid stones to form.

     Instead:
   - To prevent uric acid stones, **cut down on high-purine foods** such as red meat, organ meats, and shellfish, and ***follow a healthy diet that contains mostly vegetables and fruits, whole grains, and low fat dairy products.***
   - **Limit sugar-sweetened foods and drinks**, especially those that contain high fructose corn syrup.
   - **Limit alcohol** because it can increase uric acid levels in the blood and avoid crash diets for the same reason.
   - Eating less animal-based protein and eating more fruits and vegetables will help decrease urine acidity and this will help reduce the chance for stone formation.

Table 1: Systemic disease known to predispose to stone formation.

- Hyperparathyroidism
- Nephrocalcinosis
- Gastrointestinal diseases
  - Jejuno-ileal bypass
  - Intestinal resection
  - Crohn's disease
  - Malabsorptive conditions
  - Bariatric surgery
- Sarcoidosis
- Cushing's Disease

Table 2: Anatomical considerations that may predispose to stone formation.

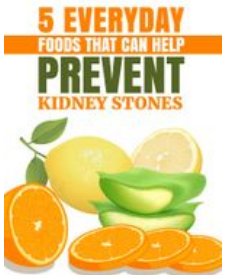
- Horseshoe kidney
- Medullary sponge kidney
- Calyceal diverticulum
- PUJ obstruction
- Ureteral stricture
- Vesico-ureteric reflux
- Neobladder / ileal conduit
- Ureterocoele

Table 3: Stone types that warrant metabolic investigations.

Stone type	Associated disease(s)
Calcium phosphate stones	Distal RTA, hyperparathyroidism, UTIs
Uric acid & urate-containing stones	Hyperuricaemia, hyperuricosuria, Metabolic syndrome
Cystine stones	Cystinuria
Pure Calcium oxalate stones	Hyperoxaluria (idiopathic / enteric / primary)

5 Everyday Foods That Can Help Prevent Kidney Stones

- The pain from having a kidney stone can be excruciating.
- This is why it is vital you ensure **you are doing all you can to prevent the formation of kidney stones in the first place through natural means.**
- Applying a prevention plan doesn't need to be complicated.



1. Aloe Vera

- A recent Thai study found that aloe gel, from the plant, was found to prevent the formation of kidney stones.
- The subjects were given 100 g of fresh aloe gel twice a day, for seven consecutive days.
- And at the end of the study the researchers concluded that changes in chemical compositions of urine after aloe consumption showed potential for preventing kidney stone formation among adults.

2. Freshly Squeezed Oranges

- A new study has found that one glass of orange juice (freshly squeezed) a day could help prevent kidney stones.
- This study was published in the Clinical Journal of the American Society of Nephrology, where 13 participants were recruited, 9 of these were healthy participants and 4 had kidney stones.
- The results found orange juice to be very beneficial due to its high amount of citrate.

3. Dandelion Greens الهند بياء

- Dandelion greens are a calcium rich food, and just one cup of chopped dandelion greens contains 103 milligrams of calcium – which is 10% of the recommended daily value.
- Dandelion greens are also a low oxalate food, which is why they are suitable for kidney stone formers.

- ***Health Tip:*** To increase your daily intake of bio-available calcium, try adding 3 cups of wild/organic dandelion greens to a smoothie.

4. When Life Gives You Lemons Make…

- All citrus fruits contain citrate, but lemon juice may be more beneficial to some due to them containing **almost five times as much as that of orange juice.**
- A recent study published in the Journal of Urology, has found that drinking 2 liters of lemonade daily doubled urinary citrate in people with decreased urinary citrate.

5. Lettuce

- Comprising of 96 per cent water – organic crisp lettuce can help you up your intake of water, as a lack of which has been found to be the leading cause of kidney stone formation in those that are prone.