Original Article

MEDICINAL PLANTS GLOBALLY EFFECTIVE FOR THE TREATMENT OF LITHIASIS AND IN VITRO PARAMETERS USED IN UROLITHIASIS

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Abstract

Renal lithiasis is a common condition that affects 4-15% of the global population and has a high recurrence rate. There is a wide range of stone compositions, however calcium oxalate makes up about 80% of uroliths. Unfortunately, neither the causes nor the current treatments for calcific stones allow for their simultaneous prevention and elimination. Because of this, a great deal of effort has gone into discovering what causes renal lithiasis and how to stop it from happening again, along with developing novel medications to treat and prevent it. This review, therefore, seeks to provide information that highlights recent developments in the study of medicinal plants believed to possess urolithiatic action. Researches looking for the active ingredients in urolithiatic herbs or compounds may find this page useful. An overview of stone formation, current treatments, and the usefulness of herbal therapy as an alternative are presented in this paper.

Keywords: Lithiasis, Herbs, Stone, Calcific, Prevention, Global population.

Abbreviations

NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases

ESWL: Extracorporeal shock wave lithotripsy

UTIs: Urinary tract infections

CaOx: Calcium oxalate

GAO: Glycolate oxidase

GAD: Glycolate dehydrogenase

LDH: Lactate dehydrogenase

Introduction

Stone disease, also known as urinary lithiasis, is a serious medical condition that affects many people. Ten percent of people in developed nations suffer from it **(Daudon 2008)**. It is characterised by the production of crystalline concretions forming in a basin and/or calyxes of kidney and producing partial or total obstruction to the regular urine flow **(Badalato *et al.*, 2011)**. Several factors can be connected to the production of these calculi such as sex, ethnic group, dietary intake, genetics, climate characteristics, and metabolic abnormalities **(Wasserstein, 2011)**. It's a disease with a 50% recurrence rate. Kidney failure is a serious consequence of several types. Urinary lithiasis is third among the causes of chronic kidney disease, accounting for 9.8% of cases **(Knoll, 2007)**. In the previous half-century, the number of cases of urinary lithiasis diagnosed each year in Western countries has nearly tripled. Salt intake increased by a factor of three, while protein consumption increased by a factor of five, as a result of the increase in disposable income **(Davoudi-Kiakalayeh *et al.*, 2017)**. Moreover, calculus has undergone a chemical transformation. While purine-based calculations were the norm at the turn of the 19th century, Oxalocalcium has become more common in the latter part of this century. The epidemiological profile of Moroccan patients' calculations is similar to that of industrialised countries **(Ramello, *et al.*, 2000)** due to the country's shifting dietary patterns between generations. Traditional medicine, which is mostly focused on the usage of plants, has been used by about 80% of the global population for a very long time **(Tabuti *et al.*, 2003)** despite the growing number of patients and the distressing symptoms associated with the disease. For generations, our forefathers acknowledged the virtues of plants. Because of this, they have passed on and expanded our understanding of how to employ medicinal plants to alleviate pain and treat injuries **(Larousse, 2001)**. The use of plants in traditional medicine is widespread even in modern times. Unfortunately, the regulations governing their application aren't always as rigorous as they should be **(Bellakhdar *et al.*, 2019)**. One of the primary assumptions underlying the traditional application of medicinal plants is that, being a natural resource, they can be used therapeutically without causing any adverse side effects. Natural is synonymous in the minds of consumers with harmless **(George, 2011)**. Studies on renal lithiasis in Eastern Morocco are limited and have mostly concentrated on elucidating complex preparations' epidemiology and chemical make-up **(Jamila, 2014)**. However, research into the use of medicinal plants for renal lithiasis treatment is lacking.

Stones occur because of an imbalance in the urine that leads to a decrease in citrate levels. Citrate and magnesium are necessary for healthy kidney function because they prevent stones from forming in the urinary tract and the kidney. A lack of citrate and magnesium inhibitors in the urine may lead to stone formation if this function is hindered **(Bellakhdar *et al.*, 2019)**. Humans face numerous serious health challenges, including a wide range of chronic ailments like heart attack, cancer, Alzheimer's disease, and so on. To make matters worse, patients are experiencing pain and discomfort due to the development of kidney, bladder, urinary system, and etc. stones. This complicated sickness is caused by a confluence of environmental, biochemical, and hereditary variables. This affects both men and women, but it is more prevalent in males than in women, and it is more common in young women. However, the most worrying trend currently is the occurrence of kidney stones in youngsters as young as five years old. Up to 80% of renal stones are caused by calcium oxalate and calcium phosphate, 10% of struvite is magnesium ammonium phosphate, 9% of renal stones are caused by uric acid, and 1% of renal stones are caused by cystine or ammonium acid urate, according to certain research. Kidney stones are most common in adults between the ages of 20 and 30, according to study. Different factors lead to an increased risk of developing and producing kidney stones **(Tabuti *et al.*, 2003)**.

