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Review

Medicinal plants in the treatment of urolithiasis: A review

[Plantas medicinales en el tratamiento de la litiasis urinaria: Una revisión]

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Abstract

Context: Urolithiasis is recognized globally as the second most burdensome renal disorder, imposing significant costs on healthcare systems.

Aims: To analyze scientific research on medicinal plants that demonstrate potential effects in the treatment of urolithiasis.

Methods: Articles that described preparation methods, plant organs used, and phytoconstituents and essential oils responsible for anti-urolithiatic activity were highlighted. Articles were extracted from Google Scholar, Science Direct, and PubMed using specific keywords.

Results: A total of 81 articles were selected. All plant organs provided anti-urolithiatic extracts, with leaves contributing 22%, followed by whole plant (17%), seeds (14%), fruits (11%), flowers (8%), aerial parts (7%), barks (4%), rhizomes (4%), and stems (3%). Cold extraction methods were used in 55% of articles, while hot methods were used in 45%. Phenolic and polyphenolic compounds were predominant, particularly flavonoids (25%); in addition to saponin glycosides (18%), alkaloids (11%), and others. Hydro-alcohols were the most utilized solvents, indicating that many polar compounds are readily soluble in urine. This suggests a potential mechanism for their action in the eradication or prevention of kidney stones.

Conclusions: Further research on synergistic formulations of these constituents and their pharmacokinetic and pharmacodynamic profiles is recommended. Extensive research is required to examine the ability of essential oils in the eradication of kidney stones, especially those with high simple phenolic and hydroxyl content. Various active phytochemical groups necessitate various modes of action, emphasizing the unique properties of medicinal plants in drug discovery and development.

Keywords: anti-urolithiatic activity; essential oils; extraction methods; kidney stones; nephrolithiasis; phytochemicals; plant organs.

Resumen

Contexto: La litiasis urinaria se reconoce a nivel mundial como la segunda enfermedad renal más grave, lo que supone un coste significativo para los sistemas sanitarios.

Objetivos: Analizar la investigación científica sobre plantas medicinales que demuestran posibles efectos en el tratamiento de la litiasis urinaria.

Métodos: Se seleccionaron artículos que describían los métodos de preparación, los órganos vegetales utilizados y los fitoconstituyentes y aceites esenciales responsables de la actividad antiurolitiasis. Los artículos se extrajeron de Google Académico, Science Direct y PubMed mediante palabras clave específicas.

Resultados: Se seleccionaron 81 artículos. Todos los órganos vegetales aportaron extractos antiurolitiasis: las hojas contribuyeron con un 22%, seguidas de la planta entera (17%), las semillas (14%), los frutos (11%), las flores (8%), las partes aéreas (7%), la corteza (4%), los rizomas (4%) y los tallos (3%). El 55% de los artículos utilizaron métodos de extracción en frío, mientras que el 45% los utilizaron en caliente. Predominaron los compuestos fenólicos y polifenólicos, en particular los flavonoides (25%), además de los glucósidos de saponina (18%), los alcaloides (11%) y otros. Los hidroalcoholes fueron los disolventes más utilizados, lo que indica que muchos compuestos polares son fácilmente solubles en la orina. Esto sugiere un posible mecanismo de acción para la erradicación o prevención de cálculos renales.

Conclusiones: Se recomienda realizar más investigaciones sobre formulaciones sinérgicas de estos componentes y sus perfiles farmacocinéticos y farmacodinámicos. Se requiere una investigación exhaustiva para estudiar la capacidad de los aceites esenciales para eliminar las piedras en los riñones, especialmente aquellos con alto contenido de compuestos fenólicos y grupos hidroxilo. Diversos grupos fitoquímicos activos requieren diversos mecanismos de acción, lo que resalta las propiedades únicas de las plantas medicinales en el descubrimiento y desarrollo de fármacos.

Palabras Clave: actividad antiurolitíaca; aceites esenciales; cálculos renales; fitoquímicos; métodos de extracción; nefrolitiasis; órganos vegetales.

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INTRODUCTION

Kidney stone disease (also known as urolithiasis) is a renal disorder characterized by the presence of stone deposits (or crystals) within the renal system. If untreated, it may cause renal failure. Globally, it was considered the second most burdensome renal disease in 2014, with an estimated cost of approximately 5 billion USD at that time. Many factors may contribute to its incidence, these factors are age, genetics, sex, diet, climate, and lifestyle (Akram et al., 2024).

Various treatments guidelines are used in prevention and eradication of kidney stones, for example, thiazide diuretics are commonly used in prevention of calcium oxalate and calcium phosphate types of kidney's stones, despite the unclear data which needs further clinical studies, the reduction of urine calcium level contributes in the role of thiazides in reducing recurrent kidney calculus formation (Hsi et al., 2024). Potassium citrate is used for alkalinization of the pH of urine, and hence, it is useful in eradicating a kidney's stone condition known as renal tubular acidosis, and causes protection against calcium phosphate stones via enhancing the excretion of citrate in the urine, also it is useful in treatment of uric acid renal stones associated with gout patients, but the main trouble with potassium citrate is the urine's pH should be extremely monitored, because high alkaline urine's pH causes calcium phosphate saturation, and this will negate the beneficial effects of potassium citrate. Calcium channel blockers and prednisolone are sometimes used to facilitate ureteral stone passage, but they are not currently recommended in treatment guidelines. Tamsulosin (an alpha-blocker agent) has successfully shown facilitation in the passage of ureteral stones, but the drug is mainly given to patients with prostate hypertrophy. The crystals of cystine stones are very rare disorder, it is a genetic disorder which affects patients suffering from kidney stones, cystinuria patients are at high risk as these crystals may get stuck in the kidneys, ureters and/or bladder in acidic urine, so tiopronin (a thiol agent) and *d*-penicillamine are used to reduce the concentration of free cystine, alkalinize the urine and hence they increase cystine's solubility in the urine (Aggarwal et al., 2017; Barnela et al., 2012).

Pharmacological therapy is recommended if the diameter of the kidney stones is less than 10 mm, but non-pharmacological therapy (such as surgical procedures) is used if the diameter of the kidney stones is greater than 10 mm. Generally, the scientific evidence for pharmacological therapy is less convincing, and it often fails to prevent new kidney stone formation due to incomplete stone clearance. These facts collectively suggest that we require new, effective pharmacological therapeutic strategies for the comprehensive treatment of kidney stones (González et al., 2020; Rule et al., 2020).

Herbal and medicinal plants are primary sources for providing us with numerous natural lead compounds and effective extracts in the treatment of various diseases, including kidney stone disorders. Khellin is a natural chromone compound isolated from *Ammi visnaga* (*Apiaceae*), which exhibits spasmolytic, muscle-relaxant, and vasodilator properties, all of which contribute to its potent dissolution of kidney stones. Therefore, medicinal plants have become an important source for discovering new compounds (or extracts) in the treatment of kidney stones, because many of these plants have polyvalent actions in reducing colic pains, preventing lithogenesis, removing stones from the kidney, and are commonly used for the treatment of kidney stones like calcium oxalate, uric acid, struvite, and cysteine (Akram and Idrees, 2019; Vaitheeswari et al., 2015). Many studies have demonstrated the efficacy of medicinal plant extracts and their isolated compounds in treating kidney and urinary tract disorders; some of these compounds act as diuretics and exhibit anti-inflammatory properties (Lu et al., 2024; Mansoor et al., 2019).

Many previous systematic reviews had reflected the importance of medicinal plants in the treatment of urolithiasis. Allam and Sabra (2024) had reviewed many related articles (PubMed/Medline) between January 2021 till December 2023, they found that most studies used ethylene glycol to induce hyperoxaluria and nephrolithiasis (*in vivo*), also they observed that different extraction methods were applied to extract various active constituents. The study recommended studying the mechanisms of action of these active extracts. Another study was carried out by Khan et al. (2021). The study made the same observations and recommended that approximately 10% of the studies had tested the antioxidant and diuretic activities of the herbs, attributing the anti-urolithiatic activity to the antioxidant, anti-inflammatory, and/or diuretic effects of the treatments. In this review, the following research question was answered: What is the significance of isolated active compounds and essential oils from medicinal plants in the treatment of urolithiasis, and how do different plant organs, extraction methods, and phytochemical classifications influence their efficacy? This review expands on previous studies about the use of medicinal plants for treating urolithiasis. Unlike prior reviews that focused only on plant extracts and fractions, this one also includes isolated active compounds and essential oils. We analyzed all relevant research articles from various sources, such as Google Scholar, to emphasize the specific plant organs used, the extraction methods, and the phytochemical classification of

the active extracts, fractions, isolated compounds, and essential oils

Hence, the objectives of this review are to collect and analyze all scientific researches done on medicinal plants (isolated compounds, essential oils and extracts or fractions) which showed promising effects in prevention or eradication of kidneys' stones in unlimited time by using Google Scholar, Science Direct and PubMed websites; we will try to shed light on articles which described the methods of preparation of those plants, parts of plants used and (if available) the phytoconstituents responsible for the activity. This is a small attempt on our part to collect all active medicinal and herbal plants, which will assist future researchers in searching for important plants and accomplishing bioassay-guided isolation and characterization of active compounds. According to our knowledge, this is the first time that reviews the role of medicinal plants in the prevention and treatment of urolithiasis, according to our stated objectives.

MATERIAL AND METHODS

Review methodology

This systematic review was conducted by following the PRISMA 2020 protocol according to Page et al. (2021).

Formulation of research question

The research questions were developed according to PICO's guidelines (Population, Intervention, Comparison, and Outcomes). The app.bigdata.com tool was utilized for information synthesis. Additionally, this tool and Rayyan.ai were used to assess the eligibility of the included scientific articles, and this process was also conducted manually and independently by several co-authors. The authors came out with the following construction, patients with urolithiasis are the population; treatment with isolated active compounds, or treatment with essential oils derived from medicinal plants, plants organs used, and method of extraction are the interventions; different extraction methods, various plant organs and different phytochemical groups are the comparison; effectiveness in treating urolithiasis, effectiveness of bioactive compounds and essential oils, and anti-urolithiatic activity of extracts and fractions, are the outcomes. These PICO's guidelines assisted the authors in formulating the research question: What is the significance of isolated active compounds and essential oils from medicinal plants in the treatment of urolithiasis, and how do different plant organs, extraction methods, and phytochemical classifications influence their efficacy?

Eligibility criteria

To address the research question, the authors collected all relevant research articles that mentioned the elements outlined in the research question, with no restrictions on publication dates and limited to articles published in English only. Conference abstracts were also included. However, some collected articles were deemed ineligible and excluded due to the absence of reported outcomes, specifically regarding the plant organ used and/or the method of preparation and extraction.

Information sources

The data was collected during the period from July 2024 to October 2024. The authors utilized three successive databases for data collection, namely Google Scholar, ScienceDirect, and PubMed websites.

Search strategy

Identification

First, the authors initiated their search strategy using Google Scholar. Next, they searched the Science Direct library, followed by a search in the PubMed database. The selected authors for data extraction worked independently; however, before moving to the next database, each author provided their colleague with complete information. Each step was validated by another author to minimize bias and ensure that no relevant articles were excluded. After searching Google Scholar, all irrelevant articles were excluded. Subsequently, irrelevant and duplicate articles obtained from Google Scholar were removed after searching the Science Direct database. Finally, all irrelevant and duplicate articles from both Google Scholar and Science Direct were excluded after searching the PubMed library. A brief searching strategy is shown in (Fig. 1). In order to minimize the risk of bias, the Rayyan.ai and app.bigdata.com tools were utilized to assess the eligibility of each included research article according to PICO's guidelines.

