Urolithiasis: Therapeutic Management and Experimental In-Vivo Models—A Comprehensive Review

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ABSTRACT:

Urolithiasis is a common and recurrent disorder of the urinary system characterized by the formation of calculi in the kidneys, ureters, bladder, or urethra, primarily due to supersaturation of urinary solutes such as calcium oxalate, calcium phosphate, and uric acid. The rising global prevalence of urolithiasis is associated with dietary habits, lifestyle changes, genetic predisposition, and metabolic abnormalities, posing a significant clinical and economic burden. Despite advancements in surgical and lithotripsy techniques, recurrence rates remain high, emphasizing the need for effective pharmacological interventions. Experimental in vivo models play a crucial role in understanding the pathophysiology of stone formation and in evaluating the antiurolithiatic potential of novel therapeutic agents, particularly those derived from natural sources. Several in vivo models are used to simulate human urolithiasis, with ethylene glycol–induced hyperoxaluria in rodents being the most common. Other models include sodium oxalate, ammonium chloride, and zinc disc implantation. These models help evaluate biochemical changes, crystal deposition, renal histopathology, oxidative stress, and inflammation. They also provide insight into mechanisms such as inhibition of crystal nucleation, growth, and aggregation, as well as promotion of crystal dissolution and diuresis.

KEYWORDS: Urolithiasis, crystal types, Therapeutic Management, Invivo Models

INTRODUCTION:

Urolithiasis is a complex urological disorder characterized by the formation of calculi in the kidneys, bladder, and urethra. The term derives from the Greek words "ouron" (urine), "oros" (flow), and "lithos" (stone). Calcium oxalate (CaOx) stones are the most common type of calculi in urolithiasis, forming when calcium and oxalate in the urine combine to create crystalline structures. Other types of calculi include uric acid, cysteine, struvite, xanthine, ammonium acid urate, drug-induced stones, and dihydroxyadenine stones. Age and sex are significant risk factors; the condition most frequently occurs in individuals in their thirties and forties, with a higher incidence in men than in women.[1] Urolithiasis affects approximately 12% of the global population, and in India, 12% of individuals are at risk for kidney stones. Nephrolithiasis can lead end stage renal failure when associated with nephrocalcinosis. Early

stages of kidney stone formation are typically asymptomatic, with symptoms developing gradually depending on the location of the stones. Management of kidney stones involves a range of therapeutic and preventive approaches.[2]

EPIDEOMOLOGY:

A significant contributor to morbidity, kidney stones impact roughly 1–15% of people worldwide. According to research from throughout the world, kidney stones have become more common in both sexes during the last quarter of the 20th century. This could be because to environmental variables including lifestyle and diet.[3]

COUNTRIES	RATE OF PREVALENCE
Asia	1 – 5 %
Europe	5 – 9 %
North America	7 – 15 %
Saudi Arabia	20 %
China	4 %

ETIOLOGY AND SYMPTOMS OF KIDNEY STONES:

- Metabolic imbalances in urine, such as elevated calcium, oxalate, or uric acid levels,
- and reduced citrate levels, promote crystal formation and stone development.
- Diets high in oxalate, purines, or sodium, along with low fluid intake, raise the concentration of stone-forming substances and results in stone development.
- Environmental factors like hot climates, chemical exposure at work, and local water composition can increase dehydration and urine concentration, promoting stone formation.
- Conditions like recurrent UTIs, inflammatory bowel disease, and metabolic disorders such as hyperparathyroidism elevate the risk of kidney stones.[4]

SYMPTOMS: Kidney stones are often asymptomatic at first but later cause severe

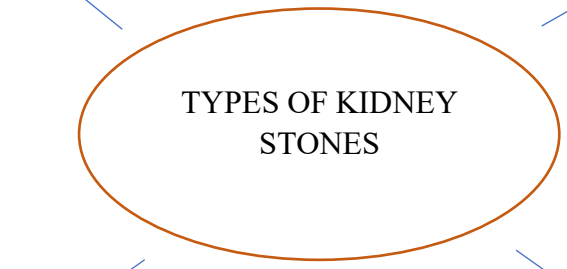
- flank pain,
- blood in urine
- urinary obstruction
- infections, and hydronephrosis, often accompanied by nausea and vomiting.[5]