According to the research, Asians have more kidney stone troubles than Africans and Americans. Aside from that, sex has a role in chronic kidney disease, with more males than women developing kidney stones. According to the NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) (NIDDK). The danger of developing kidney stones increases if we pay attention to the fact that it runs in our family. Having a family history of kidney stones, not drinking enough water, salt, glucose, or diet, hyperparathyroidism, high levels of cystine, oxalate, uric acid, or calcium, gastric bypass surgery, anti-seizure medications, and calcium-based antacids are all risk factors. I'd like to know if there are any warning signs or symptoms of kidney stone formation. Small kidney stones can sometimes be eliminated with each urine. Pain while urinating, blood in the urine, sudden and uncontrollable pain in the back or lower abdomen, nausea and vomiting, swelling in the hands or feet, puffy face,

ammonia breath, food that likes to eat like metal, upset stomach, uncertain urination, foamy or bubbly urine, brown, red, or purple urine are all symptoms associated with a larger kidney stone, and the patient should be treated accordingly **(Larousse, 2001)**.

India has been considered to as the medicinal garden of the world. India belongs under the 12 big biodiversity hubs containing 45,000 flora species. Despite the fact that over 20,000 plant species have been identified as having medicinal value in India, only about 800 are actually used by traditional tribes. Today roughly 50% of the population is entirely reliant upon the plant derived goods as a basic health care with no adverse effects. Today medicinal plants are particularly significant for the generation of new medications. People are embracing herbal medications due of its safety, efficacy and reduced adverse effects. Plants and plant materials have exploited with different success to cure and prevent diseases. There is a current, worldwide increase in the demand for items derived from natural plants. The possibilities for the rapid expansion of herbal goods and the importance of medicinal plants to the national economy have been emphasised on numerous occasions (Davoudi-Kiakalayeh et al., 2017).

Past studies on urolithiasis

Sundar Mety et al., (2022) this study aimed to investigate the conventional method of treating and avoiding kidney stones. Existing data suggests that men are more predisposed to developing kidney stones than women are between the ages of 20 and 30, when they affect 12% of the global population. But the most worrying overall trend is that children as young as five are experiencing kidney stones. The result is the formation of a solid called a kidney stone, which is made up of crystals that grow in the kidneys and eventually attract more wastes and chemicals. The size of a kidney stone can range from that of a sand grain to that of a golf ball. While there has been progress in medical technology, the lack of knowledge and experience in treating kidney stones means that their development and spread continue to be a major health problem. Kidney stone sufferers are expected to shell out at least Rs. There is a miracle ethnomedicinal natural herb available to get rid of this illness with no adverse effects if the individual begins using the chemical drug, which also causes multiple side effects and he has to take other tablets to control these negative effects. Perennial Bryophyllum pinnata has been used for centuries in both Western medicine and Ayurvedic medicine to treat a wide range of conditions, including kidney stone pain and removal.

Farah Al-Mamoori, et al., (2019) Kidney stone disease, also called as nephrolithiasis, has been around for a long time and is rather prevalent. Renal stones are a common medical problem that can affect almost anyone at any age. Renal calculi have an alarmingly high prevalence rate, both in men and women. Unfortunately, there is currently no effective medication for treating nephrolithiasis. Compilations of in vivo, in vitro, and clinical trial data suggest medicinal plants may offer an alternative therapeutic approach for the treatment of nephrolithiasis. In this review, we see that medicinal plants have a potentially useful function in both the diagnosis and treatment of kidney stones. Additional investigations are necessary to approve the safety and efficacy of these substances.