The identification process was initiated by developing the keywords, which were specified according to the research question and were applied in the search engines of the mentioned websites. The keywords used in the search engine were ["Plants" AND "kidney stones"], ["Plants" AND "Urolithiasis"], ["Volatile OR essential oil" AND "kidney stones"], ["Volatile OR essential oil" AND "Urolithiasis"], ["Phytochemical compound" AND "kidney stones"] and ["Phytochemical compound" AND "Urolithiasis"].

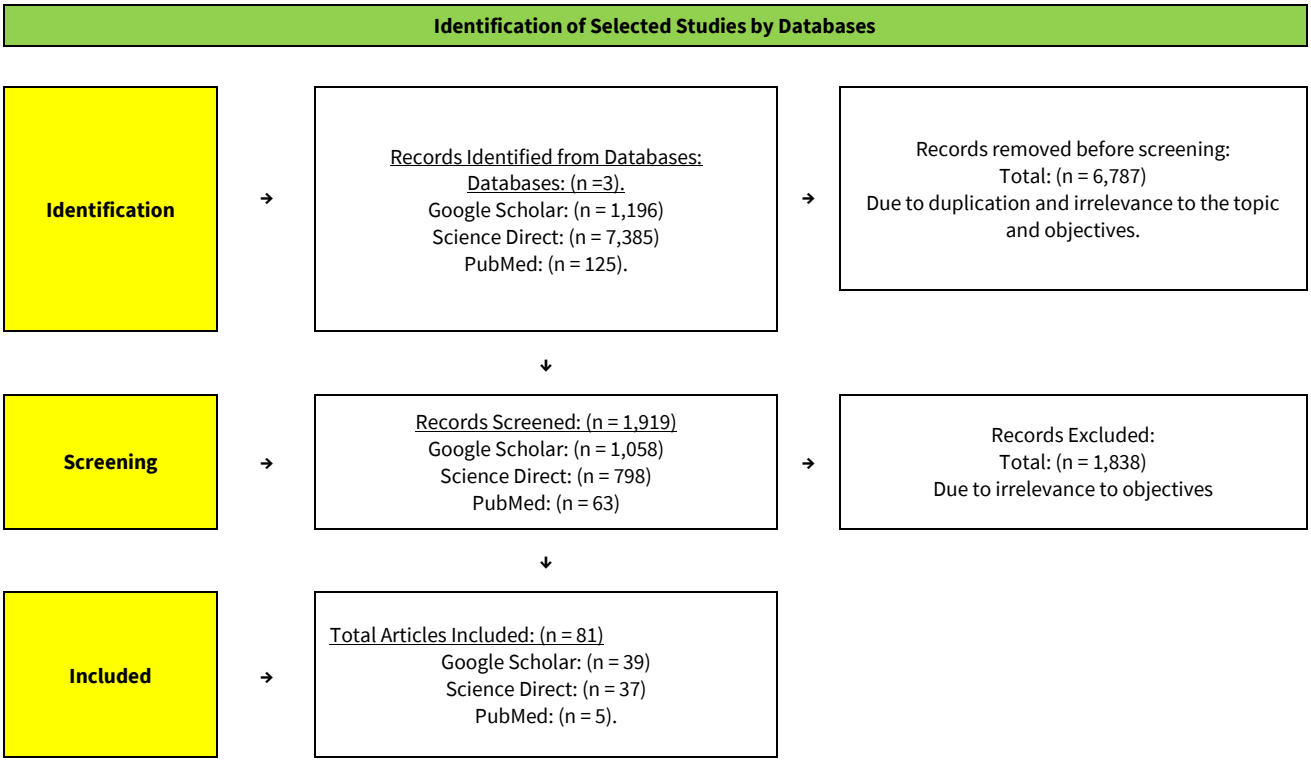

Figure 1. PRISMA flow chart.

Google Scholar and Science Direct provided the most articles in this review. Science Direct and PubMed websites have the advantage of providing the most cited articles. Google Scholar was selected because it provides comprehensive coverage in various fields and categories (including anti-urolithiatic activity of medicinal plants). However, its impact is slightly inferior due to the inclusion of some lower-quality citing articles. However, our stated outcomes, combined with the use of other websites (i.e., ScienceDirect and PubMed), provided us with many qualified articles.

Screening

The screening process involved all the articles obtained from the mentioned websites. The screening process was conducted manually, involving the reading of titles, abstracts, methods, conclusions, and occasionally the entire article, to determine whether an article should be included or excluded from this review. All selected articles, after the screening process, were downloaded and saved in a folder.

Eligibility

The next step of the research strategy is to check the eligibility of the collected articles. Again, the saved articles were double-checked to exclude untargeted and duplicated articles. A manual process was conducted to check and extract the outcomes mentioned in our research questions. Rayyan.ai and app.bigdata.com were utilized to reduce the risk of bias. The extracted information was summarized in either paragraph form or in a tabulated format (Table 1). Any article that was not within the scope and aims of the review was excluded.

Selection process

The selection process was initiated by three authors who worked independently on the chosen websites using the agreed-upon keywords. They began collecting articles from Google Scholar, followed by ScienceDirect, and then from PubMed. They then convened to review their findings on the collected articles. Any article that did not meet the eligibility criteria was excluded. In total, 39 filtered articles were obtained from Google Scholar, 37 from Science Direct, and an additional five articles were filtered from the PubMed website.

Data collection process

Data extraction was performed independently by three authors and validated by another three reviewers. The extraction form captured all medicinal plants with active isolated compounds or essential oils having anti-urolithiatic activity, as well as active extracts and fractions. Any discrepancies were resolved through discussion or consultation between all authors. Finally, the filtered articles contain the interventions and the outcomes of our review, i.e., part of the plant organ used, method of extraction, phytochemical groups of the active isolated compounds, effectiveness

of isolated compounds as anti-urolithiatic activity, effectiveness of essential oils as anti-urolithiatic activity, and effectiveness of extracts and fractions as anti-urolithiatic activity.

Data items

A set of information was gathered after the data collection phase achieved its objectives. Plant-specific details were collected, including species identification, taxonomic classification, the plant organ used, extraction and preparation methods, the phytochemical classification of the isolated active compounds, and the composition of essential oils. Additionally, the types of active extracts and/or fractions were considered important data points. Treatment parameters were documented, including the dosage and concentration of the plant extracts, fractions, compounds, or essential oils. If available, information such as the duration of treatment, route of administration, and control interventions was also recorded. Outcome measures focused on changes in urinary parameters (such as volume, pH, calcium, oxalate, and uric acid), stone characteristics (including size, density, solubility, and surface area), biochemical markers (e.g., creatinine, urea, and oxidative stress), and histopathological findings. Additionally, study design characteristics, such as sample size, *in vivo* models, *in vitro* experiments, participant demographics, and follow-up duration, were extracted from the collected articles. Finally, the potential therapeutic mechanisms of plant-derived treatments, including anti-urolithiatic properties, inhibition of crystal formation, diuretic effects, antioxidant properties, and anti-inflammatory activities, were also documented.

Study risk of bias assessment

The risk of bias of the included studies was independently assessed by two authors using the Critical Appraisal Skills Programme (CASP) checklist (Critical Appraisal Skills Programme, 2018). This tool assesses key domains, including the validity of the results, clarity of the findings, and the adequacy of the discussion surrounding the results. Each domain was rated as having a "yes," "no," or "cannot tell" risk of bias. By answering the 10 provided questions (Table S1), each study received a score out of 10, where a low score indicates a high risk of bias and a high score indicates a low risk of bias. Disagreements between the authors were resolved through discussion. The overall risk of bias for all included studies was calculated based on the average score of each study, with a low score indicating a high risk of bias and a high score indicating a low risk of bias.

Synthesis methods

The data were organized in a Microsoft Excel file, with categories refined through thorough discussions among the authors. The collected information was cleaned and clarified to facilitate systematic analysis. The synthesis involved tabulation and grouping techniques to summarize and clarify data extracted from included studies. The table was structured to record the key information obtained from each included study. Consequently, the studies were grouped based on plant species and taxonomic classification, plant organs utilized, extraction and preparation methods, phytochemical classifications, and descriptions of treatment outcomes, specifically anti-urolithiatic activity. Visual representations, in the form of pie charts, were employed to examine patterns and relationships in the extracted data, primarily as percentages of the total number of scientific articles included. This approach enabled the identification of common patterns and discrepancies among the included studies while preserving the contextual validity of the results.

Reporting bias assessment

As mentioned in the "Study Risk of Bias Assessment" section, this review utilized the Critical Appraisal Skills Programme (CASP, 2018) checklist, which contains 10 questions. The bias assessment was reported as a score ranging from 1 to 10, where a "yes" response received +1 point, a "no" response received -1 point, and a "can't tell" response received 0 points. The score for each included study was calculated, and the average score of all included studies was also determined. Consequently, a low score indicates a high risk of bias, while a high score indicates a low risk of bias.

RESULTS

Study selection

Flow of the studies

The total number of articles obtained was 8,706 after applying the specified keywords in the search engine. Specifically, 1,196 articles were retrieved from Google Scholar, 7,385 from ScienceDirect, and 125 from PubMed. The articles obtained after using "volatile oil" as a keyword were 399, 2,966, and 25 articles from Google Scholar, Science Direct, and PubMed, respectively. The articles obtained after using "phytochemical compound" as a keyword were 70, 106, and zero articles from Google Scholar, Science Direct, and PubMed, respectively.

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones.

