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# Review: Evaluating the Efficacy of Phytochemicals in Treating Urolithiasis by Inhibiting the Mechanism of Action in the Pathophysiology of Stone Formation

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#### **ABSTRACT:**

This article discussed pathophysiology, investigation, and management on recurrent kidney stone disease, The aforementioned study pertains to treatment in urolithiasis or Nephrolithiasis which refers to the condition characterized by hard mineral structures formed in the urinary tract. Urolithiasis is increasingly addressing the use of phytochemicals in treatment options because of the natural origin and minimum side effects of their interventions. The pathophysiology of urolithiasis or Nephrolithiasis encompasses: supersaturation, nucleation, crystal aggregation, growth, which interaction with epithelial cells, leading to Urolithiasis. Phytochemical of mention herbal its commonly bioactive compounds such as Saponin, flavonoids, alkaloids & glycosides, possess diuretic antioxidant, & anti-inflammatory, effects that act effectively inhibit the urolithiasis or Nephrolithiasis mechanisms.

Studies revealed that phytochemicals inhibition of supersaturation by altering urinary pH and increasing solubility of minerals forming stones. All these phytochemicals protect & treat the renal epithelial cells from oxidative stress and inflammatory responses instigated by crystal-cell interactions, further hampering the progression of stones in addition to damage to the tissue. Extracts from plants such as PHYLLANTHUS NIRURI, SYZYGIUM CUMINI, URTICA DIOICA.L, HIBISCUS SABDARIFFA, have been researched widely, showing positive results for promoting dissolution and preventing recurrence of the crystals stone.

This review will put forward the efficacy of the phytochemicals as a therapeutic approach to urolithiasis & nephrolithiasis focusing on their role targeting important inhibition of stone formation.

**Keywords:** Phytochemicals, herbal bioactive compounds, Diuretic, antioxidant, anti-inflammatory, Prevention of recurrence, dissolution of stones, protection of renal epithelial cells, Therapeutic efficacy of phytochemicals in targeting, inhibiting stone formation, Saponins, flavonoids, alkaloids, glycosides,tannins.



### INTRODUCTION

Nephrolithiasis or renal calculi is commonly referred to as kidney stones. It is the medical condition caused by the presence of stones within the kidneys. This is the presence of hard deposits formed by minerals and salts in the kidneys. Allegedly, nephrolithiasis comprises the stones in the kidney <sup>[1]</sup>. It is a condition in which stones form within the kidney itself and is also known as renal calculi. The term is derived from two words - Nephros, which means of the kidney, and lithos, which means stone. Stones or renal calculi are formed when water cannot dissolve some salts and minerals, forming hard deposits. They are known as kidney stones, renal stones, or urinary calculi <sup>[2]</sup>. Or Urolithiasis - From the Greek words ouron (urine) and lithos (stone), Urolithiasis literally means urinary stone disease. In practical terms, Urolithiasis is defined as the formation of hard, solid and non-metallic minerals such as uric acid, lithiasis in the urinary tract.[3]

### PATHOPHYIOLOGY: - [4]

- 1. Supersaturation- The solution is supersaturated when it is able to keep dissolving solute in any concentration beyond the limit that can be dissolved under normal conditions. The absorption takes place when all amino acids and proteins are gathered in the tubules in a soft form and are then exported through the tubules into the kidney. Under this condition solutes precipitate in urine cause nucleation and crystal formation.
- 2. Nucleation- Supersaturation when urine is retained in the kidney has energy as cluster less than the energy of liquid. Nucleation is a change from liquid to solid phase in syperatisable soluble charge molecules such as calcium and oxalate which come together to form calcium oxalate crystals and furthermore crystals become insoluble at the early stages of this process consists of the coalescence of stone sites in clusters which growth of their crystals by nucleation and aggregation process. Nucleation may be homogenous if consists only of solute molecules or else it is heterogeneous if nucleating agents are involved like redundant cellular debris, tea epithelial cells, red blood cells, urinary casters and proteins.