Muhammad Akram (2019) with an emphasis on medicinal uses, pharmacological activity, and scientific study, set out to compile a list of some of the most promising and recently developed medicinal plants for the treatment of kidney stones. Kidney stones are a worldwide epidemic that cause significant morbidity and economic expenses. The high cost of kidney stones is primarily attributable to medical expenses. Keywords like "phytotherapy of kidney stones," "medicinal plants employed in kidney stones," and "lithotriptic action of plants" have been used to search for in in vitro and in vivo research on alternative treatment for kidney stones. The lithotriptic potential of medicinal herbs was demonstrated in the studied literature. A number of people have found relief from kidney stones by using medicinal plants. To provide safe, cost-efficient, and effective management choices for kidney stones, and so minimise the burden of disease, this study set out to investigate and expound on the efficacy and availability of alternative therapies. Patients and the healthcare system may both benefit from increased treatment efficiency if it could be achieved at a lower cost. Further randomised clinical trials should be done to investigate the safety and efficacy of therapeutic plants.

Muhammad Akram and Muhammad Idrees (2019) Using an emphasis on medicinal applications, pharmacological activity, and research study set out to examine some of the novel and regularly used medicinal plants in the treatment of kidney stones. Globally, renal stones are a major cause of morbidity and economic expenditures. The large economic burden associated with kidney stones is linked mostly with healthcare costs. Keywords like "phytotherapy of kidney stones," "medicinal plants employed in kidney stones," and "lithotriptic action of plants" have been used to search for in vitro and in vivo studies on alternative treatment for kidney stones. The lithotriptic potential of medicinal herbs was established by the literature. A number of people have found relief from kidney stones by using medicinal plants. To provide safe, cost-efficient, and effective management choices for kidney stones, and so minimise the burden of disease, this study set out to investigate and expound on the efficacy and availability of alternative therapies. Patients and the healthcare system may both benefit from increased treatment efficiency if it could be achieved at a lower cost. More controlled clinical trials involving medicinal plants are needed to determine their safety and effectiveness.

Mina Cheraghi Nirumand et al., (2018) Kidney stones are one of the oldest well-known and widespread disorders in the urinary tract system. Vegetable and fruit rich diets have been linked in several human studies to reduced risk of kidney stones. In this review, we have presented an overview of these dietary plants, their key chemical ingredients, and their putative modes of action. *Camellia sinensis* (green tea), *Rubus idaeus* (raspberry), *Rubia cordifolia* (common madder), *Petroselinum crispum* (parsley), *Punica granatum* (pomegranate), *Pistacia lentiscus* (mastic), *Solanum xanthocarpum* (yellow-fruit nightshade), *Urtica dioica* (stinging nettle), *Dolichos biflorus* (horse gramme), *Ammi visnaga* (khella), *Nigella sativa* (black-cumin), *Hibiscus sabdariffa* (roselle), and *Origanum vulgare* (oregano) have gained widespread interest based on scientific evidence. Phytochemicals such catechin, epicatechin, epigallocatechin-3-gallate, diosmin, rutin, quercetin, hyperoside, and curcumin, which function as antioxidant dietary phyto-phenols, were also found to be useful in preventing urolithiasis in addition to the aforementioned plants (the process of stone formation in the urinary tract). Inhibiting crystallisation, nucleation, and aggregation of crystals, as well as diuretic and antispasmodic action, are the primary mechanisms by which these dietary plants and their separated phytonutrients aid in the management of urolithiasis. This research shows that including plants and phytophenols in your diet can help reduce your risk of developing kidney stones and can help you manage them if you already have them. Further investigations are required to establish the safety and efficacy of these substances.

S. Gupta and S. S. Kanwar (2018) Urolithiasis and kidney stones have not been common in humans for ages. Kidney stones have been on the rise in both rural and urban areas over the past decade, and have a high recurrence rate. The rate and prevalence of urolithiasis has been ascribed to a number of factors such as age, fluid intake, infections of the urinary system, climatic conditions sex, genetic susceptibility, ethnicity as well as food. Surgery to remove or break kidney stones is sometimes necessary because they can cause excruciating pain, a clogged urinary system, hydronephrosis, and serious bleeding. Extracorporeal shock wave lithotripsy (ESWL) and medication therapy are two options for dealing with kidney stones, but their high costs and serious side effects, such as acute renal damage, reduced renal function, and increased stone recurrence, severely limit their utility. As advocated by various in vivo and in vitro investigations and clinical trials, employing phyto-molecules in the treatment and management of kidney stones has emerged as a unique approach. This article discusses the numerous plant options for treating kidney stones, the chemical ingredients involved, and the underlying mechanism of action.