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Aegle marmelos (L.) Corrêa (*Rutaceae*)	Flowers	Maceration/ ethanol and hexane. Decoction/ aqueous. All extracts were dissolved in DMSO for the biological test	The extracts were examined *in vitro*. The synthetic urine contains calcium oxalate (prepared by adding calcium chloride and sodium oxalate together). Ethanolic and hexane extracts showed better inhibition at 1,000 µg/mL in terms of calcium oxalate crystal nucleation; the aqueous extract showed better inhibition of crystal aggregation and growth. Phytochemically, the plant was found to contain reducing sugars, proteins, anthracene glycosides, and saponins.	(Hewagama and Hewawasam , 2022)
Aerva lanata (L.) Juss. ex Schult. (*Amaranthaceae*)	Flowers	Percolation/ ethyl acetate	The extract was examined *in vitro* in a prepared calcium oxalate solution, and good dissolution of calcium oxalate was detected. Flavonoids and tannins were detected by HPLC. The study suggested the anti-urolithiatic activity may be due to these constituents.	(Kaviraj et al., 2022)
Aerva lanata (L.) Juss. ex Schult. (*Amaranthaceae*)	Whole plant	Quercetin and betulin (Fig. 2) were isolated from ethyl acetate and *n*-butanol fractions of the hydro-alcoholic extract	The two isolated compounds were examined *in vivo* in rats. The calcium oxalate crystals were induced by 0.75% ethylene glycol. At a dose of 2 mg/kg body weight/day for 28 days, the results showed an increase in urine volume. Additionally, a reduction in the size of renal calculi and an increase in the excretion of calcium and phosphate were detected. Blood urea nitrogen and creatinine levels decreased after serum analysis, and a noticeable reduction in calculi size was observed.	(Dinnimath et al., 2017)
Allium jesdianum Boiss. & Buhse (*Amaryllidaceae*)	Aerial parts	Hydro-ethanolic extract, in which 3 phenolic compounds and 2 steroidal compounds had been identified	The hydro-alcoholic extract was examined *in vitro* and showed remarkable inhibition of crystal growth and a decrease in particle size, especially at a dose of 32 mg/mL. Phytochemical detection revealed that the extract contains phenolic compounds, which have the ability to eradicate calculi through a scavenging process.	(Mahan et al., 2024)
Allium noeoanum Reut. ex Regel (*Amaryllidaceae*)	Aerial parts	Maceration/ ethanol 70%	The extract and the isolated flavonoidal compound by TLC were detected in Wistar rats in which the kidney stones were induced by 1% ethylene glycol; the results showed a reduction in the number of oxalates, urinary calcium, and citrates (especially the flavonoidal compound).	(Goudarzi et al., 2021)
Allium schoenoprasum L. (*Amaryllidaceae*)	Leaves	Maceration/ ethanol and acetyl acetate	The total phenolic and flavonoids contents were detected, the ethanolic extract showed high total phenolic content (111.28±1.29 mg/g extract), while ethyl acetate extract showed high flavonoids content (34.64±1.60 mg/g extract) and high antioxidant activity; both extracts showed anti-lithogenesis activity (*in vitro* incubation of kidney stones in atomic absorption spectroscopy at 37°C for 6 hours) with 2.5% concentration of ethyl acetate extract, as it gives 95.55% solubility of calcium oxalate.	(Sinaga et al., 2018)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Ammi visnaga (L.) Lam. (*Apiaceae*) (This name is a synonym of *Visnaga daucoides* Gaertn.) Two types: Turkish and Egyptian.	Seeds	Hot infusion/ aqueous	Both types of khella extracts (Egyptian and Turkish khella) prolonged the induction time of calcium oxalate, thereby affecting the formation of crystals. They also affected the crystal's morphology of calcium oxide monohydrate to the dihydrate form, which is less harmful. The Turkish Khella showed better results in inhibiting calcium oxalate monohydrate, which is attributed to the presence of khellin and visnagin (Fig. 2), not found in the Egyptian khella.	(Abdel-Aal et al., 2009)
Anneslea fragrans Walls. (*Pentaphylacaceae*)	Leaves	Continuous extraction method/ methanol	The extract exhibited significant in vitro anti-urolithiatic activity, as evidenced by changes in turbidity in artificial urine, as well as nucleation and aggregation assays, with maximum percentage inhibition at 1,000 µg/mL (78.1%, 32.32%, and 57.11%, respectively).	(Kumar, 2022)
Aquilaria malaccensis Benth. (*Thymelaeaceae*) [This name is a synonym of *Aquilaria sinensis* (Lour.) Spreng.]	Whole plant	Decoction/ aqueous	The extract was examined using an *in vitro* model of calcium oxalate. The results were detected by turbidity analysis of the extract, and calcium oxalate showed a high inhibition percentage (approximately 77.27%) compared to the standard Cystone. Sterols and saponins were identified.	(Sairi et al., 2019)
Bergenia ciliata (Haw.) Sternb. (*Saxifragaceae*)	Leaves	Continuous extraction method/ ethanol, then fractionated by petroleum ether, chloroform, *n*-butanol, and ethyl acetate	The extract and fractions were examined *in vivo* in rats and *in vitro* by using calcium oxalate and calcium phosphate stones, the isolated crude phenolic compound from the ethyl acetate fraction gave the highest dissolution of both stones when compared to the tested extract at 10 mg concentration, as it dissolved calcium phosphate stones (67.74%) and oxalate crystals (36.95%), the reference Cystone was found to be more effective (48.48%) when compared to the phenolic constituents.	(Byahatti et al., 2010)
Bergenia ciliata (Haw.) Sternb. (*Saxifragaceae*)	Rhizomes	Maceration/ hydro-methanolic 70%	The extract inhibits nucleation and aggregation of calcium oxalate crystallization, *in vitro*, in a dose-dependent manner (from 1-10 mg/mL extract) by using the Cystone control system, but the mechanism needs more investigation by using an animal model.	(Saha and Verma, 2013)
Bergenia ligulate (Wall.) Engl. (*Saxifragaceae*) [This name is a synonym of *Bergenia pacumbis* (Buch.-Ham. ex D.Don) C.Y.Wu & J.T.Pan]	Rhizomes	Hydro-methanolic extract	The anti-urolithiatic activity was detected *in vivo* in Wistar rats, where the kidney stones were induced by 0.75% ethylene glycol. The results showed the prevention of calcium oxalate deposition and its amount, compared to the untreated group. *In vitro*, the extract showed significant inhibition of calcium oxalate formation and crystal aggregation.	(Bashir and Gilani, 2009)
Boldoa purpurascens Cav. (*Nyctaginaceae*) (This name is a synonym of *Salpianthus purpurascens* Hook. & Arn.)	Leaves	Heat reflux/ aqueous	The extract was examined *in vitro* and *in vivo*; urolithiasis was induced in rats by administering ethyl acetate (0.75%) and ammonium chloride orally for 10 days. The extract was applied at different concentrations (i.e., 100, 200, and 400 mg/kg). Inhibition of nucleation, aggregation, and a significant reduction in dissolution, as well as a reduction in uric acid levels, were all identified, especially at 400 mg/kg.	(Mosquera et al., 2020)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Brassica oleracea L. (Brassicaceae) and *Desmostachya bipinnata* (L.) Stapf (Poaceae)	Aerial parts	Decoction/ aqueous extracts	Aqueous extracts were tested, individually, on albino Wistar rats induced to form kidney stones by ethylene glycol 0.75% and ammonium chloride 2%; after day 10, urine samples were collected and showed a significant decrease in calcium oxalate production and biochemical parameters (like uric acid and creatine) in both aqueous extracts tested individually and in combination at 400 mg/Kg body weight P.O. Further studies are needed to know the mechanism of action and phytochemicals responsible for the anti-urolithiatic activity.	(Naga et al., 2014)
Camellia sinensis (L.) Kuntze (*Theaceae*)	Leaves	Epigallocatechin-3-gallate (Fig. 2) was isolated	Epigallocatechin-3-gallate was examined for anti-urolithiatic activity using an *in vitro* model with different concentrations. The inhibition of crystal growth was detected at all concentrations in a dose-dependent manner (0.1, 1, 10, and 100 µM). It also affected the aggregation and altered the expression of heat shock protein in renal cells (i.e., the calcium oxalate crystal receptor), especially at 10µM concentration.	(Kanlaya and Thongboonkerd, 2019; Kanlaya et al., 2024)
Cerasus avium (L.) Moench (*Rosaceae*) [This name is a synonym of *Prunus avium* (L.) L.]	Stem	Maceration/ distilled water	This study was done in Wistar rats, in which kidney stones were induced by receiving 1% ethylene glycol. The 200 and 400 mg/kg doses of the extract showed a significant decrease in the number of deposits compared with the ethylene glycol group on day 30.	(Azaryan et al., 2017)
Chromolaena odorata (L.) R.M.King & H.Rob. (*Asteraceae*)	Leaves	Maceration/ *n*-hexane, ethyl acetate, and methanol	The methanolic extract (10,000 µg/mL) can dissolve calcium kidney stones by 19.2 µg/mL, phytochemical screening showed the presence of saponins, tannins, alkaloids, flavonoids, and steroids, LCMS/MS analysis revealed 3 active phyto-constituents against kidney stones (3,5,7,4'-tetrahydroxy-8,3'-dimethoxy flavone; 5,7,4'-trihydroxy-3',5'-dimethoxy flavones (tricin) and 5,6,7,8,4'-pentamethoxyflavone (tangeretin) (Fig. 2).	(Indriatmoko et al., 2022)
Cinnamomum zeylanicum Blume (*Lauraceae*) (This name is a synonym of *Cinnamomum verum* J.Presl)	Inner bark	Hydro-alcoholic extract	The extract exhibited a significant reduction in crystal nucleation at doses of 4, 8, and 10 mg/mL. At 2 mg/mL, the extract showed 92.46% growth inhibition. The highest inhibition of aggregation was observed at 4 mg/mL for both the extract and the standard (Cystone).	(Zaki et al., 2019)
Cirsium setidens (Dunn) Nakai (*Asteraceae*)	Herb	Pectolinarigenin (dimethoxy flavone natural compound) (Fig. 2)	The results showed that pectolingargenin decreased renal crystal deposition and exhibited noticeable inhibition of HIF-1 alpha, indicating its anti-inflammatory role.	(Yao et al., 2024)
Citrullus lanatus (Thunb.) Matsum. & Nakai (*Cucurbitaceae*)	Fruit pulp	-	The pulp extract inhibited calcium oxalate formation and decreased urinary parameters, and diuretic activity (which reduces stone formation) was also observed in both *in vivo* and *in vitro* experiments. Sterols and alkanes were the main constituents of this extract, as detected by gas chromatography and mass spectroscopy; their activity may be attributed to these compounds.	(Siddiqui et al., 2018)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Costus igneus N.E.Br. (*Costaceae*) [This name is a synonym of *Chamaecostus cuspidatus* (Nees & Mart.) C.D.Specht & D.W.Stev.]	Stem	Continuous extraction method (ethanol) and decoction (distilled water)	The calcium oxalate crystal deposition in the kidney was significantly decreased by both alcoholic and aqueous extracts in ethylene glycol-induced urolithic rats. Treatment with lupeol and stigmasterol (Fig. 2) significantly reduced the deposition of calcium and oxalate in both the kidney and blood serum.	(Manjula, 2012)
Cucumis melo L. (*Cucurbitaceae*)	The peel and the pulp (Fruit)	Continuous extraction method (*n*-hexane, chloroform, and methanol) and maceration (ethanol and water)	The experiment was conducted *in vivo* in mice with induced kidney stones. Among all tested extracts, chloroform and methanol extracts showed significant potential to reduce renal calculi by lowering serum levels of creatinine, uric acid, and blood urea nitrogen.	(Saleem et al., 2021)
Curcuma longa L. (*Zingiberaceae*)	Rhizomes	Maceration/ ethanol	The ethanol extract showed significant kidney stone dissolving properties, as the standard Cystone tablet *in vitro.*	(Islam et al., 2022)
Cydonia oblonga Mill. (*Rosaceae*)	Leaves	Infusion/ methanol and acetone	The two extracts were examined using a synthetic model of calcium oxalate crystals, and their antioxidant activity was also assessed, demonstrating a significant inhibitory effect on the dissolution of calcium oxalate. Flavonols and polyphenolic compounds were detected.	(Elhadari et al., 2024)
Cynodon dactylon (L.) Pers. (*Poaceae*)	Roots	Decoction/ aqueous (fractionated in *n*-butanol and ethyl acetate)	The experiment was done in male Wistar rats, induced renal calculi by 1% ethylene glycol, in curative groups, after day 35th, all kidneys were removed and examined histologically, *n*-butanol fraction of *C. dactylon* group showed the best result (significant reduction in calcium oxalate deposits), as well as the ethyl acetate fraction group; further studies are required to detect the active constituents.	(Rad et al., 2011)
Drymoglossum piloselloides C.Presl (*Polypodiaceae*) [This name is a synonym of *Pyrrosia piloselloides* (L.) M.G.Price]	Leaves	Maceration/ ethanol and hexane. Decoction/ aqueous. All extracts were dissolved in DMSO for the biological test	The extracts were examined in synthetic urine (*in vitro*), which contains calcium oxalate. Dose-dependent inhibition was shown in all extracts on the nucleation of calcium oxalate crystals; the ethanolic extract at 800 and 1,000 µg/mL showed the same percentage of inhibition (71.13%), which was the highest percentage of inhibition among all extracts, compared to the standard Cystone, ethanolic, and hexane extracts showed higher percentages of inhibition. The maximum inhibition of calcium oxalate growth was observed in the ethanolic extract (93.33%) at a concentration of 1,000 µg/mL, which was significantly higher than that of Cystone. Phytochemically, the extracts contain reducing sugars, proteins, flavonoids, tannins, and polyphenolic compounds.	(Hewagama and Hewawasam, 2022)
Ensete superbum (Roxb.) Cheesman (*Musaceae*)	Seeds	Decoction/ aqueous	The extract was tested in an *in vitro* model using calcium hydrogen phosphate. The results showed a remarkable effect on the morphology of crystals and also demonstrated inhibition of crystal deposition.	(Diana and George, 2013)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Euphorbia hirta L. (*Euphorbiaceae*)	Leaves	Continuous extraction method/ ethanol	Significant percentage inhibition against nucleation of calcium oxalate stones was observed, with a maximum of 55.81% inhibition at 1,000 µg/mL, and a maximum of 73.17% inhibition at 1,000 µg/mL of the aggregation of calcium oxalate to form a stone-like structure.	(Kain et al., 2021)
Euphorbia hirta L. (Euphorbiaceae) and *Orthosiphon stamineus* Benth. (*Lamiaceae*) (This name is a synonym of *Orthosiphon aristatus* var. *aristatus*)	Leaves	Maceration/ hexane, ethyl acetate, methanol, and aqueous	The best inhibition percentage aggregation of calcium oxalate was exhibited by the hexane extract of *E. hirta* (95.78%), and the lowest inhibition was shown by the hexane extract of *O. stamineus* (20%). The study suggested that this could be related to the high content of alkaloids in the hexane extract of *E. hirta* compared to other extracts. The rate of inhibition percentage for both plants varies depending on the type of solvent used.	(Pauzi et al., 2019)
Foeniculum vulgare Mill. (*Apiaceae*) and *Cymbopogon proximus* (Hochst. ex A.Rich.) Chiov. (*Poaceae*) [This name is a synonym of *Cymbopogon schoenanthus* subsp. *proximus* (Hochst. ex A.Rich.) Maire & Weiller]	Herbs	A certain weight of each dried plant was taken, and different ratios of their combinations were prepared as tea bags; the mixture was dissolved in hot water	Phytochemical screening of the two plant extracts showed high content of flavonoids and polyphenols. The mixture of the extracts was examined in calcium oxalate-induced renal calculi in albino rats. The two formulations ratio of 0.5:1.5% and 0.0:2.0% from *F. vulgare* and *C. proximus*, respectively, showed the most effective cure for kidney stones.	(İbrahim and El-Khateeb, 2013)
Gossypium herbaceum L. (*Malvaceae*)	Leaves	Maceration/ ethanol and water	Dissolution of calcium oxalate was shown in both ethanolic and aqueous extracts in the *in vitro* model, but the ethanolic extract was more efficient than the aqueous extract in the dissolution of the crystals.	(Niharika et al., 2018)
Hedychium coronarium J.Koenig (*Zingiberaceae*)	Roots	Continuous extraction method/ alcoholic and maceration/aqueous	The two extracts were examined experimentally on prepared calcium oxalate kidney stones using an *in vitro* model. The alcoholic extract showed better dissolution of calcium oxalate at a 10 mg concentration, exhibiting an effect equal to that of the control, Cystone.	(Bahuguna and Kumar, 2014)
Helichrysum graveolens Boiss. and *Helichrysum stoechas* (L.) DC. (*Asteraceae*)	Inflorescence (capitulum)	Decoction/ aqueous	*H. stoechas* extract showed a prominent effect against kidney stone induced in albino Wistar rats at 156 mg/kg dose, whereas the number of kidney stones was higher in sodium oxalate group, also there is reduction in uric acid and oxalate levels in urine samples and increase in the urine citrate levels are significant and promising in extract groups, it also showed significant change in hematological, biochemical and enzymatic makers after using the extracts.	(Orhan et al., 2015)