TYPES OF KIDNEY STONES :

CALCIUM STONES:

Studies worldwide show that calcium-based stones, mainly composed of calcium oxalate and sometimes mixed with calcium phosphate, are the most common type of kidney stones.[6]

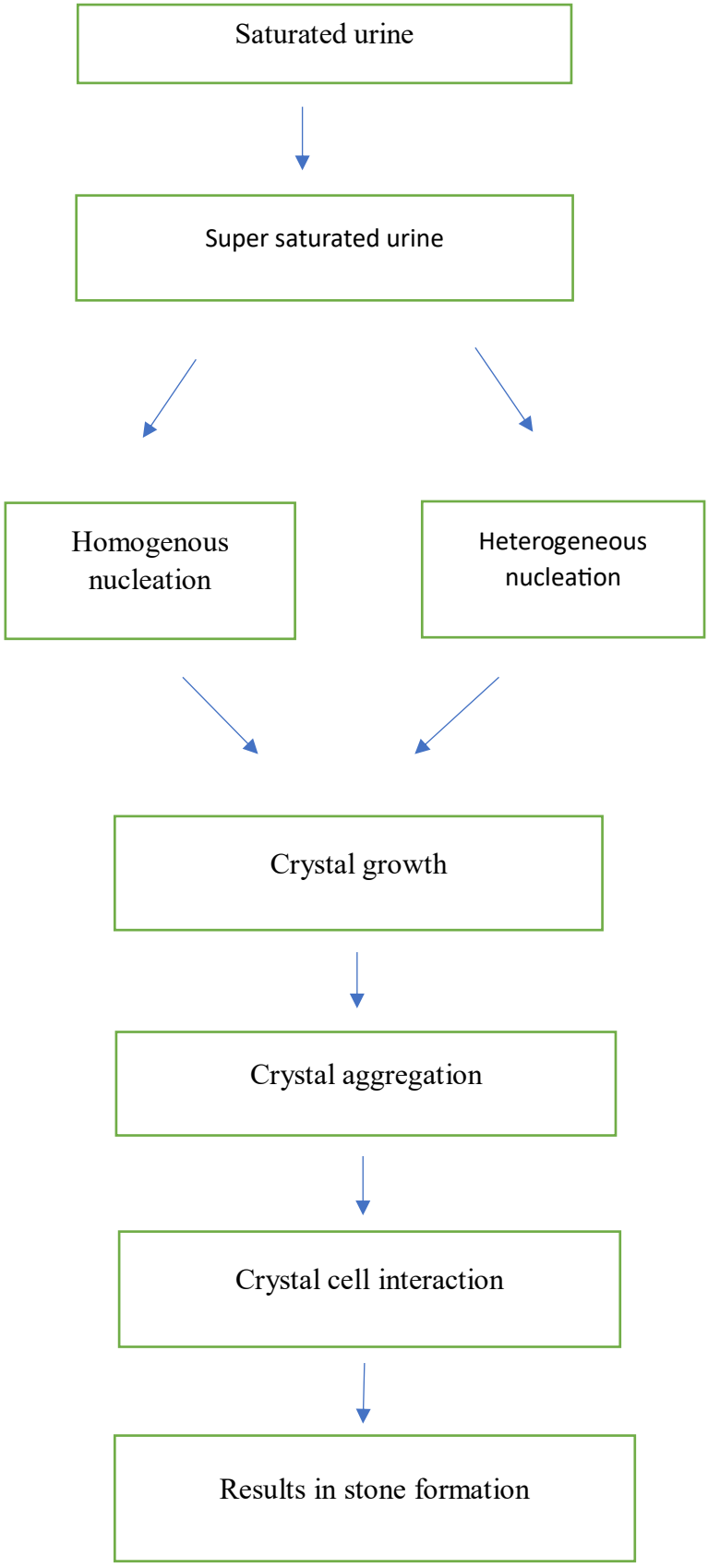
STRUVITE STONES :Struvite (magnesium ammonium phosphate) stones form in the urinary tract, typically due to urease-producing bacteria like *Proteus* or *Klebsiella*. Though less common than calcium oxalate stones, they account for about 10–15% of cases and are more frequent in women and those with recurrent urinary tract infections.[4]