M. Bahmani *et al.*, (2016) when compared to UTIs and prostate pathology, kidney stones are the third most common ailment of the urinary tract. Pain and a complete inability to urinate are two of the possible side effects of kidney stones. The drugs used to treat them often have undesirable side effects. For centuries, people all over the world have turned to medicinal plants as a safe and effective alternative to synthetic pharmaceuticals. The purpose of this research was to identify the local plants utilised by Shiraz's traditional healers to combat kidney stones. The ethno-medicinal data were acquired between July and September 2012 by face-to-face conversation with local herbalist. Eighteen plant species representing nineteen different families were found in the area under study. *Alhagi maurorum* (51.58%), Tribulus terrestris (51.58%), and *Nigella sativa* (51.58%) were mentioned more often than any other species (48.14). Plants' leaves, flowers, and fruits were all used regularly. The majority

of these directions call for decoction (68%). Most of the plants that Shirazian herbalists offer for treating illness have not been studied in animal and humane models of kidney stone, thus this is an exciting new topic for investigation. Finally, if they prove to be safe and effective, they can be transformed into all-natural pharmaceuticals.

Urolithiasis is inhibited by triterpenes

Various pharmacological effects have been attributed to naturally occurring pentacyclic triterpenes derived from plants. Animal studies have shown that the chemical compound lupeol (Lupa-21, 20 (29) dien, 3b-ol) is effective in lowering the risk of stone formation by avoiding crystal-induced tissue damage and diluting the urinary stone-forming ingredients. This study compared the antilithiatic effects of two structurally similar triterpenes, lupeol and betulin (Lupa-20 (29) ene-3, 28 diol. Foreign body implantation approach followed by supplementation of ammonium oxalate was modified to cause stone development in the bladder. The result was a decline in antioxidant capacity and an increase in lipid peroxidation in the kidneys. Crystal-induced renal peroxidative alterations, as assessed by malondialdehyde and subsequent tissue damage, were both well mitigated by both triterpenes. Both the kidney and bladder of stone-forming animals showed dramatically diminished antioxidant status, including both enzymatic and non-enzymatic components. The thiol status and antioxidant enzymes like superoxide dismutase, catalase, and glutathione peroxidase were similarly restored by lupeol and betulin. Calcium oxalate crystal aggregation inhibition and strengthening of the body's defence mechanisms may play a role in the protective effects of the two substances **(Malini *et al.,* 2000)**.

Clinical and pharmacology studies

Some proprietary compositae herbal medications, such as Cystone **(Jehti *et al.,* 1983)**, have also been released in recent years for dissolving renal calculi. (Himalaya Drug Co. Bombay) and Calcuri (Charak Pharmaceuticals Bombay) (Charak Pharmaceuticals Bombay). In India, the usage of these substances is widespread. Both of these herbo-mineral supplements share the plant components Saxifraga ligueata and Tribulus terrestris. Therapy with the herbo-mineral makeup 'Cystone' resulted in the disappearance of ureteric calculi within 55 days **(Muthusamy, 1980)**. Cystone's high concentration of naturally occurring mineral salts makes it an effective diuretic by soothing the detrusor muscles. Other indigenous herbo-mineral drug calculi (2 TDS) in 40 cases of ureteric calculi, revealed transit of disintegrated or intact stones through urine in 25 (62.85%) cases **(Yadav *et al.,* 1981)**. Cystone has also been proven to be beneficial in urolithiasis, crystalluria, and urinary tract infection. Pharmacologically, Berginia ligulata has showed no impact in preventing the stone development but was proven useful in dissolving zinc calculi in the urinary bladder in experimental rats **(Seth *et al.,* 1974)**. The experimental rates of stone deposition were reduced by using Varuna, Ghokhru, and Kulatha. Varuva and kulatha were ineffective against oxalate (Vataj) and uric acid (Pitiaj) stones. Urate and cystine stones can be partially broken down by drinking gokhru decoctions.