Helichrysum graveolens Boiss. and *Helichrysum stoechans* (L.) DC. (*Astraceae*)	Inflorescence (capitulum)	Infusion	The extracts were used *in vivo* in a rat model, where calcium oxalate was induced by administering sodium oxalate (70 mg/kg, i.p.). Following the injection of sodium oxalate for 5 days, potassium citrate (positive control) and both extracts were examined. The results showed that there is a reduction in oxalate and uric acid levels in collected urine samples (especially *H. stoechans* at 156 mg/kg dose).	(Onaran et al., 2016)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Herniaria hirsuta L. (*Caryophyllaceae*)	Whole herb	Decoction/ aqueous	The inhibition percent of calcium oxalate increases after treating with the herb extract (especially at a higher concentration, which is 1 mg/mL).	(Atmani and Khan, 2000)
Herniana hirsuta L. (*Caryophyllaceae*)	Whole plant	Decoction/ aqueous	The extract was examined in rats using the ethylene glycol and ammonium chloride-induced urolithiasis model for 3 days; urine samples were taken on days 1, 3, 7, and 14. The treated and untreated groups showed no differences in pH. Histological results of the removed kidneys from the treated group showed less calcium oxalate crystal deposition, unlike those from the untreated group.	(Atmani et al., 2003)
Hibiscus sabdariffa L. (*Malvaceae*)	Flowers	Continuous extraction method (chloroform and ethanol) and decoction (water)	All extracts showed inhibition of calcium oxalate stone crystallization. The highest effect was observed in the aqueous extract, followed by the ethanolic extract, and lastly, the chloroform extract.	(Saleh et al., 2013)
Humulus lupulus L. (*Cannabaceae*)	Whole plant	Aqueous slightly alkaline extract, then fractionated into soluble methanolic and insoluble methanolic fractions	The extract was examined *in vitro* by using a prepared litholytic model of calcium oxalate and real kidney stones, which were removed after surgery. Remarkable results were shown in the inhibition of kidney stones; the extract was fractionated into two fractions. A fraction containing sugars and organic acids demonstrated good efficacy in dissolving kidney stones. The other fraction, which is not soluble in methanol, contains only sugar derivatives; it caused a significant change in the shape of the crystals, so both fractions were effective. Further *in vivo* studies are required.	(Frąckowiak et al., 2010)
Incarvillea diffusa Royle (*Bignoniaceae*)	Herb	-	The extract was examined (*in vivo*) in Sprague-Dawley rats, after inducing kidney stones by ethylene glycol and ammonium chloride, and the urine was collected. A reduction in blood urea nitrogen was detected; the extract also exhibited antioxidant activity, in addition to a decrease in calcium oxalate levels.	(William et al., 2025)
Kalanchoe laciniata (L.) DC. (*Crassulaceae*)	Leaves	Maceration/ ethanol and hexane. Decoction/ aqueous. All extracts were dissolved in DMSO for the biological test	The experiment was done *in vitro*. Hexane extract showed good results against calcium oxalate nucleation in a dose-dependent manner. The maximum inhibition was at 500 µg/mL (97.69%), which was much higher than the standard Cystone at 500 µg/mL (66.67%). The ethanolic extract showed the highest percentage of inhibition at 500 µg/mL (96.10%). The aqueous fraction showed the highest inhibition at 100 µg/mL (73.16%). Phytochemically, the plant showed the presence of reducing sugars, proteins, flavonoids, tannins, and other polyphenolic compounds.	(Hewagama and Hewawasam, 2022)
Kalanchoe pinnata (Lam.) Pers. (*Crassulaceae*)	Leaves	Maceration/ deionized water	In this *in vitro* study, crystal growth in supersaturated solutions and artificial urine was inhibited by 41% and 15%, respectively. The results showed that the organic acid content in the extract is important for anti-urolithic activity.	(Ranaweera et al., 2023)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Launaea procumbens (Roxb.) Ramayya & Rajagopal (*Asteraceae*)	Leaves	Continuous extraction method/ methanol	The extracts at 150 and 300 mg/kg were examined in rats, in which renal calculi were induced. The results revealed hyperoxaluria due to increased elimination of uric acid and oxalates. Additionally, a noticeable reduction in elevated calcium levels in renal tissue was detected in a dose-dependent manner. It also showed activity in decreasing the risk for glomerular and tubular damage. When the tissues of the treated group were examined histopathologically, no calculi were observed.	(Makasanaa et al., 2014)
Malus domestica (Suckow) Borkh. (Rosaceae)	Fruits	Maceration/ methanol	*In vitro* anti-urolithiatic activity was tested using different concentrations of the methanolic extract of M. domestica. It was found that 500 µg/mL showed a promising inhibition of calcium oxalate crystal aggregation compared to the positive control (potassium citrate). The methanolic extract exhibited a high flavonoid content.	(Hiponia et al., 2019)
Mentha × piperita L. (*Lamiaceae*)	Aerial parts	Essential oil	The kidney stones were induced in rats by administering ethylene glycol and ammonium chloride. The essential oil was effective against urolithiasis-associated changes, including crystalluria, polyuria, and acidic urine. It also neutralized the levels of urinary uric acid, magnesium, total protein, serum blood urea nitrogen, and serum creatinine.	(Jamshed and Jabeen, 2021)
Mimosa bimucronata (DC.) Kuntze (*Fabaceae*)	Leaves	Gallic acid and methyl gallate (Fig. 2) were isolated from the ethyl acetate fraction of the plant's extract	The anti-urolithiatic activity of gallic acid and methyl gallate was evaluated at different concentrations (0.003-0.03 mg/mL). They were examined *in vitro* on calcium oxalate crystals, noticeable inhibition of total calcium oxalate crystals was noticed, gallic acid inhibited about 44.57%, while methyl gallate inhibited about 48.35%, comparing to the negative control, which is distilled water, after using UV spectrometry on the one treated with these phenolic compounds, it showed reduction of absorbance, which is a sign of reduction of synthetic crystals.	(Cechinel-Zanchett et al., 2021)
Moringa oleifera Lam. (*Moringaceae*)	Bark	Maceration/ methanol 70%	Significant inhibition of nucleation was observed with the alcoholic extract, similar to that of citrates. İnhibition of crystallization was also observed (*in vitro*). So, it has a promising effect, and *in vivo* experiments are needed.	(Menon et al., 2024)
Moringa oleifera Lam. and *Moringa peregrina* (Forssk.) Fiori (*Moringaceae*)	Leaves	Maceration/ hydro-alcoholic extract	Inhibition of the crystallization process was detected in both extracts (*in vitro*); the *M. oleifera* extract showed better results than the *M. peregrina* extract. So, further *in vivo* studies are recommended.	(Menon et al., 2022)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Paronychia argentea Lam. (*Caryophyllaceae*)	Aerial parts	Continuous extraction method/ hexane and methanol (fractionated by ethyl acetate, isopropanol, and acetone)	The result showed that ethyl acetate fraction reduced the crystal size and activated the formation of calcium oxalate dihydrate (COD) crystals out from calcium oxalate monohydrate (COM) with concentration dependent process, it reduced the crystal size and ion concentration (*in vitro* model), this extract after phytochemical screening showed high content of saponins, so some of this anti-lithogenisis activity was due to the diuretic characteristics of these saponins.	(Magharbeh et al., 2020)
Pedalium murex L. (*Pedaliaceae*)	Whole plant	Continuous extraction method/ ethyl acetate	The *in vitro* activity of ethyl acetate extract against several urease producing bacteria (the main reason of struvite stone formation) showed minimum bactericidal concentration (MBC) against *Escherichia coli* and *Staphylococcus aureus* (>125); *in vivo* experiment in rats induced kidney stone showed good result in 1% (300 mg) treated group than the standard; histological examination showed noticeable reduction in renal damage and glomerular formation.	(Kaleeswaran et al., 2019)
Peganum harmala L. (*Nitrariaceae*)	Seeds and isolated β-carboline alkaloids (harmine and harmalacidine) (Fig. 2)	Alcoholic extract, then fractionated in petroleum ether, n-butanol, and others	The alcoholic extract and the two isolated compounds were examined in rats with induced urolithiasis using ethylene glycol. A decrease in calcium oxalate crystals, blood urea nitrogen, uric acid, and inflammatory mediators, along with an increase in urine volume and a decrease in the number and size of calculi, was identified. Histologically, examining the tissue supported the findings. The extract and isolated compounds exhibit both therapeutic and preventive characteristics.	(Rashid et al., 2023)
Peltophorum pterocarpum (DC.) Backer ex K.Heyne (*Fabaceae*)	Fresh leaves	Maceration/ hydro-methanolic	*In vitro* anti-urolithiatic model results showed that the aqueous fraction has the highest dissolution of kidney stones compared to the other fractions; the plant extract contains phenolic and flavonoid compounds.	(Jha et al., 2016)
Phaseolus vulgaris L. (*Fabaceae*)	Green fruit pods	The juice obtained from the pods was dissolved in water, and then several formulations were prepared as a syrup dosage form	The extract (syrup) was examined *in vitro* and *in vivo* in Wistar rats. The calcium oxalate crystals were induced by ethylene glycol; the results showed inhibition of aggregation at all concentrations (200-600 µg/mL), i.e., 200, 400, and 600 µg/mL. Significant reduction of calcium oxalate crystals was also detected.	(Noorulla et al., 2024)
Piper attenuatum Humb. ex Link (*Piperaceae*) (This name is a synonym of *Piper laevigatum* Kunth)	Leaves	Ethanolic extract and isolation of some phytoconstituents	The ethanolic extract demonstrated a significant anti-lithiatic effect in treated rats, particularly at a dose of 400 mg/kg. After phytochemical analysis and molecular docking to detect binding to the protein, it was found that aristolactam A II, cepharadione A and B, piperolactam A, norcepharadione B, and pipoxide chlorohydrin (Fig. 2) are responsible for the activity in renal function.	(Sharma et al., 2024)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Pistacia lentiscus L. (*Anacardiaceae*)	Fruits	Ethanolic extract	The extract was examined in human's kidney which was incubated with calcium oxide monohydrate, by using the microscope, staining and counting, the image examination of the treated kidney showed decrease in E-cadherin expression and decrease in the huge amount of H_2O_2 induced by calcium oxide monohydrate, the extract reduced the particle size and decreased the concentration of calcium oxide monohydrate, it prevents calcium oxide monohydrate adhesion to tubular apical membrane, so, it showed preventive effect against nephrolithiasis.	(Cheraft-Bahloul et al., 2017)
Plectranthus tomentosus Benth. (*Lamiaceae*) [This name is a synonym of *Coleus hadiensis* (Forssk.) A.J.Paton]	Seeds and roots	Decoction/ aqueous	The experiment was *in vivo*, lithogenesis was induced with ethylene glycol in albino Wistar rats, furosemide (20 mg/kg) was used as standard positive control, the aqueous extracts of roots and seeds (500 and 1,000 mg/kg, respectively) gave good activity in decreasing kidney stones and serum levels of calcium, phosphorous, creatinine and urea, but less than furosemide.	(Madhu et al., 2012)
Punica granatum L. (*Lythraceae*)	Fruits peels	Continuous extraction method/ ethanol and infusion/ aqueous.	The two extracts, at doses of 200 and 400 mg/kg/day, showed significant anti-urolitholytic properties in a rat model, in which calcium oxalate was induced by ethylene glycol and ammonium chloride. They exhibited a diuretic effect, particularly with the infusion extract at 400 mg/kg, with no crystals detected. Also, they showed anti-microbial properties.	(Kachkoul et al., 2023)
Rhus chinensis Mill. (*Anacardiaceae*)	Fruits pulps	Decoction/ aqueous	The extract was examined *in vitro* on synthetic crystals of calcium oxalate, which showed inhibition of nucleation and aggregation of calcium oxalate crystals, resulting in a significant decrease in crystal density. These results were similar to those obtained with standard malic acid, citric acid, and Cystone, with concentrations ranging from 1 to 10 mg/mL. Tannins, flavonoids, polyphenolics, terpenoids, and glycosides were detected after phytochemical examination.	(Heirangkhongjam and Ngaseppam, 2021)
Rubia tinctorum L. (*Rubiaceae*)	Roots	Continuous extraction method/ ethanol and ethyl acetate	Both extracts significantly reduced the presence of calcium oxalate in the rat model. The extracts demonstrated antioxidant activity and were rich in polyphenolic constituents.	(Marhoume et al., 2021)
Scolymus hispanicus L. (*Asteraceae*)	Roots and shell parts	Maceration and percolation/ ethyl acetate	The experiment was conducted in rats with induced kidney stones using 1% ethylene glycol in drinking water; the extract showed a significant decrease in stone size.	(Coşkun et al., 2022)
Solanum xanthocarpum Schrad. & J.C.Wendl. (*Solanaceae*) (This name is a synonym of *Solanum virginianum* L.)	Fruits	Saponin-rich fruit fraction from macerated hydro-alcoholic extract	*İn vitro* and *in vivo* experiments were done. Ethylene glycol was administered to induce the formation of renal stones in rats. At two doses, 20 and 40 mg/kg, the *in vitro* results showed a significant decrease in nucleation and aggregation of calcium oxalate crystals.	(Patel et al., 2012)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Spinacia oleracea L. (*Amaranthaceae*) and *Coriandrum sativum* L. (*Apiaceae*)	Seeds	Decoction/ aqueous	Phytochemical screening of both extracts showed the presence of phenolic compounds, flavonoids, and alkaloids. The mixture contained a higher percentage of these phytochemicals compared to each extract alone; it also contained saponins, glycosides, tannins, steroids, terpenoids, and triterpenoids. The mixture of both extracts was examined for anti-urolithiatic activity against synthetic urine and stones at a concentration of 1,000 µg/mL; the mixture exhibited a synergistic effect, which supported its traditional use in treating kidney stones.	(Raj et al., 2024)
Terminalia arjuna (Roxb. ex DC.) Wight & Arn. (*Combretaceae*)	Dried barks	Decoction/ aqueous, then fractionated	The aqueous extract was effective on the growth of mineral phase of calcium phosphate (CaP) ions, the maximum inhibition of calcium ion was at 1.5 mL (48%) followed by 1.0 (41%), 0.8 (37%), 0.4 (36%) and 0.2 mL (15%); inhibition of phosphate ion was found to be maximum with 0.2 mL (50%) of the extract followed by 1.5 (40%), 0.8 (35%), 1.0 (29%) and 0.4 mL (24%), the results of inhibiting the growth of calcium oxalate monohydrate crystals at 30 sec was 20%, and was 48% at 120 sec when 1.5 µL of aqueous extract of *T. arjuna* was used. After fractionation, the *n*-butanol fraction exhibited significant growth inhibition of CaP at various concentrations and time intervals. The *n*-butanol fraction was abundant with saponins and tannins.	(Chaudhary et al., 2010)
Trigonella foenum-graecum L. (*Fabaceae*)	Seeds	Infusion/ aqueous NaCl 0.9% solution	The aqueous extract demonstrated a more effective dissolution of cystine and carbapatite stones, with mass losses of 94 mg and 73 mg, respectively, in an *in vitro* experiment. The reason for this was the formation of complexes between the stones and polyphenols or flavonoids present in the extracts. Another study tested the effect of trigonelline (Fig. 2), an alkaloidal compound isolated from *T. foenum-graecum* and other plants, it was found by light microscope (400×) that trigonelline showed inhibition of calcium oxalate mono- hydrate size, number and mass during crystallization process, mostly, with the highest tested concentration (100 µg); the crystal growth and crystal-cell adhesion was due to down regulation of the crystal receptors at apical membranes of renal tubular cells.	(Peerapen et al., 2022; Yachi et al., 2018)
Zaleya pentandra (L.) C.Jeffrey (*Aizoaceae*)	Herb	Ethanolic extract	The results showed a dose-dependent manner, which is (30-300 mg/kg) as a diuretic after in vivo examination in rats, in which their calcium oxalate crystals were induced by ethylene glycol, the extract gave similar effects as hydrochlorothiazide, and it also showed remarkable antioxidant activity. The *in vitro* synthetic calcium oxalate showed noticeable crystal inhibition. Further clinical trial examinations are needed.	(William et al., 2025)