Fig: - Schematics of stone aggregation, progression and formation [4]



- 3. Aggregation- This is the growing of supersaturated crystals by sticking small crystals to grow into larger crystals by example calcium oxide aggregate to form calcium oxalate and many such soft crystals are also formed.
- 4. Crystal growth- The formation of a tiny, hard stone, also known as crystal growth, is the process by which urinary crystalline components gather and conjoin in order to develop a hard, firm stone.
- 5. Crystal cell interaction- The interaction of crystals with cells may be observed during progressive growth of crystals. When a crystal interacts with epithelial and endocytic tissues, it ruptures tissues by movement of crystals on the necrosing cells; this interaction can lead cell injury in epithelial cells, resulting in increased expression and synthesis of proinflammatory macromolecule. This predisposes the formation of stones.
- 6. Stone formation- Consequently, their clumping with other crystals and organic substances finally results in the formation of kidney stones, which may cause kidney failure if not treated in time.

EPIDEMIOLOGY: Urolithiasis Approximately 12% of people will have this disease at some time during their lives, the incidence increasing with age; thus, nearly half of enough people will suffer from a recurrence within 5–10 years and approximately 75% will again suffer from a relapse within 20 years. The last 30 years have seen remarkable increases in incidence, particularly among women within the developed world, whose incidence is now approximately equivalent to that of men. Kidney stone is one of the oldest recorded disorders of human and one of the major health burdens.[5] Now a days large number of peoples are affected with this disorder all over the world, mostly between ages 20 to 60, while it also prevails more in hot climates. Three common terms used in epidemiological study of renal calculi are incidence, prevalence and life time prevalence. Since incidence is the number of new renal stone patients found in a selective population at a particular time point, prevalence refers to the total number of renal stone patients considering the same selected population at a particular time point and life time prevalence is the presence of old nephritic stone in number of patients.[6] Studies and surveys on the last half-century time have shown that nephrolithiasis produces a lot of human suffering. The cases are constantly on the increase as reported by researchers and surveys done in the last half century. Nephrolithiasis is a global problem affecting all geographical regions throughout the globe. Annual approximate prevalence is 3-5% and approximate life time prevalence is 15-25%. Most renal calculi show the tendency of recurrence among them. Recurrence rates of renal stone were approximately 10% yearG1, 50% over a period of 5-10 years and 75% over 20 years period11. The incidence rate of nephrolithiasis varies with geographical region of an individual country. After the first attack, renal calculi recurred in the patient at a rate of 14% in 1 year, 35% in 5 years, and 52% by the end of 10 years. Higher incidence of renal calculi in adults in the western region as compared to the eastern region. Approximately 200 million people every year in India are becoming victim to nephrolithiasis. Several regions of the country are said to have names tagged with "stone belt" such as Gujarat, Maharashtra, Punjab, Rajasthan, Delhi, Haryana, and some of the states on North-East side. South India is also rich in urinary stone cases resulting from high consumption of tamarind in the daily diet. In the upper urinary tracts, predominantly uroliths are found in the form of pure calcium oxalate crystals, as seen in a case study at AIIMS, New Delhi. Hence the Kutchchh and Saurashtra region of Gujarat also has this high prevalence of renal calculi. An India approximates about 50 percent of its population suffering from renal calculi, which may end up towards renal damage or loss of kidney function. The nephrolithiasis incidence rate, mostly among staghorn calculi, is very high in Manipur, and a few reports indicate an increase prevalence in the North



Western region of India as well. During the years 1999-20013, there was an increase in renal stone cases in the northeastern part of Bihar from Purina division. Pediatric renal calculi cases have recently fallen under some epidemiological studies in the last few decades [7]