Kaphaj (phosphetic) stones were dissolving in all the three medications. Stones become friable and dissolve significantly when exposed to kulatha **(Kumar *et al.,* 1981)**. Many of the herbal concoctions recorded in Ayurvedic texts centre on kulatha. Charak, Sushruta, and other authorities refer to it as an Ashmarighana (Destroyer of stone). Sushruta cites its efficiency in vataj ashmari with the features of oxalate stone. According to clinical studies, 9 out of 15 individuals with urinary calculi passed their stones within 8-10 days of treatment with Dolichos biflorus. Spontaneous transit of stones was prevalent depending upon the size, location and mobility of the calculus **(Singh and Kumar 1973)**; **(Havagiray *et al.,* 2010)**.

Mechanism of action of phytotherapeutic agents:

- Benefits renal function by correcting the crystalloid-colloid imbalance: Colloids (mucin and sulphuric acid) in urine keep a variety of crystalloids (oxalate, uric acid, calcium, and cystine) in solution while they are absorbed. Renal stones arise when there is an elevation in crystalloids and a decrease in colloid levels, or when the colloid loses its solvent action or adhesive characteristic, both of which can lead to the production of urinary stones. Ethylene glycol-induced urolithic rats had an elevation in urine phosphorus excretion. Stone formers have been shown to excrete more phosphorus than average **(Soundararajan *et al.*, 2016)**. Increased urinary phosphorus excretion and oxalate stress appear to create a favourable environment for stone formation by inducing calcium oxalate deposition epitaxially through the production of calcium phosphate crystals. Both people prone to developing kidney stones and rats with a genetic disorder called hyperoxaluria have been shown to excrete more uric acid than usual. When calcium oxalate is dissolved in uric acid, the inhibitory effect of GAGS is diminished and calcium oxalate becomes insoluble. Because uric acid crystals are so much more common in calcium oxalate stones, and because uric acid binding proteins can bind to calcium oxalate and control its crystallisation, uric acid appears to play a central role in stone formation. When these colloids in urine reach a supersaturation level, they precipitate as crystal initiation particles, which, once caught, serve as a nidus for further crystal formation. By lowering the excretion of urinary calcium, oxalate, uric acid, phosphorus, and protein, the polyherbal formulation Cystone **(Karadi *et al.*, (2006)** helps maintain crystalloid-colloid equilibrium in urolithiasis.

- Renal Improvement: When the urinary tract is blocked by stones, a condition known as urolithiasis, waste products, especially nitrogenous chemicals such urea, creatinine, and uric acid, build in the blood **(Ghodkar *et al.*, 1994)**. Elevated urea and creatinine output are two of the ways in which herbal therapy boosts renal function. In fact, this mechanism accounts for the vast majority of the antiurolithiatic impact of phytothereupatic agents. Moringa oleifera and *Rubia cordifolia* considerably lower serum levels of accumulated waste products BUN and creatinine is attributable to the improved GFR **(Divakar *et al.*, 2010)**.

- Hyperoxaluria is a major contributor to the development of renal stones, so it's important to keep oxalate metabolism under control. Some studies have shown that oxalate has a 15-fold larger influence on stone formation than urine calcium. CaOx crystals precipitate and accumulate due to a high oxalate content. *Tribulus terrestris* aqueous extract disrupts oxalate metabolism in male rats given sodium glycolate. Hyperoxaluria, elevated liver oxalate synthesising enzyme activities (glycolate oxidase [GAO], glycolate dehydrogenase [GAD], and lactate dehydrogenase [LDH]), and decreased kidney LDH activity were all the results of a diet high in glucose. When *T. terrestris* was given to rats that had been fed sodium glycolate, the animals' urinary oxalate excretion decreased and their urine glyoxylate excretion increased, in comparison to rats who had been fed sodium glycolate alone **(Sangeeta *et al.*, 1994)**.

- Some herbal medicines have an antilithogenic effect, and this is in part due to their antibacterial qualities. Important risk factors in the development of urinary stone disease include a lack of the crystallisation inhibitory impact of urine and the presence of promoters. The anti-adherent layer of GAGS provides protection from urinary stone disease when environmental factors like these promote stone development. As a result of bacterial infection, if this layer is compromised, a stone nucleus can form, and eventually a whole stone can form in the urinary system. Since the anti-adherent glycosaminoglycan layer covering the epithelium of the collecting system is protected by several extracts that display antibacterial activities, these extracts are now considered antilithogenic **(Sellaturay *et al.*, 2008)**. Infections (DTIs) are a common complication of renal stones. Matrix, a non-crystalline substance, can also be found in kidney stones. When there is also a urinary tract infection present, the matrix percentage of a stone can rise to as high as 65% by weight. Changes in renal enzyme output (less urokinase and more sialidase) may promote matrix formation, it has been hypothesised. Matrix formation, triggered by bacteria like Proteus mirabilis and Escherichia coli, increases crystal adherence to the renal epithelium. Besides treating urolithiasis, Cystone has been shown to be beneficial in treating urinary tract infections and infective stones **(Kumaran *et al.*, 2007)**.