URIC ACID STONES :Uric acid stones form from uric acid crystals that precipitate in acidic urine, usually in the dihydrate form. They are more common in individuals with type 2 diabetes or obesity, with a rising prevalence among men in recent years.[6]

CYSTEIN STONES :Cystine stones are rare and occur due to cystinuria, an inherited disorder caused by mutations in the **SLC3A1** gene. This defect impairs cystine reabsorption in the kidneys, leading to elevated cystine levels in urine and stone formation

MECHANISM OF KIDNEY STONES FORMATION:



SUPERSATURATION:

A supersaturated solution contains more dissolved solute like calcium, oxalate, phosphate, uric acid, results in solute precipitation in urine and leading to nucleation and crystal formation.[7]

NUCLEATION PROCESS:

Nucleation is the process where a supersaturated solution transitions from liquid to solid, forming clusters of stone salts that grow as more material accumulates. It may occur homogeneously or heterogeneously in the presence of nucleating agents.[7]

CRYSTAL GROWTH

Crystal growth is the process of adding crystal components to an existing nucleus.[7]

CRYSTAL CELL INTERACTION

During crystal growth, interactions such as adhesion and endocytosis play a key role in urinary stone formation. Crystals may move to the interstitium and cause epithelial cell injury, triggering proinflammatory molecule production that promotes stone development.[7]

DIAGONISTIC TECHNIQUES:

This crucial step helps identify the nature and cause of the disease, guiding appropriate treatment. Various diagnostic tools are used to confirm urolithiasis.[8]

URINE TEST STRIPS:

Urine test strips detect hematuria, nitrituria, leukocyturia, glycosuria, proteinuria, and estimate urine pH and density.[8]

URINE ANALYSIS:

Urine analysis for kidney stones includes a 24-hour urine test to measure calcium, oxalate, citrate, and uric acid levels that indicate the risk of stone formation.[8]

IMAGING TECHINQUES:

CT SCAN

CT scans can detect stones of any size, type, or location, except for indinavir and pure matrix protein stones found in some HIV patients. CT is also useful for evaluating congenital urinary tract anomalies, renal or urothelial tumors, and secondary obstructions, such as hydroureteronephrosis or perinephric edema. Dual-energy CT (DECT) differentiates stone types and predicts ESWL effectiveness. CT remains the gold standard for identifying residual stones and post-treatment complications. Contrast-enhanced CT distinguishes phleboliths from distal ureteral stones and detects renal calculi smaller than 3 mm with high sensitivity. [4]

ULTRASONOGRAPHY:

Ultrasonography (US) provides an accurate assessment of the renal collecting systems, renal tissue, and bladder; however, visualizing the ureters can be challenging, especially in individuals with significant intestinal gas or excess subcutaneous fat. Despite these obstacles, US remains a valuable first-line imaging method, particularly for those more vulnerable to radiation, such as children and pregnant women, who often experience urolithiasis.[4]

MAGNETIC RESONANCE UROGRAPHY:

Despite being less frequently used, magnetic resonance urography (MRU) is a helpful alternative to computed tomography (CT) in the diagnosis and treatment of urolithiasis. This is especially true for individuals who need to limit their radiation exposure, like youngsters, expectant mothers, or people with renal disease who are contrast agent intolerant. By offering

a comprehensive assessment of the anatomy of the urinary system and the soft tissues around it, MRU helps identify and cure stones. Particularly in pregnant women, MRU can assist in differentiating between pathological and healthy ureteral blockage.[4]

THERAPEUTIC STRATEGIES:

MEDICATION FOR CALCIUM STONES:

THIAZIDES:

Thiazides are used as a medical preventive medication to lower urine calcium in people with hypercalciuria . By promoting calcium reabsorption in the distal renal tubules, thiazide diuretics reduce the amount of calcium excreted in the urine.[9] Hydrochlorothiazide (25 mg twice a day), chlorthalidone (24 mg/day), and indapamide (1.25 to 2.5 mg/day) have been linked to decreased stone formation. The hypercalciuric effects of thiazide diuretics can be enhanced by decreasing dietary salt. Restricting sodium intake reduces potassium loss caused by thiazides.[10]