### **DRUG FOR UROLITHIASIS: -**

**SYZYGIUM CUMINI** - The common name of Syzygium cumini is Jamun or Java Plum and belongs to family Myrtaceae and the mainly found chemical constituents are saponin, Flavonoids [8]. Follows the Mechanism of action where the diuretic activities exhibited by Syzygium cumini could be caused by the phytochemical compositions of flavonoids, tannins and essential oils, which confer a powerful effect on renal physiology. Such compounds increase renal blood flow and glomerular filtration rate (GFR), thus enhancing urine output. Syzygium cumini also modulates the ionic channels and transporters in the renal tubule that mediate sodium and water excretion while maintaining the balance of electrolytes. The antioxidant status also protects the renal tissues from oxidative stress caused often with diuretic treatments to ensure continued kidney function. This type of diverse action has the potential of natural diuretic as an agent in managing fluid retention and its associated conditions [9].it is mainly found in India, Malaysia, Sri Lanka, & Thailand [10] & Side effects are Digestive Distress.[11]



Fig: Syzygium cumini

**TETRAPELURA TETRAPETRA: -** The common name of Tetrapleura tetraptera is Aridan or Prekese. It is also referred to as Aidan fruit & belonging to the Family – Fabaceae and the mainly found chemical constituents are saponin, alkaloids, tannins, flavonoids [12]. Follows the Mechanism of action where Tetrapleura tetraptera fruit is predominantly used as a spice and condiment in Cameroon. This present study revealed that fruit extracts contained high amounts of polyphenols and flavonoids. The present findings support earlier evidence that the plant's antiplasmodial effects are likely related to its high phenolic content. The antioxidants by well-known properties of polyphenols are due to the redox potential of these compounds to neutralize free radicals or break down peroxides and singlet oxygen. The FRAP assay gave an indication of the total antioxidant capacity by which these compounds can reduce the TPTZ-Fe (III) complex to TPTZ-Fe (II) by donating electrons. Our findings provided enough evidence for the water-ethanol extracts from Tetrapleura tetraptera having remarkably higher antioxidant potential than many other ethnomedicinal plants, such as Harungana madagascariensis. A similar trend was also



observed for the activity - that the total antioxidant activity correlates positively with phenolic content - increasing antioxidant capacity with increasing phenolic concentration. This suggests that those phenolic compounds play a significant role in determining the antioxidant activity of Tetrapleura tetraptera[13]. It is mainly found in lowland forest of tropical Africa [14], & Side effects are arthritis and other inflammatory conditions, asthma, diabetes mellitus, hypertension, epilepsy, schistosomiasis [15]



Fig: Tetrapelura tetrapetra

**BORASSUS FLABELLIFER:** - The common name of Borassus flabellifer is the palmyra palm or toddy palm & belongs to the Family - Arecaceae and the mainly found chemical constituents are Tannain, Saponin, Alkaloids, Flavonoids[16]. Follows the Mechanism of action where the sap of the Palmyra palm, Borassus flabellifer, called Legen, is said to have diuretic as well as antiurolithiatic properties because it can dissolve brushite crystals in the kidney, thus preventing stone formation. This sap possesses some diuretic chemical agents which stimulate the urinary system, increasing urine output and enhancing the calcium and magnesium ion excretion of those commonly associated with the waters and soils of Tuban, East Java, Indonesia. Because of this diuretic effect, crystal aggregation is inhibited, rendered possible the dissolution and the elimination of the pre-existing kidney stones. It is also manifested in the usage according to tradition, as it is said that this Legen, when taken once daily for 30 days, will cure kidney stones; whereas, maintained in regulated amounts, it serves as a preventive measure against reoccurrences. The diuretic properties of the plant are in line with its full ethnomedicinal uses as a stimulant, antileprotic, and antiphlogistic agent as substantiated in earlier studies [17] It is mainly found in Tamil Nadu[18] and there was no Side effects found.