- Active Ingredients with Pain-Relieving and Inflammatory-Suppressing Properties Patients with renal or ureteric colic due to an obstructing stone often report with acute loin pain that comes on suddenly, most frequently during the night when urine concentration is at its highest. The onset of renal colic might be rapid or more gradual.

When the agony reaches a critical point, the patient often thrashes around rather than can't get comfortable **(Leye *et al.*, 2007)**. In a clinical investigation, individuals treated with Cystone experienced a considerable symptomatic alleviation from abdominal pain and dysuria. From the beginning of treatment to the finish, the average number of pain episodes decreased dramatically. In studies with rabbits and guinea pigs, cysteine showed promising spasmolytic action **(Phukan, 1977)**. Urolithiasis patients can benefit from the anti-inflammatory properties of Solidago virgaurea and Phyllanthus niruri **(Melzig *et al.*, 2004)**.

Traditional Medicine In Renal Lithiasis: A Therapeutic Answer

For as long as there have been humans, people have turned to plants for healing when they had no other options. Legends, pictographs, and numerous monographs have carried this information down to the present day **(Rodrguez *et al.*, 2015)**. A Sumerian clay slab from Nagpur, dating back around 5,000 years, contains the earliest known written record of the use of medicinal herbs in the production of medications. Connections can also be found in "The Ebers Papyrus," which dates back to around 1550 B.C., "The Indian holy texts Vedas," and "The Chinese book on roots and grasses," written around 2500 B.C. by Emperor Shen Nung **(Petrovska, 2012)**. Eighty percent of the world's population relies on plants for medical treatment, according to WHO statistics **(Escalona *et al.*, 2015)**. To the contrary, it is well-documented **(Majouli *et al.*, 2017)** that between twenty and thirty percent of commercially marketed medicines are created using ingredients found in nature.

Several multi-national corporations have benefited to the tune of $ 7.00 billion in Europe, $ 3.2 billion in the United States, and $ 2.3 billion in Asia thanks to the growing popularity of medical plant use and commercialization. This growth can be attributed to a number of factors: an interest in alternative therapies; a preference for preventative care as a result of an ageing population; and the widespread belief that herbal drugs have no side effects.

Opportunities exist in the study of herbal medicines as therapeutic alternatives for a number of diseases, particularly in cases where conventional medicine has not been very effective. This is due to the widespread acceptance of herbal medicine among the population, the wealth of traditional knowledge about medicinal plants, the small number of scientific studies supporting the therapeutic properties of these, and the interest of the pharmaceutical industry in the development of phytopharmaceuticals. Herbal remedies, on the other hand, frequently include multiple pharmacologically active substances. Synergistic effects between herbs have the potential to outperform those of synthetic medications in the treatment of certain disorders, making this a useful quality for the therapeutic use of herbal medicine. Because minimal access surgery and pharmacological therapy are the standard of care for renal lithiasis, numerous studies have looked to herbal medicine as an alternative. For herbal therapy to be taken seriously, scientific research must confirm the traditional knowledge of medicinal plants, which serves as the initial clinical evidence for the treatment's effectiveness. There has been a recent publication of a catalogue of antilithiatic plants utilised by people all around the world; so far, scientists have identified 500 species from 106 families. Based on sample size, the most well-represented families in this research were the Asteraceae (87), Fabaceae (71), Lamiaceae (58), Rubiaceae (17), Solanaceae (12), Phyllanthaceae (9), Zingiberaceae (9), Rutaceae (9), Polygonaceae (8), and Urticaceae (8) **(Ahmed *et al.*, 2017)**. Rosaceae (41 species), Poaceae (24), Malvaceae (23), Brassicaceae (20), and Boraginaceae (10 species) were also recorded (13). Studies using herbal medicine for lithiasis have a better likelihood of success due to the widespread ancient traditions of antilithiatic herbs.