POTASSIUM CITRATE:

Urinary pH and citrate levels are raised by alkali citrates like potassium citrate . By attaching to calcium in the urine, citrates lower urinary calcium excretion and prevent calcium crystallization in hypocitraturia patients. Following shock wave lithotripsy or percutaneous nephrolithotomy, potassium citrate has also been shown to increase the stone-free rate and stop the production of new stones.[10]

ALLOPURINOL:

Uric acid stones can be prevented and treated with allopurinol, a xanthine oxidase inhibitor.

Allopurinol, however, is also useful to prevent calcium oxalate stones in people with hyperuricosuria.[10]

MEDICATION FOR STRUVITE STONES:

Eliminating the infection with antibiotics and removing the bacteria-laden stones surgically as soon as possible are the mainstays of treatment for struvite stones. Unless patients are too sick for surgery or refuse stone removal, medical care combined with long-term antibiotic medication is rarely effective and is not advised. The sole medication authorized to treat struvite nephrolithiasis is acetohydroxamic acid, a urease inhibitor; nevertheless, its usage is restricted due to adverse effects such as rash, hemolytic anemia, nausea, and thrombophlebitis.[11]

MEDICATION FOR URIC ACID STONES:

Management of cystinuria focuses on lowering urinary cystine levels to below 250 mg/L. This can be achieved by increasing fluid intake, limiting dietary sodium, and reducing the intake of methionine and cystine through restricted consumption of animal protein. Maintaining urine pH between 7.0 and 7.5 enhances cystine solubility. While dietary protein control can help achieve this, alkalinizing agents such as potassium citrate or sodium bicarbonate are usually required for effective pH regulation.[11]

INVASIVE TREATMENT TECHNIQUES :

The placement and size of the stones serve as indicators to start the management process. Due to the increasing efficacy of minimally invasive techniques like ureteroscopy (URS) and ESWL, open surgeries are being utilized less frequently to treat ureteric stones, renal stones (20 mm), and lower renal pole stones (10 mm). Additionally, renal stones bigger than 2 mm or lower renal pole stones less than 1 mm can be treated using percutaneous nephrolithotomy (PCNL).[4]

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL):

Extracorporeal Shock Wave Lithotripsy (ESWL), , is a minimally invasive method used to manage urinary stones, achieving a success rate of about 70–80% after treatment. It is widely regarded as the preferred option for small to medium-sized stones—specifically, renal stones under 20 mm and lower pole stones smaller than 10 mm, as recommended by international guidelines.[4]

URETEROSCOPES:

Flexible ureteroscopes are essential for performing endoscopic removal of kidney stones via the body's natural passages. Evidence from multiple randomized controlled trials has shown that ureteroscopy achieves high success rates in the management of ureteral stones.[4]

PERCUTANEOUS NEPHROLITHOTOMY (PCNL):

Percutaneous nephrolithotomy (PCNL) is the preferred treatment for staghorn calculi, offering a stone clearance rate of 85% to 93%. However, this procedure is not suitable for patients who are pregnant, have bleeding disorders, or suffer from uncontrolled urinary tract infections (UTIs).[4]

HERBAL TREATMENTS FOR UROLITHIASIS:

The scientific benefits of herbs and herbal remedies have drawn public interest. Approximately 75% of people on the planet, primarily in developing nations, rely on herbal remedies to meet their basic medical needs. Approximately 25% of the current pharmacopoeia consists of compounds that were originally isolated from plants, while another 25% consists of altered forms of compounds that were initially found in natural products. Regarding herbal remedies, there are several species that are classified as therapies for urolithiasis in the pharmacopoeia of numerous nations across the world. Numerous herbs include diuretic, antilithic, alkalizing, antispasmodic, and anti-inflammatory qualities that can help promote kidney health, prevent stone formation, encourage stone breakdown, and relieve symptoms.