Fig : Borassus flabellifer



**CORN SILK (ZEA MAYS):** - The common name of corn silk refers to the long, thread-like styles that grow from the ears of corn and belongs to the Family - Poaceae and the mainly found chemical constituents are flavonoids [19] and Follows the Mechanism of action where the starch tissue and uricosuric effects of corn silks (stigma/style of Zea mays L.) are through renal functioning and solute excretion. Water, sodium (Na+), potassium (K+), and uric acid urinary excretion are enhanced following aqueous extract of corn silks. Alterations in glomerular function, proximal tubular activity, and sodium tubular handling are responsible for these changes. These processes are by modulating renal activities, leading to diuretic and uricosuric effects, thus linking it to traditional uses for the management of fluid retention and hyperuricemia [20]. It is mainly found in the ear shoot [21] & Side effects decreased potassium and sodium levels in the blood [22]



JAVA TEA (ORTHOSIPHON STTAMINWUS): - The common name of Java tea refers to the plant Orthosiphon aristatus and belongs to the Family – Lamiaceae and the mainly found chemical constituents are flavonoids, glycosides [23] and Follows the Mechanism of action where the water extract of Orthosiphon Stamineus led to increased urine output in Sprague-Dawley rats and was previously shown as having dose-dependent diuretic activity. The activity of the extract was lower compared to furosemide and hydrochlorothiazide which are the commonly used drugs for diuresis. There was also observed abnormal high urinary potassium excretion and increased levels of blood urea nitrogen, creatinine, and glucose, all of which were within normal limits. The methanol-water extract from leaves of Orthosiphon stamineus had a diuretic action similar to that seen with hydrochlorothiazide for both acute and chronic administration. Reported reduction in uric acid level after six hours, like that of allopurinol for hypouricemic rats. The diuretic activity of Orthosiphon stamineus was attributed to the presence of methoxy flavonoids (sinensetin and tetramethylscutellarein) with an antagonizing activity on the adenosine receptors. Thus, the diuretic properties of Orthosiphon stamineus are attributed to the affinity of active compounds to adenosine receptor ligands [23] & it is mainly found in the southern China [24] & Side effects are taking java tea might decrease how well the body gets rid of lithium. This could increase how much lithium is in the body and result in serious side effects.[24]



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Fig: Java tea (orthosiphon sttaminwus)

PETROSELINUM CRISPUM: - The common name of petroselinum crispum refers to parsley and belongs to the Family – Apiaceae and the mainly found chemical constituents are Flavonoids & polyphenolic compounds [25]. And follows the mechanism of action where the diuretic effect of Petroselinum crispum (parsley) arises from renal sodium and potassium management. Increased urinary volume in rats was demonstrated by the method of 24-hour comparison or by in situ perfusion of kidneys with parsley seed aqueous extract. Effects of the extract on Na<sup>+</sup>-K<sup>+</sup> ATPase pump have been vital in bringing about this diuretic action. The extract inhibits activity of the sodium-potassium ATPase in both the renal cortex and medulla, resulting in impaired sodium reabsorption and reduced potassium secretion. This inhibition thus holds the potassium for increased retention in the renal tubules and intercellular spaces. Increased concentration of potassium disrupts normal reabsorption of sodium and potassium, giving rise to generating osmotic gradients wherein water is drawn into the renal lumen, thus inducing diuresis. This fact was verified further since the diuretic effect is maintained even in the presence of amiloride and furosemide, while sodiated condition is absent but not the potassium. Thus, parsley acts diuretically primarily by inhibiting the  $Na^+-K^+$  ATPase pump [26] & it is mainly found in the eastern Mediterranean [27] and Side effects are ingestion of parsley oil include headache, giddiness, loss of balance, convulsions, and renal damage.[28]



**Fig: Petroselinum crispum** 



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**PHYLLANTHUS NIRURI:** - The common name of Java tea refers to the plant Orthosiphon aristatus and belongs to the Family-Phyllanthaceae and the mainly found chemical constituents are saponin, flavonoids & alkaloids [29] and follows the mechanism of action where Phyllanthus niruri has exhibited a propensity for being used as therapeutic agents in urolithiasis through multi-faceted action mechanisms. The plant interferes with several stages of kidney stone formation by reducing crystal aggregation, altering the structure and composition of crystals, and preventing their interaction with tubular cells. This disruption impairs the endocytosis of crystals by renal tubular cells and may limit their formation and growth. Clinically, Phyllanthus niruri may promote ureteral relaxation thereby aiding in the passage of calculi or assisting with the clearance of stone fragments after lithotripsy. This plant also has the potential to minimize the excretion of urinary crystallization promoters like calcium and hence prevent stone formation. It's worth mentioning that no adverse effects - renal, cardiovascular, neurological or toxic were recorded in the studies, suggesting that Phyllanthus niruri would be safe and effective for preventive and therapeutic aspects of urolithiasis. Further long-term randomized clinical trials should be directed to inflammation in order to prove it for clinical efficacy and applicability of the plant for human use [30] & it is mainly found in the India [31] & Side effects are its prevalence is high worldwide with an increase in morbidity.[32]