Discussion

Due to its widespread prevalence and the absence of effective pharmaceutical therapies, renal lithiasis is a major global kidney issue. To now, there is just one method for eliminating renal calculi, and that is minimally extensive surgery. As a result, medicinal plants have risen to prominence in the realm of medicine as scientists continue

their pursuit of better therapeutic options. The absence of scientific investigations, particularly clinical studies, supporting the medicinal capabilities of plants has restricted their therapeutic application, notwithstanding their extensive usage in traditional medicine. However, Newman and Cragg (2016) found that half of all approved medications between 1981 and 2014 have their pharmacological basis in natural ingredients **(Newman *et al.*, 2016)**. Though this data demonstrates that plants are a useful tool in the treatment of ailments, further research is needed to back up their use in therapeutics; this is a limitation of herbal medicine's clinical applicability. Plants traditionally used to treat renal lithiasis have shown promise in *in vitro*, *in vivo*, and clinical trials, however these studies have not been backed up by adequate phytochemical analysis. Therefore, the investigations' generalizability is constrained because of the lack of phytochemical characterisation, which makes quality control challenging and replication of results dubious. Available data suggests that plant extracts may have diuretic, antioxidant, or antibacterial properties; increase the excretion of urine citrate; decrease the excretion of urinary calcium and oxalate; and prevent the crystallisation of oxalate calcium **(Butterweck, 2009)**. In conclusion, there is evidence to suggest that plants may be an effective therapeutic resource for the treatment of renal lithiasis, including universal popularity of natural products, pharmaceutical industry interest in developing these, traditional knowledge of a wide range of plants for the treatment of lithiasis, and promising results from scientific studies.

Conclusion

This review shows that several therapeutic herbs are tested using different experimental models of urolithiasis, with a focus on calcium oxalate and magnesium ammonium phosphate kidney stones. The majority of these investigations were exploratory in nature and were conducted on animals, neither of which are suitable for the creation of a pharmaceutical. There is still a need for extensive preclinical and clinical studies to assess the efficacy and safety of these plant products. In addition, the plants' active ingredients must be isolated and researched through chemical experiments in search of a promising Lead molecule. Surgical techniques and extra corporeal shock wave Lithotripsy are being used often in the management of urinary stones. The most significant downside of these methods is that stones tend to return. Natural products are a possible source of bioactive molecules for this ailment, and their increased incidence and prevalence, as well as the lack of a suitable pharmacological therapy for their treatment, have drawn the attention of various researchers.

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Table 1: Plants Historically Employed in the Therapy of Urolithiasis

Phytotherapeutic agent	**Type of study**	**Mechanism of action**
Herniaria hirsute	*in vitro*, cell culture, *in vivo*	Decrease crystal size & rise COD, diuretic
Amni visnaga	*in vivo* animals, cell culture	Potent diuretic, khellin & visnagin prevent renal epithelial celldamage caused by oxalate & COM
Tribulus terrestris	*in vitro*, cell culture, *in vivo* animals	COM, Decrease oxalate
Bergenia ligulata	*In vitro, in vivo* animals	COM, Decreases calcium
Dolichos	*In vitro*	oxalate crystals

biflorus		
Aerva lanata	*in vivo* animals	Decrease crystal ppt
Vediuppu chunnam	*in vivo* animals	Decrease urinary calcium oxalate, uric acid & Diuretic
Raphanus sativus	*in vivo* animals	Diuretic
Achyranthus Aspera	*In vitro*, cell culture, animals *in vivo*	Prevent renal epithelial damage, Diuretic
Quercus salicina	cell culture	Reduction in oxalate induced renal epithelial cell injury
Phyllanthus niruri	*In vitro, in vivo* animals	Antispasmodic & relaxant
Cranberry juice	Humans *in vivo*	Decrease urinary oxalates
Cynodon dactylon	*In vivo* animals	Rise COD as contrast to COM
Grapefruit juice	Humans *in vivo*	Rises urinary excretion
Paronychia argentea	*In vivo* animals	Antioxidant activity
Lemonade juice	Humans *in vivo*	Increases urinary excretion
Pyracantha crenulated	*In vivo* animals	Increase diuresis and lowering of urinary conc. of stone forming constituents
Trachyspermum ammi	*In vivo* animals	Maintain renal functioning; Reduce renal injury and decrease crystal excretion in urine and retention in renal tissues
Moringa oliefera	*In vivo* animals	Diuretic, improved renal function
Costus spiralis	Animals *in vivo*	Decrease stone size