Some of the herbal medicinal plants include *Aerva lanata* (Amaranthaceae), *Boerhaavia diffusa* Linn. (Nyctaginaceace), *Bombax ceiba L.* (Malvaceae), *Bryophyllum prinnatum Lam* (Crassulaceae), *Pedalium murex* (Zygophyllaceae), *Tribulus terrestris* (Zygophyllaceae), *Tridex procumbens L.* (Asteraceae). Three marketed compound herbal formulations have been effectively used in therapeutic settings to remove renal and bladder urinary calculi: Calcuri (Charak Pharmaceuticals, Bombay, India), Cystone (Himalaya Drug Company, India), and Chandraprabha bati (Baidyanath, India).[12]

DIETARY MODIFICATION:

In order to prevent or treat a variety of urological disorders and to promote urological health, dietary changes are essential. Certain dietary adjustments can help lower the chance of developing these illnesses or lessen their symptoms. The following dietary changes are helpful to urological health:

Hydration , Reducing sodium intake , Limiting oxalate-rich foods , Balanced diet , Avoiding caffeine and carbonated beverages , Fiber-rich foods.[13]

GUT MICROBIOME – A PREBIOTICS AND PROBIOTICS:

The gut microbiota influences urolithiasis through multiple pathways, including direct effects on oxalate metabolism and indirect modulation of inflammation, immunity, and gut barrier integrity. These interactions play a key role in stone formation and offer opportunities for targeted therapies.

Certain gut bacteria can reduce stone risk by degrading oxalate, the main component of calcium oxalate stones, which represent about 75% of all cases (Hunthai et al., 2024). *Oxalobacter formigenes*, an anaerobic gram-negative species, is particularly important for this process, utilizing enzymes such as formyl-CoA transferase and oxalyl-CoA decarboxylase to break down oxalate.

The presence of *Oxalobacter formigenes* in the gut lowers intestinal oxalate absorption and consequently reduces urinary oxalate levels (Chmiel et al., 2022). However, clinical studies using oxalate-degrading probiotics, including *O. formigenes*, have shown inconsistent results. A key limitation is the bacterium's high susceptibility to commonly used antibiotics, which hinders stable colonization (Lange et al., 2012). Moreover, some colonized individuals still develop stones, indicating that additional microbial species and host factors also contribute to oxalate handling and stone risk.[14]

INNOVATIVE TREATMENT APPROACHES FOR UROLITHIASIS :

LASER TECHNOLOGY

Thulium fibre laser (TFL) is a newer lithotripsy technology with several advantages over Ho:YAG [Holmium: yttrium-aluminum-garnet] Operating at 1940 nm—near the water absorption peak—it requires significantly less energy to fragment stones while remaining effective across all stone types. TFL supports a broad operational range, delivering pulse energies from 0.025 to 6 J at frequencies up to 2000 Hz, producing peak powers around 500 W. These settings allow the use of much smaller fibres (≈50 µm versus ≥200 µm with Ho:YAG), improving instrument flexibility, irrigation, and reducing stone retropulsion due to smaller bubble formation and higher pulse frequencies.[15]

ARTIFICIAL INTELLIGENCE STRATEGIES:

In the branch of computer science known as artificial intelligence (AI), machines are designed to mimic and carry out cognitive functions typically performed by the human brain. AI is rapidly incorporated in all fields of medicine, since it has got demonstrably better accuracy than traditional statistical approaches, and can incorporate novel data sources, eg, image or pathology data, and permits the creation of predictive models that are very accurate, using huge amounts of data. AI has already been tested for the diagnosis of stone illness, the identification of stone composition, and other elements of medical or surgical treatment. Langkvist et al colleagues employed a machine learning neural network to differentiate between phleboliths and stones in the CT scan, obtaining a sensitivity of 100%.[15]

ROBOTIC URETEROSCOPY (ROBOURS)

Desai et colleagues first described the use of a robotic system for URS in porcine models.66 They proposed enhanced ergonomics when employing the Sensei robot, based on surgeons' replies on a visual analogue scale for instrument stability (10/10), reproducibility of access (10/10) and auto-retraction (8/10). Geavlete et al did a comparison study using RoboURS and normal flexible ureteroscopy, showing a considerably lower retreatment rate when employing robotic devices (9.1% vs 15%). Summarizing available literature, robotic systems are in their infancy but apparently contribute to improved ergonomics, less utilization of fluoroscopy and shorter operative time due to the memory of these systems; however, cost implication should be considered as well.[15]