**Fig: Phyllanthus niruri** 

**ALISMA ORIENTALIS:** - The common name of Alisma orientalis is oriental water plantain and belongs to the Family – Alismataceae and the mainly found chemical constituents are saponin and follows the mechanism of action where the bioactive components in Alisma orientalis act as a safeguard against the formation of renal oxalate calcium stones in a rat model of urolithiasis. The mechanism is purported to be related to the modulation of bikunin mRNA expression, an important regulatory protein implicated in the formation of urinary stones. In this research hyperoxaluria with calcium oxalate stone formation was



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induced in the rats by giving 1% ethylene glycol and 2% ammonium chloride consumption. The treatment using Alisma orientalis extracts resulted in significant stone formation reduction when compared to stoneformers. This effect is presumably due to the active constituents of Alisma orientalis which probably modulate the expression of bikunin, a protein involved in reducing the aggregation of crystals and enhancing the clearing of urinary stones. Alisma orientalis prevents the causation of calcium oxalate stones through the modulation of molecular pathways influencing nucleation, aggregation, and retention of the crystals. The findings indicate upregulation of bikunin as a mechanism behind the action of Alisma orientalis, suggesting a possible therapeutic direction in preventing and managing kidney stone disease by regulating vital biochemical parameters on urolithiasis [33]& typically identified in the moist, wetland areas like shallow waters, ponds, lakes, marshes, and river banks, it is native to regions in East Asia, including China, Korea, Japan, and Southeast Asia.



Fig: Alisma orientalis

MANGIFERA INDICA: - The common name of Mangifera indica is mango and belongs to the family Anacardiaceae and the mainly found chemical constituents are Tannin, Alkaloids, Flavonoids [34] and follows the mechanism of action where the mangiferin is a natural C-glucosyl xanthonoid polyphenol, which possesses very potent reno-protective effects in various kidney disorders through its multifaceted pharmacological actions. Mangiferin is effective by the activation of antioxidant responses that protect against renal inflammation and oxidative stress, thus contributing much to kidney injury. Apoptosis in renal cells is inhibited by mangiferin, which is one of the contributory processes of renal damage in diabetic nephropathy and renal fibrosis. In addition, mangiferin promotes a process called autophagy, through which a cell maintains its functions through the elimination of damaged organelles. Mangiferin shows pharmacological properties, modulating immune response activities with activations of renal urate transporters, responsible for their downward hyperuricemia and evoked renal derangements. The primary activities associated with it are through the modulation of some key signaling pathways, mainly through regulating NF-kB, which primarily involves suppression of sEH related to inflammation and activation of oxidative stress. In-silico molecular docking studies endorse this mechanism by showing that mangiferin interacts with NF-kB and sEH. Overall, mangiferin would be relatively effective in renal protection with respect to inflammatory and oxidative stress, apoptosis, and autophagic effects. Thus, it can be considered as an effective natural therapeutic agent for kidney disorders [35] & it is mainly found in the India and Myanmar [36] & Side effects - antibacterial, anti-fungal, anthelmintic, anti-parasitic, anti-tumor, anti-



HIV, antibone resorption, antispasmodic, antipyretic, antidiarrhoeal, antiallergic, immunomodulation, hypolipidemic, anti-microbial, hepatoprotective, gastroprotective [37]