Table 1. List of medicinal plants that showed prevention and eradication of kidney stones (continued...)

Scientific name (family)	Part of plant used	Method of extraction/ solvent	Experimental description and outcomes	Ref.
Ziziphus jujuba Mill. (*Rhamnaceae*)	Leaves	Maceration/ absolute ethanol	The experiment was conducted in male Wistar rats, in which kidney stones were induced by administering 1% ethylene glycol and 0.25% ammonium chloride in drinking water for 28 days. The extract showed that the most effective dose for inhibiting calcium oxalate is 500 mg/kg.	(Pourahmadi et al., 2023)

Scientific names and families were confirmed on the World Flora Online website: https://www.worldfloraonline.org/

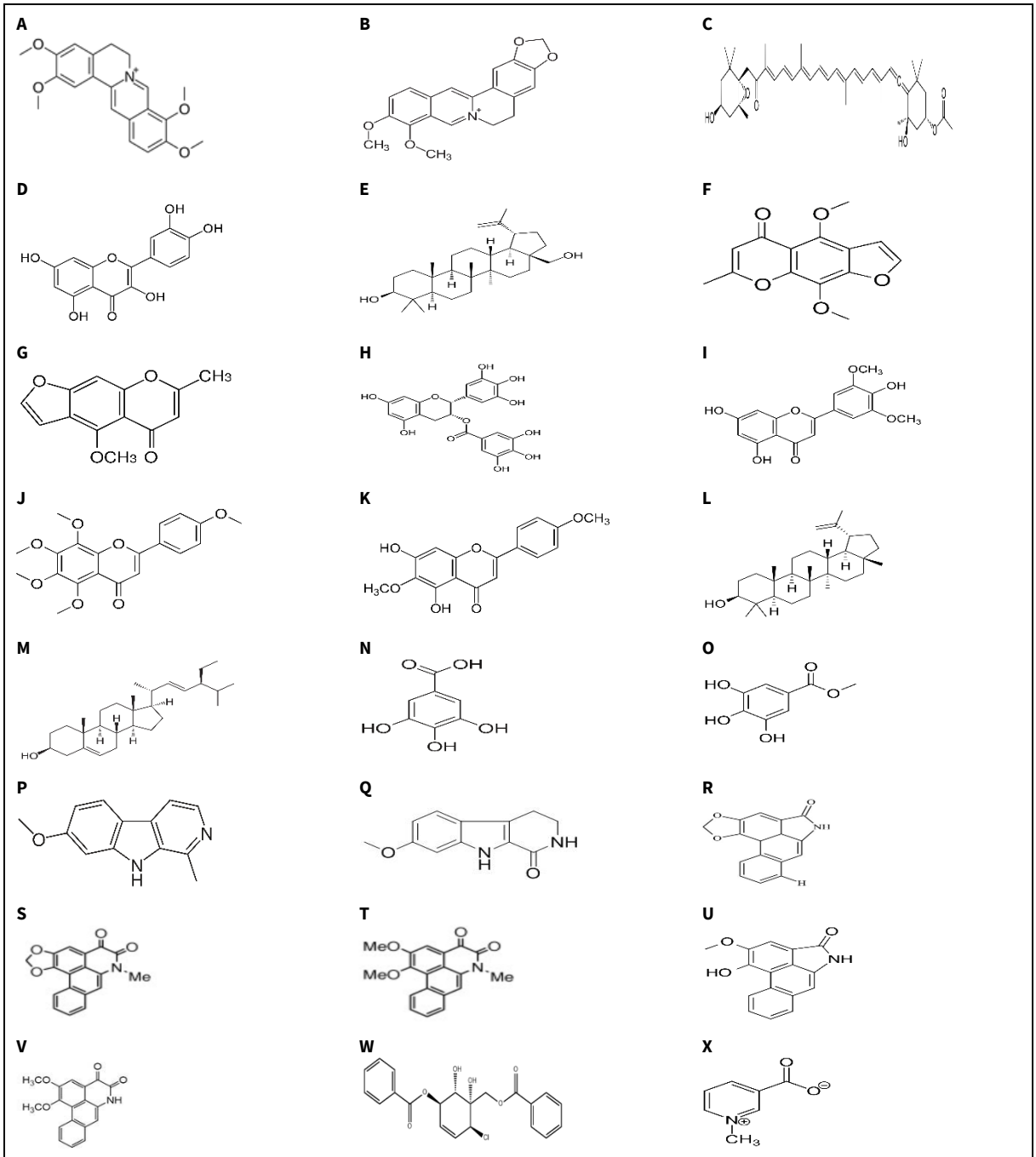

Figure 2. Chemical structures of some natural compounds with anti-urolithiatic activity isolated from medicinal plants.