MINIATURIZATION OF PCNL SHEATH:

Technological developments permitted the refinement of instruments used during PCNL. The reduction of access sheaths from 24–30 Fr (regular PCNL) to 14–20 Fr (mini-PCNL) is one of the most significant changes.70. The primary benefits of mPCNL are decreased bleeding and transfusion rates, higher rates of tubeless procedures (75–80%), and shorter hospital stays. However, the use of laser lithotripsy during mPCNL results in longer operating times.[15]

NANOTECHNOLOGY FOR UROLITHIASIS TREATMENT:

Renal calcium oxalate stones are largely caused by oxidative stress damage to renal epithelial cells. Numerous mechanisms can lead to oxidative stress, which raises the chance of kidney stone formation. The inflammatory response that results from kidney stone production further intensifies oxidative stress, creating a vicious cycle.

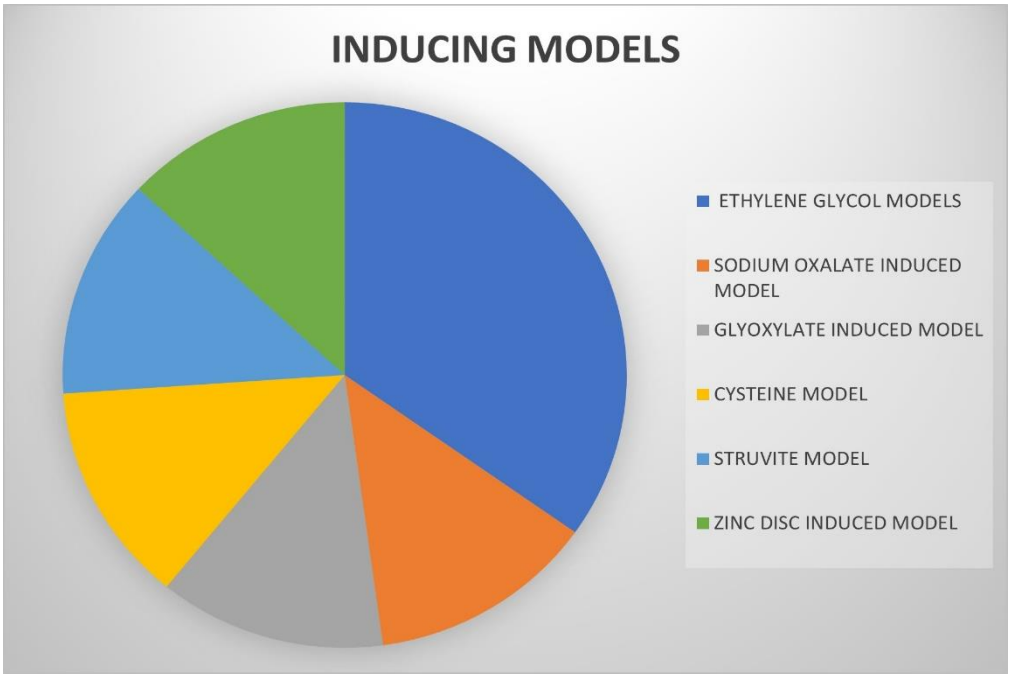
Antioxidants can prevent the development of stones and counteract the oxidative stress damage that hyperoxaluria causes to renal cells. Currently, certain nanomaterials having catalytic and enzymatic qualities—known as nanozymes—have been found. Antioxidant therapy mediated by nano enzymes is currently regarded as a potential approach for the management of inflammation caused by oxidative stress.[15]

CeO_2 nanozymes possess a cubic fluorite structure rich in oxygen vacancies, enabling Ce atoms to shift between +3 and +4 oxidation states—an essential feature for their enzyme-like activity. Their ROS-scavenging performance varies with crystal form, morphology, and particle size. Deng et al. reported that porous CeO_2 nanorods efficiently neutralize excess free radicals by leveraging Ce’s reversible valence states, thereby lowering oxidative stress in renal tubular

epithelial cells and preventing calcium oxalate crystal formation, without causing noticeable toxicity to other organs.[16]

EXPERIMENTAL IN-VIVO APPROACHES FOR MODELING UROLITHIASIS

Preclinical animal models of urolithiasis have become indispensable for evaluating the efficacy of herbal extracts, pharmaceuticals, and novel drug candidates. These models help determine their ability to reduce crystal deposition, correct metabolic abnormalities, and protect renal tissue.