Fig: Mangifera indica

HIBISCUS SABDARIFFA: - The common name of Hibiscus sabdariffa is roselle or jamaica and belongs to the Family – Malvaceae and the mainly found chemical constituents are Steroids, tannins & flavonoids [38] and follows the mechanism of action: - Most of the beneficial effects of Hibiscus sabdariffa Linn. (roselle) have been attributed to modulation of important inflammatory pathways regarding antiinflammatory action within urinary tract infection (UTI) and renal inflammation. Clinical observances in long-term care facilities showed that ingestion of roselle drink reduced incidence of infection of urinary tract, particularly in patients who had urinary catheters. In experimental animals, roselle inhibited lipopolysaccharide (LPS)-induced renal inflammation in mice. The mechanism of action is based on the receptor blocking downregulation of nuclear factor-kB (NF-kB) activation, which is a major mediator of the inflammatory response. Besides, using roselle reduced LPS-induced interleukin-1ß production in a dose-dependent manner. Immunohistochemical staining also revealed that roselle inhibited the stimulation of NF- $\kappa$ B and-aggressed infiltration by inflammatory cells into the kidneys. Further support for these findings came from gene expression profiling which showed that roselle downregulated the expression of pro-inflammatory cytokine genes and enzymes involved in the production of prostaglandins and nitric oxide. This means that the reno-protective effects of roselle are through an inhibition of the NF-κB signaling pathway, resulting in reduced inflammatory gene expression and consequent decrease in production of pro-inflammatory mediators. In summary, the anti-inflammatory effect of roselle on UTI is associated with its immunomodulation effect and the modulation of the inflammatory pathways, therefore having a likely therapeutic value in preventing and treating UTI and related renal inflammation [39] & it is mainly found in tropical Asia & Side effects - stomach upset, gas, and constipation.[40]

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Fig: Hibiscus sabdariffa

#### DRUG USE FOR NEPROLITHIASIS

THALICTRUM FOLIOLOSUM: - The common name of Thalictrum foliolosum is Indian meadow-rue and belongs to the family Ranunculaceae and the mainly found chemical constituents are Alkaloids [41] and follows the mechanism of action where thalictrum foliolosum DC. boasts anti-urolithiatic activity through its capacity to hinder critical stages of stone formation in the kidneys, namely nucleation, aggregation, and crystallization. These mechanisms have been validated in a variety of in vitro assays and kinetic studies. The bioactive components of the plant, for instance, berberine and palmatine, determined by high-performance thin-layer chromatography (HPTLC), would likely inhibit crystal growth and aggregation. The herb also contains antioxidants that can potentially inhibit oxidative damage or inflammation affecting renal tissues and may further protect them from the possible consequences of urolithiasis [42]& it is mainly found in North America, particularly in the northeastern United States, and can be found in temperate regions with slightly acidic to neutral soil conditions & the Side effects are multifaceted actions justify the traditional usage of T. foliolosum as diuretic/anti-urolithiatic. It demonstrates the remarkable therapeutic capability of this plant in treating kidney stone disease [43]



fig : Thalictrum foliolosum

**OCIMUM BASILICUM.L.:** - The common name of Ocimum basilicum is basil and belongs to the family Lamiaceae and the mainly found chemical constituents are flavonoids & phenolics and follows the mechanism of action where the active antioxidant property of the Ocimum basilicum L. and Origanum vulgare L. extracts seemed mediated through their ability to neutralize reactive oxygen species (ROS) and to inhibit lipid peroxidation. As such, the EtOAc, n-BuOH, and H2O extracts demonstrated strong free radical scavenging activity, effectively neutralizing DPPH, NO,  $O_2^{\bullet-}$ , OH radicals, and H<sub>2</sub>O<sub>2</sub>. In addition,



these extracts significantly inhibited lipid peroxidation in liposomes, determined by a TBA assay, thus demonstrating protection against oxidative damage. The high antioxidant potential of these extracts worked well with their higher total phenolic and flavonoid levels. However, Et<sub>2</sub>O and CHCl<sub>3</sub> extracts showed weak radical scavenging and prooxidative tendencies in neutralization of OH radicals and inhibition of lipid peroxidation. Thus, the results suggest that the antioxidant mechanism depends mostly on phenolic and flavonoid contents contributing to the redox potential of the extracts that reduce oxidative damage [44] & it is mainly found in tropical Asia, Africa and America [45] & Side effects are nausea or diarrhea [46]



Fig: OCIMUM BASILICUM.L.