(A) Palmatine; **(B)** Berberine; **(C)** Fucoxanthin; **(D)** Quercetin; **(E)** Betulin; **(F)** Khellin; **(G)** Visnagin; **(H)** Epigallocatechin-3-gallate; **(I):** Tricin; **(J)** Tangeretin; **(K)** Pectolinarigenin; **(L)** Lupeol; **(M)** Stigmasterol; **(N)** Gallic acid; **(O)** Methyl gallate; **(P)** Harmine; **(Q)** Harmalacidine; **(R)** Aristolactam AII; **(S)** Cepharadione A; **(T)** Cepharadione B; **(U)** Piperolactam A; **(V)** Norcepharadione B; **(W)** Pipoxide chlorohydrin; **(X)** Trigonelline.

Excluded studies

The articles that met the stated inclusion criteria were finally filtered into 39, 37, and five articles from Google Scholar, ScienceDirect, and PubMed, respectively. Each article was studied qualitatively, and the required information was summarized either as paragraphs or in tabulated form. Therefore, the total number of 81 articles was included (Table 1).

Study characteristics

Below are the findings and a summary of the 81 articles included.

***Hibiscus rosa-sinensis* L. (*Malvaceae*)**

The flowers of *H. rosa-sinensis* were macerated by hydro-ethanol. The anti-urolithiatic activity of the extract was evaluated *in vivo* using Wistar rats (doses of 300 and 600 mg/kg in two groups). Calcium oxalate urolithiasis was induced in rats by administering an ethylene glycol/ammonium chloride mixture in their drinking water. At the end of the experiment, all kidney samples were collected, and their sections were examined under a light microscope. Additionally, urinary parameters were estimated. The results revealed that the group treated with *H. rosa-sinensis* showed a significant decrease in urine secretion of calcium oxalate and citrates, which are responsible for inducing oxalate crystals, compared with the control group. Histological studies confirmed the urinary parameters, revealing minimal damage with a small amount of calcium oxalate deposits in the kidneys. These results indicate that *H. rosa-sinensis* can reduce and prevent the growth of kidney stones (Sahu and Singh, 2022).

***Rubus idaeus* Thunb. (*Rosaceae*)**

The roots of *R. idaeus* were extracted by Soxhlet's apparatus using alcoholic solvent. The extract was applied to assess its effects on experimentally induced calcium oxalate nephrolithiasis in mice by using glyoxylate for 12 days. The dose of glyoxylate was 80 mg/kg/day by intra-abdominal injection, while the doses of *R. idaeus* extract were 100 mg/kg/day and 200 mg/kg/day, given to two groups through oral gavage accompanied by glyoxylate injection. Histological and biochemical tests were taken after the end of the experiment. The results showed a significant reduction in the urinary excretion values of oxalate, calcium, and phosphorus in the extract-treated groups compared to the untreated mice group, while creatinine urinary excretion was increased. The serum values of oxalate, calcium, and creatinine were also significantly reduced; however, the phosphorus values remained unchanged. The kidney content of calcium was higher in the untreated group. It was also found that there was a significant increase in superoxide dismutase, catalase, glutathione reductase (GSH), and G6PD activities in the treated groups rather than the untreated group. Moreover, hyperoxaluria-induced generation of malondialdehyde (MDA) and protein carbonyls was significantly prevented in the treated groups. A high content of vitamin E was observed in the treated groups (*R. idaeus* groups). Histologically, calcium oxalate crystals were deposited and observed in the untreated group. Hence, *R. idaeus* showed a magnificent prophylactic effect on calcium oxalate stones in nephrolithic mice (Ghalayini et al., 2011).

***Malva neglecta* Wallr. (*Malvaceae*)**

The leaves of *M. neglecta* were soaked in distilled water for 72 hours, and the extract was examined against ethylene glycol-induced kidney stones in male Wistar rats. The rats were randomly distributed into eight groups. The first group received tap drinking water for 28 days (Normal group), and the second group received drinking water containing 1% ethylene glycol plus 0.25% ammonium chloride (Disease group). Groups 3 and 4 received by i.p. route 200 mg/kg/day and 800 mg/kg/day of *M. neglecta* aqueous extract, respectively, for 28 days. Groups 5 and 6 received drinking water containing 1% ethylene glycol, 0.25% ammonium chloride, and *M. neglecta* extract by the i.p. route at 200 mg/kg/day and 800 mg/kg/day, respectively, for 28 days (Preventive groups). Lastly, groups 7 and 8 received drinking water containing 1% ethylene glycol plus 0.25% ammonium chloride for 28 days, and *M. neglecta* extract was administered intraperitoneally at 200 mg/kg/day and 800 mg/kg/day, respectively, from day 14 to day 28 (Curative groups). After day 28, all kidneys were removed and examined; the results showed a significant decrease in calcium oxalate deposits and tubulo-interstitial damage in groups 5 and 6, particularly in the curative groups, such as the high-dose aqueous extract group, where there was a marked reduction in oxalate deposits and tubulo-interstitial damage. However, the high-dose groups in both preventive and curative settings seemed to be more effective (Saremi et al., 2015).

***Nigella sativa* L. (*Ranunculaceae*)**

N. sativa seeds showed promising results in prevention and treatment of kidney stones; in a preclinical study, it was applied to examine renal stone's dissolving efficacy in random clinical trial, sixty patients with kidney stones were divided randomly into 2 groups of a randomized triple-blind placebo-controlled clinical trial, the patients were treated by *N. sativa* capsules (500 mg) or placebo b.i.d. for 10 weeks. The size of the kidney stones was measured using sonography before and after the study. 44.4% of patients who took *N. sativa* capsules excreted their stones completely, and the

size of the stones remained unchanged, decreased in 3.7% and 51.8%, respectively. On the other hand, in patients who received a placebo, 15.3% completely excreted their stones, 11.5% experienced a reduction in stone size, 15.3% had an increase in stone size, and 57.6% showed no change in stone size. *N. sativa* has shown positive effects in the treatment of kidney stones and reduction in their size (Ardakani Movaghati et al., 2019).

Another study examined the ethylene glycol-induced kidney stones in rats, and the essential oil and methanolic extract of *N. sativa* seeds were both investigated. The results revealed higher efficacy in preventing calcium oxalate crystal accumulation in the urinary tract and treating kidney stones (Zarei and Rhmani, 2015).

Another study was conducted in Iran to investigate the activity of *N. sativa* in treating kidney stones, particularly its alcoholic extract. The experiment was a clinical trial conducted from June 2020 to December 2021 on 50 patients with kidney stones, who were divided into two groups using the randomized block sampling method. For 12 weeks, the intervention group received a capsule containing 100 mg alcoholic extract of *N sativa* b.i.d., and the control group received their usual treatment. The urinary oxalate, pH, citrate levels, and the size of the stones (as measured by sonography) were assessed before and after the interventions. The result showed a decline in kidney stone size in the intervention group, but it was statistically insignificant. The urinary oxalate amount in the intervention group was reduced compared to the control group; however, there were no differences in pH, urine volume, or citrate levels between the two groups (Aghamirei et al., 2022).

Another study was conducted on *N. sativa* hydro-alcoholic extract in combination with honey to assess its synergistic effects on male mice induced to develop kidney stones by administering 1% ethylene glycol in their drinking water. The mice were randomly divided into seven groups, each with five mice. The decrease in urinary oxalate in the combined group of honey and black seed (125 mg/kg) was 0.3 ± 0.07. The urine calcium concentration was also decreased significantly in the combined group (5.70 ± 0.75). In addition, the serum and tissue parameters in the honey and black seed groups alone (125 and 250 mg/kg, respectively) and the honey and black seed group (125 mg/kg) also showed significant changes (Rashidi et al., 2022).

Bryophyllum pinnatum (Lam.) Oken (*Crassulaceae*)

B. pinnatum (a synonym of *Kalanchoe pinnata* (Lam.) Pers.) leaves extract was prepared by macerating the leaf powder with hydro-ethanol 70%. The albino Wistar rats were randomly assigned to the testing groups and then subjected to sodium oxalate (70 mg/kg i.p.) to induce renal calculi. The extract was administered orally in two doses to two groups, i.e., 50 and 200 mg/kg/day, for 14 days. Cystone, administered at 500 mg/kg/day, served as a reference standard agent. After day 14, the results showed a significant increase in urine volume compared to Cystone ($p<0.05$). Additionally, a reduction in urinary oxalate, uric acid, phosphorus, magnesium, and creatinine was reported, especially in the 200 mg/kg/day group, indicating dose-dependent anti-urolithiatic activity. Histopathological examination of the removed renal tissues from treated groups revealed a dose-dependent reduction in the amount of calcium oxalate deposits in the renal tubules compared with the untreated group; additionally, the renal function test results were better than those of the untreated group (Pandhare et al., 2021).

Another study on the same species, but this time using an ethyl acetate extract, showed a promising anti-urolithiatic activity at a 10 mg concentration compared to the positive control (Neeri). A good result was also recorded for the dissolution of calcium oxalate crystals (Kaviraj et al., 2022).

Leea macrophylla Roxb. ex Hornem. *(Vitacaceae)*

L. macrophylla powdered whole plant extract was extracted with absolute ethanol for 15 days. The dried extract was examined in albino Wistar rats, which were divided into two groups: preventive and therapeutic groups. For the preventive group, 500 mg/kg/day was administered to each rat for 14 days; however, the therapeutic group received the same dose for 28 days. After 24 hours, urine samples were collected on a regular basis. At the end of the experiment, the kidneys of the treated rats were removed and examined. The results showed a significant decrease in calcium, phosphate, and oxalate levels in both experimental groups, but an increase in creatinine and magnesium levels was observed. The results of the therapeutic group were more effective than those of the preventive group. After patho-histological examination, no oxalate crystal deposition was detected. The extract also showed no toxicity up to 3.5 g/kg/day. The study recommended that more experiments are needed to detect the specific mechanism of action (Nizami et al., 2012).

Chenopodium album L. (*Amaranthaceae*)

C. album leaves powder was extracted with distilled water for 48 hours, the anti-urolithiatic activity of the aqueous extract was examined (*in vitro* model) on calcium oxalate crystals. The extract was prepared at two concentrations (500 and 1,000 µg/mL), with Cystone at 1,000 µg/mL as the control. The results showed

inhibition of nucleation at 58.33%, 12.5%, and 37.5%, respectively. Cystone and the aqueous extract (500 µg/mL) yielded the same percentage of inhibition on crystal growth and aggregation (66.66%). It also showed a noticeable effect on crystal growth at a concentration of 1,000 µg/mL, resulting in 39.57% inhibition compared to the standard Cystone, which achieved 50.96% inhibition. The results also showed an inhibition of brushite crystal growth, with a decrease in thickness from 52.64 µm in the control to 17.28-14.15 µm with the aqueous extract at 500 and 1,000 µg/mL, respectively. The phytochemical screening revealed that this plant extract contains a higher content of phenolic compounds (239.8 mg), flavonoids (87.23 mg quercetin/g of extract), and saponin content of 1.6 mg saponins per 100 g of the powder mass (Sharma et al., 2016).