SODIUM OXALATE INDUCED UROLITHIASIS:

Sodium oxalate–induced urolithiasis develops when excessive oxalate intake elevates urinary oxalate levels, promoting calcium oxalate crystal formation. After ingestion, sodium oxalate is absorbed from the gastrointestinal tract into the bloodstream and subsequently filtered by the kidneys. Under normal conditions, only small amounts of soluble oxalate are excreted in urine. However, high oxalate intake increases urinary oxalate concentration, reducing its solubility. Excess oxalate then readily binds to calcium ions, leading to the precipitation of calcium oxalate crystals and contributing to kidney stone formation.[17]

GLYCOLIC ACID INDUCED UROLITHIASIS:

Glycolic acid–induced urolithiasis occurs when glycolic acid metabolism increases oxalate production, promoting calcium oxalate stone formation. In the liver, glycolic acid is converted to glyoxylate by glycolate oxidase. Under normal conditions, glyoxylate is transformed into glycine by alanine–glyoxylate aminotransferase (AGT). In disorders such as primary hyperoxaluria type 1, AGT deficiency leads to glyoxylate accumulation, which is then converted into oxalate. Excess oxalate binds to calcium, forming calcium oxalate crystals that can deposit in the urinary tract and cause symptoms such as flank pain, hematuria, and recurrent urinary infections.[17]

ETHYLENE GLYCOL INDUCED UROLITHIASIS:

Ethylene glycol–induced urolithiasis develops when the compound is metabolized into oxalate, which promotes calcium oxalate stone formation. After ingestion, ethylene glycol is processed in the liver by alcohol dehydrogenase and aldehyde dehydrogenase, producing glycolic acid, glyoxylic acid, and ultimately oxalic acid. The resulting oxalic acid readily binds with calcium to form calcium oxalate crystals, which can accumulate in the urinary tract and lead to kidney stone development.[17]

ZINC DISC IMPLANTATION MODEL OF UROLITHIASIS:

In the zinc disc implantation model of urolithiasis, bladder stone formation is induced by surgically inserting pre-weighed and sterilized zinc discs into the urinary bladder of rats. The animals are anesthetized with intraperitoneal sodium pentobarbitone (40 mg/kg), and the bladder is accessed through a suprapubic incision. A small incision is made on the bladder wall, urine is aseptically collected for pH and bacteriological analysis, and the zinc disc is then placed into the bladder. The incision is closed with absorbable sutures, and animals are allowed to recover for about one week. This model results in a marked rise in urinary albumin and creatinine levels. Male rats, in particular, show greater stone formation and bladder smooth muscle hypertrophy at 4 and 8 weeks post-implantation due to the presence of the zinc foreign body.[17]

CONCLUSION:

Urolithiasis is a multifactorial disorder primarily involving calcium oxalate stone formation, influenced by metabolic, physiological, and lifestyle factors. Men are more commonly affected than women, with diet and fluid intake playing key roles in disease prevalence. Emerging

evidence on stone promoters and inhibitors, immune mechanisms, the gut microbiome, and sex hormones has improved understanding of stone pathogenesis. Progress in personalized medicine, novel therapeutics, and advanced diagnostic and surgical techniques offers improved management. An integrated approach that combines medical, nutritional, and surgical strategies is essential to reduce recurrence, improve patient outcomes, and lower the healthcare burden of kidney stones.

ACKNOWLEDGEMENT:

I, **THAMARAISELVI K** express my sincere gratitude to my respected guide, **ABIRAMI RAJA ,** and **DR. AMUDHA P** (Head of the Department of Pharmacology) for the continuous support, valuable guidance, and constant encouragement throughout the review paper work.