**TRIDAX PROCUMBENS.L.:** - The common name of Tridax procumbens is Coat Buttons or Tridax Daisy and belongs to the family Asteraceae and the mainly found chemical constituents are flavonoids & phenolics [47] and follows the mechanism of action where the antiurolithiatic and antioxidant activities of Tridax procumbens Linn. should be due to ability of the plant in reducing hyperoxaluria-induced oxidative stress and calcium oxalate crystallization. The ethanolic extract of T. procumbens lowers urinary calcium, oxalate, and creatinine levels, which reduces the supersaturation of stone-forming constituents, thus precluding renal deposition of calcium oxalate crystals. Its antioxidant activity counteracts the oxidative stress caused by the oxalate toxicity in renal epithelial cells, thus providing protection against cellular damage. Histopathological analysis also confirms the protective effects of T. procumbens and captures reduced calcium oxalate crystal deposition with reduced renal tubular damage. Thus, these studies suggest that the plant extract acts by modulating urinary biochemistry, inhibiting crystal aggregation, and alleviating oxidative damage, making it a potential therapeutic agent for urolithiasis[48] & it is mainly found in Central and South America[49].



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Fig: Tridax procumbens.L.

ADIANTUM CAPILLUSVENERIS. L.: - The common name of adiantum capillusveneris. 1. is Maidenhair Fern and belongs to the Family - Pteridaceae and the mainly found chemical constituents are Flavonoids[50] and follows the mechanism of action where the potential of hydroalcoholic extract of Adiantum capillus-veneris Linn. as an Anti-urolithic agent is evidenced by its ability to prevent calcium oxalate crystallization and aggregation. This extract showed considerable reduction in crystal size and number according to urine sample observation under light microscopy in in vitro studies, in addition to reduced rate of crystal aggregation. Nucleation appears to have not been inhibited, but again total number of crystals was fairly reduced, suggesting it might prevent the formation of early-stage crystals. All these effects were also confirmed from in vivo experiments in male Sprague Dawley rats having urolithiasis induced by ethylene glycol and ammonium chloride, where estimates following treatment with the extract showed a significant decline in urinary crystals along with total normalization of serum calcium, phosphorus, and blood urea levels. However, serum creatinine levels remained at par with control, thus suggesting preserved renal function. Histopathology revealed near-normal kidney architecture in treated groups, along with significant improvement in body weight. Thus, it is presumed that the extract works by inhibiting crystallization and aggregation process, maintains renal homeostasis, and protects kidney tissue, rendering it a promising candidate therapeutic agent for urolithiasis[50] & it is mainly found in tropical parts of South America, particularly in Brazil & Side effects are very large amounts may cause vomiting[51].



fig: Adiantum capillusveneris. L



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CYNODON DACTYLON.L.: - The common name of Cynodon dactylon L. is Bermuda Grass or Doob Grass and belongs to the Family - Poaceae (Grass family) and the mainly found chemical constituents are Saponin, flavonoids, alkaloids[52] and follows the mechanism of action where the antioxidant and diuretic properties of Cynodon dactylon (C. dactylon) are responsible for its protective impact against kidney stone disease. In this study, aqueous decoction of C. dactylon showed the reduction in the formation of calcium oxalate (CaOx) stones and improvement of antioxidant status both among serum and kidney tissues of male Wistar rats induced with ethylene glycol (EG). The highest dosage of C. dactylon given at 200 mg/kg resulted in the significant reduction of incidence of stone formation, decreased urine volume, and increased total antioxidant capacity, as determined by FRAP and total thiol level, when compared with the control group that received the EG treatment. It also was shown to bring down malondialdehyde (MDA), a marker of lipid peroxidation, suggesting its capability to combat oxidative stress. The histopathological result also corroborated the reduction of CaOx deposits in kidney tissues. Besides that, C. dactylon treatment did not change water intake but increased kidney weight and improved kidney function. Hence, these outcomes suggest that C. dactylon promotes antioxidant defense mechanisms to limit oxidative damage and inhibit the formation and aggregation of calcium oxalate crystals, hence being able to act as a promising natural remedy for prevention and treatment of the disease of kidney stones [53]& it is mainly found in sub-Saharan Africa and/or on islands in the western parts of the Indian Ocean [54]