Another study was conducted on *C. album* using a rat model (*in vivo*) with an ethylene glycol model. Methanolic and aqueous leaf extracts were prepared at different concentrations (100, 200, and 400 mg/kg) for comparison with the standard Cystone. The results revealed significant inhibition of calcium oxalate deposition and reduction in crystallization in the treated group. After phytochemical screening, flavonoids and phenolic compounds were detected at concentrations of 98.5 mg and 239.8 mg, respectively. 236 mg and 87.23 mg quercetin equivalent/g of extract, with methanolic and aqueous extracts, respectively. The study concluded that the anti-urolithiatic activity probably refers to these phenolic compounds (Sikarwar et al., 2017).

Enhydra fluctuans Lour. (*Asteraceae*)

The whole plant of *E. fluctuans* was extracted with distilled water (decoction) for 4 hours. The anti-urolithiatic activity of the aqueous extract was detected (*in vitro*) against calcium phosphate (brushite) crystals. Three different concentrations were prepared (i.e., 50, 100, and 200 µg/mL). All concentrations exhibited an inhibitory effect on crystal growth. The length of the deposited crystals and the crystal bed were decreased by the aqueous extract, as was the case with citric acid; however, the crystal bed was inhibited more by the extract at concentrations of 200 and 100 µg/mL. The study recommended that further *in vivo* studies are needed to detect the active compound(s) responsible for the activity (Chattaraj et al., 2023).

Didymocarpus pedicellatus R.Br. (*Gesneriaceae*)

The extracted leaves of *D. pedicellatus* was examined, *in vivo*, for anti-urolithiatic activity in albino rats, the kidney stones were induced by 0.75% ethylene glycol + 1% ammonium chloride, the experimental rats were divided into five groups, a group given ethylene glycol, the second group was treated as normal control, the third group was treated with Neeri (as standard), while the last two groups were treated with the extract (200 mg/kg and 300 mg/kg), respectively. After 24 hours, the urine collection of the last two groups showed lower calcium concentration, but an increase in potassium and sodium levels compared to the control. The standard group showed a reduction in blood urea nitrogen and creatinine compared to the control. The treated group, at 300 mg/kg, exhibited the highest reduction in creatinine, and no crystals were observed after histological examination. Further studies are needed to identify the biologically active ingredients in this plant and the mechanism of action responsible for its activity against kidney stones (Ahmad et al., 2022).

Thalictrum foliolosum DC. (*Ranunculaceae*)

The root extract of *T. foliolosum* showed a remarkable effect in inhibiting nucleation, aggregation, and changing the shape of calcium oxalate crystals (*in vitro*). The anti-urolithiatic activity of the extract was dose dependent effect, 50% inhibition of calcium oxalate formation was found at 114.36 µg/mL, quantitative analysis showed that it contains berberine and palmatine (alkaloidal compounds) (Fig. 2A-B), they inhibited 50% of calcium oxalate formation at 10.41 and 10.69 µg/mL for berberine and palmatine, respectively. Additionally, the antioxidant and anti-inflammatory properties were also detected (Chaudhary et al., 2022).

Another study was conducted on berberine, an isolated natural compound with anti-urolithiatic properties. It is a known isoquinoline alkaloid derived from various plants, including *Hydrastis canadensis*, *Coptis chinensis*, *Berberis aquifolium*, *Berberis aristata*, and *Berberis vulgaris*. Anti-urolithiatic activity was detected (*in vivo*) in Wistar albino rats. The kidney stones were induced by giving calcium oxalate at different concentrations (5, 10 and 20 mg/kg), the compound showed an increase in urine output in the treated groups, especially with 5 and 20 mg/kg groups, also, increasing in sodium and potassium elimination levels and decreasing in calcium elimination level claims its diuretic activity (as hydro-chlorothiazide). Prevention of calcium oxalate deposition was also observed, particularly in the 10 mg/kg group. The doses (50-150 µg/mL) exhibited antioxidant activity by inhibiting peroxidation induced in the rat's kidneys, with an effect more efficient than the reference butylated hydroxytoluene (Bashir and Gilani, 2011).

Persea americana Mill. (*Lauraceae*)

The ethanolic extract of avocado (*P. americana*) leaves was tested against kidney stones in white male rats, the experiment groups were divided into four

groups, five rats each, group A was untreated group, group B was positive control group in which the rats treated by 0.75% ethyl glycol + 2% ammonium chloride, groups C and D they were treated as group B in addition to the alcoholic extract at doses (100 and 300 mg/kg per body weight), respectively. Both treatment groups (C and D) exhibited a decrease in calcium oxalate levels compared to the other groups. Following phytochemical analysis, it was found that the plant extract contains secondary metabolites, primarily high amounts of flavonoids. Further studies are needed to determine the exact mechanism, as the extract has shown preventative effects (Wientarsih et al., 2012).

Fucoxanthin

Fucoxanthin is a natural carotenoid (Fig. 2C) that occurs as an accessory pigment in brown algae. It demonstrated anti-urolithiatic activity when examined *in vivo* in rats, where renal calculi were induced by administering 0.75% ethylene glycol in their drinking water. The effect was examined at different concentrations, ranging from 40 to 80 mg/kg body weight. After histopathological examination of the tissue in the glomeruli, no calculi were observed in the treatment group; therefore, there was an inhibition of calcium deposition. Therefore, fucoxanthin prevented tubular membrane damage and the deposition of calculi in the glomeruli (Wang et al., 2020).

Table 1 summarizes other articles that were collected for this review.

Fig. 3 represents a proposed flowchart illustrating the primary mechanisms of action of active natural compounds identified from the reviewed articles.

DISCUSSION

Natural products, particularly medicinal plants, play a crucial role in drug discovery and development by providing important lead compounds and drug prototypes. Urolithiasis is a widespread renal disorder globally, imposing significant costs on healthcare systems. This condition can be effectively prevented and treated primarily through the use of natural products and medicinal plants. Therefore, the aim of our review is to compile and analyze the current state of knowledge regarding the role of medicinal plants in the prevention and treatment of urolithiasis, with a focus on isolated active natural compounds and essential oils. We will present nearly all isolated and characterized active natural compounds (Fig. 2) as well as the major phytochemical groups responsible for anti-urolithiatic activity. This review represents a modest effort on our part to guide researchers in their future endeavors to discover and develop new molecules derived from medicinal plants for the treatment and prevention of urolithiasis.

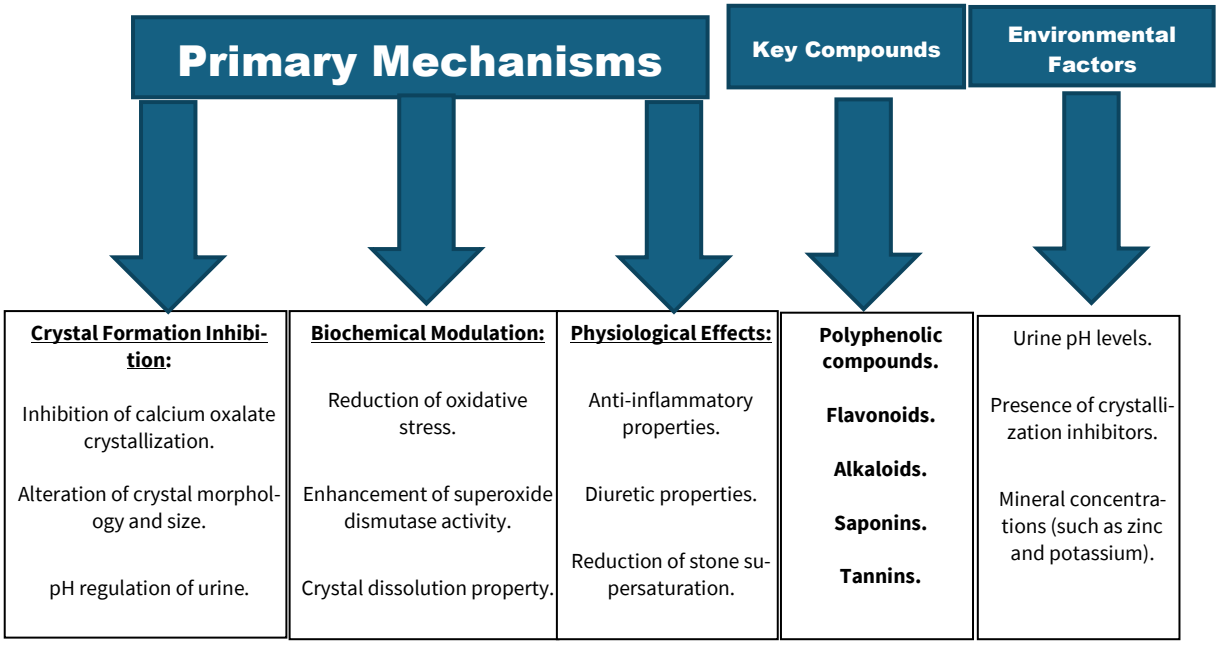

Figure 3. Flowchart illustrating the primary mechanisms of action of natural compounds in the treatment of urolithiasis.

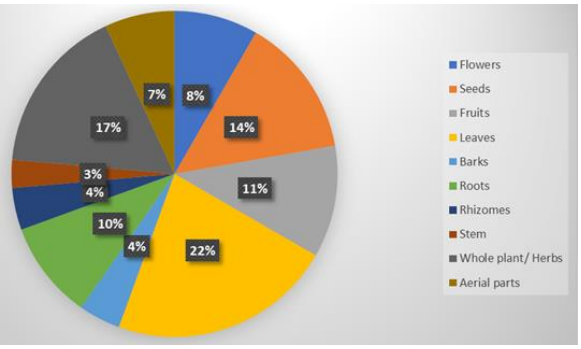

Figure 4. The percentage of plant parts contributed to the anti-urolithiatic activity of medicinal plants.

In this study, 81 articles were reviewed. Generally, was observed that all plant parts had provided us with anti-urolithiatic active extracts, essential oils and pure active compounds (Fig. 4), the leaves were the most dominant part with 22% of contribution, followed by the whole plant parts and herbs (17%), followed by seeds (14%), fruits (11%), roots (10%), flowers and inflorescence (8%) and aerial parts (7%). The barks, rhizomes, and stems contributed 4%, 3% and 3%, respectively. These variations of plants' organs necessitate various phytochemical active constituents (Fig. 2). Also, various plant parts (organs) with various tissues and cells structures and characters, necessitate that there is no specific method of extraction, this point was obviously recognized that both hot extraction and cold methods of extraction had shared almost the same percentage in our reviewed articles (Fig. 5), 45% and 55%, respectively.

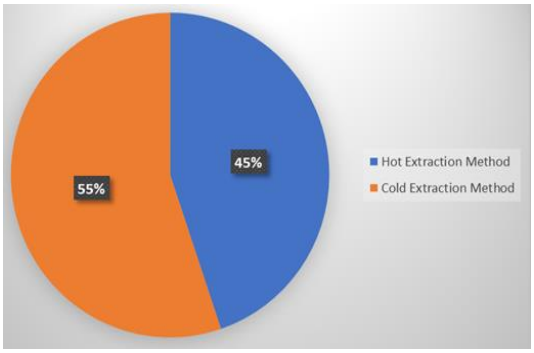

Figure 5. The percentage of the method of extraction contributed to the anti-urolithiatic activity of medicinal plants.