REFERENCE:

1. Allam EA. Urolithiasis unveiled: pathophysiology, stone dynamics, types, and inhibitory mechanisms: a review. African Journal of Urology. 2024 Jul 23;30(1):34.

2. Vilapurathu JK, Carlmana CA, Francisa D, Varghesea S. A comprehensive investigation of the prevalence and risk factors associated with renal calculi in Southern India: A prospective study. Urological Science. 2025 Mar 1;36(1):20-4.

3. Moftakhar L, Jafari F, Ghoddusi Johari M, Rezaeianzadeh R, Hosseini SV, Rezaianzadeh A. Prevalence and risk factors of kidney stone disease in population aged 40–70 years old in Kharameh cohort study: a cross-sectional population-based study in southern Iran. BMC urology. 2022 Dec 19;22(1):205.

4. Yamgar PV, Nimbalkar VV, Pagar HJ. Urolithiasis: Mechanism of stone formation, diagnostic modalities and treatment protocols [Internet]. IP Int J Compr Adv Pharmacol. 2024 [cited 2025 Nov 05];9(4):227-235. Available from: https://doi.org/10.18231/j.ijcaap.2024.034]

5. Alelign T, Petros B. Kidney stone disease: an update on current concepts. Advances in urology. 2018;2018(1):3068365.

6. Peerapen P, Thongboonkerd V. Kidney stone prevention. Advances in Nutrition. 2023 Mar 9;14(3):555.

7. Tamborino F, Cicchetti R, Mascitti M, Litterio G, Orsini A, Ferretti S, Basconi M, De Palma A, Ferro M, Marchioni M, Schips L. Pathophysiology and main molecular mechanisms of urinary stone formation and recurrence. International journal of molecular sciences. 2024 Mar 6;25(5):3075.

8. Kachkoul R, Touimi GB, El Mouhri G, El Habbani R, Mohim M, Lahrichi A. Urolithiasis: History, epidemiology, aetiologic factors and management. The Malaysian journal of pathology. 2023 Dec 1;45(3):333-52.

9. Jahrreiss V, Seitz C, Quhal F. Medical management of urolithiasis: Great efforts and limited progress. Asian Journal of Urology. 2024 Apr 1;11(2):149-55.

10. Gul Z, Monga M. Medical and dietary therapy for kidney stone prevention. Korean Journal of urology. 2014 Nov 28;55(12):775.

11. Shastri S, Patel J, Sambandam KK, Lederer ED. Kidney stone pathophysiology, evaluation and management: core curriculum 2023. American journal of kidney diseases. 2023 Nov 1;82(5):617-34.

12. Khanam A, Singh G, Narwal S. Treatment and prevention of recurrent urolithiasis: insights on molecular mechanism of occurrence and medical care. Food Chemistry Advances. 2024 Dec 1;5:100751.

13. Alghamdi AM, Alqurashi EA, Alsubaie AT, Alamri AM, Alamri AM, Abdulmajeed AH, Asiri SA, Alenezi NK. Management of recurrent urolithiasis: advances in prevention strategies. Int J Community Med Public Health [Internet]. 2025 Jun. 13 [cited 2025 Dec. 1];12(7):3389-94.

14. Li D, Li Z, Liu W. The Gut-Kidney Axis in Urolithiasis: Roles of 1 Gut Microbiota, Metabolites, and 2 Therapeutic Implications 3. Frontiers in Microbiology. 2025 Oct 10;16:1655808.

15. Tzelves L, Geraghty RM, Hughes T, Juliebø-Jones P, Somani BK. Innovations in kidney stone removal. Research and reports in urology. 2023 Dec 31:131-9.

16. Wang Y, Yang J, Amier Y, Yuan D, Xun Y, Yu X. Advancements in Nanomedicine for the Diagnosis and Treatment of Kidney Stones. International Journal of Nanomedicine. 2025 Dec 31:1401-23.

17. Satapathy T, Pradhan B, Sen K. Experimental animal models for urolithiasis (kidney stone): A comprehensive review. Animals and Zoonoses. 2025 Mar 7.