fig : Cynodon dactylon.L

**TAXAXACUM OFFICINALE:** The common name of taxaxacum officinale is Dandelion and belongs to the Family – Asteraceae and the mainly found chemical constituents are Flavonoids & phenolics[55] and follows the mechanism of action where Taraxacum species, commonly referred to as dandelion, have well-known pharmacological effects because of their many bioactive compounds with diverse therapeutic actions, the biological evidence supports its diuretic, choleretic, anti-inflammatory, antioxidant, anticarcinogenic, analgesic, anti-hyperglycemic, anti-coagulatory, and prebiotic effects. These are associated, apparently, with the plant's rich phytochemical content of active principles such as flavonoids, sesquiterpene lactones, triterpenes, and polysaccharides. Possibly, diuretic action caused renal excretion of water and electrolytes, whereas choleretic property stimulated bile secretion aiding in digestion and



liver function. Scavenging free radicals that mediate oxidative stress and inhibition of pro-inflammatory cytokines protect tissues for anti-inflammatory and antioxidant actions. In a manner involving modulation of cell signaling pathways regulating cell proliferation and apoptosis, the anticancer activity makes possible an analgesic anti-hyperglycemic role in alleviating pain and controlling blood sugar, respectively. Its prebiotic activity would contribute to gut health through its development of beneficial gut bacteria. It will require further studies to determine specific components in Taraxacum and their relative pharmacological activities [56] & it is mainly found in Europe and Asia [57]& Side effects are abdominal discomfort, diarrhea, heartburn, increased heart rate, bruising and bleeding, excessive urination, and increased potassium levels (hyperkalemia)[58].



fig: Taxaxacum officinale

URTICA DIOICA.L.: - The common name of urtica dioica.l. is Stinging Nettle and belongs to the Family - Urticaceae and the mainly found chemical constituents are Flavonoids & phenolics [59] and follows the mechanism of action where Phytochemical complexity mediates the pharmacological effects of Urtica dioica (stinging nettle) flavonoids, tannins, saponins, proteins, amino acids, and phytosterols. These bioactive compounds mediate the pharmacological activities of the plants in various therapeutic effects such as antioxidant, antibacterial, analgesic, antiviral, anti-inflammatory, hepatoprotective, anticancer, and immune-regulatory effects. The antioxidant activity probably comes from scavenging free radicals, and hence protects the cell from oxidative damage. The anti-inflammatory and analgesic activities would be the inhibition of pro-inflammatory cytokines and other enzymes involved in pathways of pain and inflammation. Antimicrobial and antiviral activities are produced through the disruption of microbial cell membranes and interferes with the viral replication. Urtica dioica also protects the liver by increasing liver enzyme function and decreasing liver damage. Its anticancer activity may include modulation of cell signaling pathways regulating cell growth and apoptosis, and immune-regulatory effects also support immune function through modulation of immune cell activity. Thus, the diverse pharmacological features show that Urtica dioica is indeed a multifunctional medicinal plant for treating various diseases [60]& it is mainly found in Europe [61] & Side effects are diarrhea, constipation, and upset stomach.[62]



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Fig: Urtica dioica.L

#### **Conclusion:**

Review of above-mentioned Herbal drug commonly evaluate chemical constituent such as saponin, flavonoids, tannin, alkaloids etc. are showing commonly inhibit mechanism of kidney stone formation in nephrolithiasis or urolithiasis. Research concluded that saponin, flavonoids, tannin, and alkaloids basically 80-90 percent of drug inhibits the kidney stone formation.

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