Decoction, infusion, and continuous extraction methods (using Soxhlet's apparatus) were common hot extraction methods, while maceration, percolation, and fractionation (using a separatory funnel) were the most common cold extraction methods applied in extraction and isolation processes. Alcohol and water were used as solvents more frequently than other organic solvents. It is well known that alcohol is a universal solvent with moderate polarity, allowing it to extract and isolate a majority of phytochemical constituents. The use of water suggests that many polar compounds are readily soluble in urine, which may indicate their potential mechanisms of action in the eradication or prevention of kidney stones. Our findings align with previous systematic reviews that concluded that nearly all plant organs extracted using various methods of extraction demonstrated significant anti-urolithiatic activity (Allam and Sabra, 2024; Khan et al., 2021). Khan et al. (2021) concluded in their review that various mechanisms of action are involved in the eradication of kidney stones, along with antioxidant and anti-inflammatory effects.

Previous studies have identified various types of phytochemical constituents present in active extracts (or fractions) that exhibit remarkable anti-urolithiatic activity. Almost all phytochemical groups have provided with active compounds with anti-urolithiatic activity (Fig. 6).

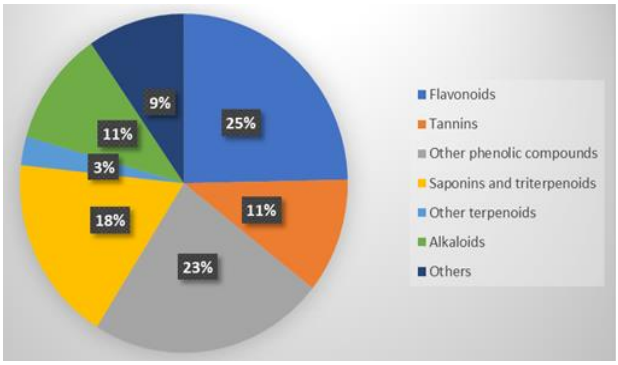

Figure 6. The percentage of active phytochemical constituents contributed to the anti-urolithiatic activity of medicinal plants.

The isolated active compounds prove our findings because they are belonging to different phytochemical groups (Fig. 2). We observed that phenolic and polyphenolic compounds are the dominant, as flavonoids and tannins contributed with 25% and 11%, respectively, while other phenolic compounds (like coumarins, chromones and their furano-derivatives) showed out with 23%. Saponin glycosides, including steroidal and triterpenoidal constituents, contributed 18%, while alkaloids contributed 11%. Therefore, almost all secondary metabolites supplied us with different active phytochemical constituents that have huge differences in their chemical structures. This indicates that natural products (especially medicinal plants) are rich in many chemical compounds that can act as anti-urolithiatic by different and various mechanisms of action. These variations in the chemical structures of active constituents, with their variations in mechanisms of action, allow us to think and search more on synergistic formulations of these constituents, and studying their pharmacokinetic and pharmacodynamics profiles, this

is the unique properties of discovering and developing new drugs from natural products and medicinal plants.

Regarding essential oils, our review revealed that only two articles demonstrated significant anti-urolithiatic activity through the use of essential oils derived from *Nigella sativa* and *Mentha piperita*. This raises two possibilities: either essential oils have not been extensively studied for their anti-urolithiatic effects, or they may not be effective in this regard. Generally, essential oils consist of molecules that belong to categories such as monoterpenes, sesquiterpenes, low-molecular-weight hydrocarbons, or low-molecular-weight phenolic and hydroxyl compounds. For a molecule to exert its pharmacological effects as an anti-urolithiatic agent, it must be polar (or moderately polar) to ensure solubility in urine. Considering the active essential oils identified in our review, their effectiveness may be attributed to the phenolic and hydroxyl content, as these are moderately polar molecules that facilitate solubility in urine. These observations underscore the importance of conducting extensive research on essential oils, particularly those characterized by a high content of phenolic and hydroxyl compounds, such as *Nigella sativa* and *Mentha piperita*.

CONCLUSION

All plant parts (organs) have provided us with anti-urolithiatic active extracts, fractions, pure active compounds, and essential oils. The variations in cellular structures of these organs necessitate different extraction methods; therefore, cold extraction methods were applied in approximately 55% of the collected articles, compared to 45% that used hot extraction methods. Almost all phytochemical compounds and secondary metabolites provided us with potential anti-urolithiatic activity; phenolic and polyphenolic compounds were the dominant, mainly flavonoids, followed by saponin glycosides, alkaloids, and others. The differences in chemical structures, biologically, indicate different mechanisms of action. Extensive research is required to examine the ability of essential oils in the eradication of kidney stones, especially those with high simple phenolic and hydroxyl content. Therefore, we recommend conducting further research on synergistic formulations of these constituents and investigating their pharmacokinetic and pharmacodynamic profiles.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Contribution	Osman W	Elsadig T	Mirghani M	Mohamed MS	Elamin KM	Alqarni MH	Foudah AI	Ashour A	Sherif AE
Concepts or ideas	x	x	x						
Design				x	x		x		
Definition of intellectual content				x					
Literature search	x	x	x						
Experimental studies									
Data acquisition	x	x					x	x	
Data analysis					x	x			x
Statistical analysis					x	x			x
Manuscript preparation	x	x							
Manuscript editing			x	x		x	x	x	x
Manuscript review	x	x	x	x	x	x	x	x	x

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Supplementary Data

Table S1. Risk of bias assessment according to Critical Appraisal Skills Programme (CASP, 2018) checklist, which contains 10 questions.

No.	Included studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	score
1	Ahmad et al., 2022	√	√	√	√	√	√	√	√	√	√	10
2	Ardakani et al., 2019	√	√	√	√	√	√	√	√	√	√	10
3	Atmani et al., 2003	√	√	√	√	√	√	√	√	√	√	10
4	Azaryan et al., 2017	√	√	√	√	√	√	√	√	√	√	10
5	Bahuguna and Kumar, 2014	√	√	√	√	√	√	√	√	√	√	10
6	Bashir and Gilani, 2009	√	√	√	√	√	√	√	√	√	√	10
7	Bashir and Gilani, 2011	√	√	√	√	√	√	√	√	√	√	10
8	Byahatti et al., 2010	√	√	√	√	√	√	√	√	√	√	10
9	Cechinel-Zanchett et al., 2021	√	√	√	√	√	√	√	√	√	√	10
10	Chattaraj et al., 2023	√	√	√	√	√	√	√	√	√	√	10
11	Chaudhary et al., 2022	√	√	√	√	√	√	√	√	√	√	10
12	Cheraft-Bahloul et al., 2017	√	√	√	√	√	√	√	√	√	√	10
13	Diana and George, 2013	√	√	√	√	√	CT	√	√	√	√	10
14	Elhadari et al., 2024	√	√	√	√	√	√	√	√	√	√	10
15	Ghalayini et al., 2011	√	√	√	√	√	√	√	√	√	√	10
16	Goudarzi et al., 2021	√	√	√	√	√	√	√	√	√	√	10
17	Heirangkhongjam and Ngaseppam, 2021	√	√	√	√	√	√	√	√	√	√	10
18	Hewagama and Hewawasam, 2022	√	√	√	√	√	√	√	√	√	√	10
19	Hiponia et al., 2019	√	√	√	√	√	√	√	√	√	√	10
20	Islam et al., 2022	√	√	√	√	√	√	√	√	√	√	10
21	Jamshed and Jabeen, 2021	√	√	√	√	√	√	√	√	√	√	10
22	Jha et al., 2016	√	√	√	√	√	√	√	√	√	√	10
23	Kain et al., 2021	√	√	√	√	√	√	√	√	√	√	10
24	Kaleeswaran et al., 2019	√	√	√	√	√	√	√	√	√	√	10
25	Kanlaya and Thongboonkerd, 2019	√	√	√	√	√	√	√	√	√	√	10
26	Kaviraj et al., 2022	√	√	√	√	√	√	√	√	√	√	10
27	Kumar, 2022	√	√	√	√	√	√	√	√	√	√	10
28	Madhu et al., 2012	√	√	√	√	√	√	√	√	√	√	10
29	Magharbeh et al., 2020	√	√	√	√	√	√	√	√	√	√	10
30	Mahan et al., 2024	√	√	√	√	√	√	√	√	√	√	10
31	Makasanaa et al., 2014	√	√	√	√	√	√	√	√	√	√	10
32	Manjula, 2012	√	√	√	√	√	√	√	√	√	√	10
33	Marhoume et al., 2021	√	√	√	√	√	√	√	√	√	√	10
34	Menon et al., 2022	√	√	√	√	√	√	√	√	√	√	10
35	Menon et al., 2024	√	√	√	√	√	√	√	√	√	√	**10**
36	Mosquera et al., 2020	√	√	√	√	√	√	√	√	√	√	10
37	Naga et al., 2014	√	√	√	√	√	√	√	√	√	√	10
38	Nizami et al., 2012	√	√	√	√	√	√	√	√	√	√	10
39	Noorulla et al., 2024	√	√	√	√	√	√	√	√	√	√	10
40	Orhan et al., 2015	√	√	√	√	√	√	√	√	√	√	10
41	Pandhare et al., 2021	√	√	√	√	√	√	√	√	√	√	10
42	Patel et al., 2012	√	√	√	√	√	√	√	√	√	√	10
43	Peerapen et al., 2022	√	√	√	√	√	√	√	√	√	√	10
44	Pourahmadi et al., 2023	√	√	√	√	√	√	√	√	√	√	10
45	Rad et al., 2011	√	√	√	√	√	√	√	√	√	√	10
46	Rashid et al., 2023	√	√	√	√	√	√	√	√	√	√	10
47	Rashidi et al., 2022	√	√	√	√	√	√	√	√	√	√	10
48	Sahu and Singh, 2022	√	√	√	√	√	√	√	√	√	√	10
49	Saleem et al., 2021	√	√	√	√	√	√	√	√	√	√	10
50	Saremi et al., 2015	√	√	√	√	√	√	√	√	√	√	10
51	Sharma et al., 2016	√	√	√	√	√	√	√	√	√	√	10
52	Sharma et al., 2024	√	√	√	√	√	√	√	√	√	√	10
53	Sikarwar et al., 2017	√	√	√	√	√	√	√	√	√	√	10
54	Sinaga et al., 2018	√	√	√	√	√	√	√	√	√	√	10
55	Wang et al., 2020	√	√	√	√	√	√	√	√	√	√	10
56	Wientarsih et al., 2012	√	√	√	√	√	√	√	√	√	√	10
57	Yachi et al., 2018	√	√	√	√	√	√	√	√	√	√	10
58	Yao et al., 2024	√	√	√	√	√	√	√	√	√	√	10
59	Zaki et al., 2019	√	√	√	√	√	√	√	√	√	√	10
60	Abdel-Aal et al., 2009	√	√	√	√	√	CT	√	√	√	√	09
61	Aghamirei et al., 2022	√	√	√	√	√	CT	√	√	√	√	09

Table S1. Risk of bias assessment according to Critical Appraisal Skills Programme (CASP, 2018) checklist, which contains 10 questions (continue...)

No.	Included studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	score
62	Dinnimath et al., 2017	√	√	√	√	√	CT	√	√	√	√	09
63	Frąckowiak et al., 2010	√	√	√	CT	√	√	√	√	√	√	09
64	İbrahim and El-Khateeb, 2013	√	√	√	CT	√	√	√	√	√	√	09
65	Indriatmoko et al., 2022	√	√	√	√	√	CT	√	√	√	√	09
66	Kachkoul et al., 2023	√	√	√	√	√	CT	√	√	√	√	09
67	Kanlaya et al., 2024	√	√	√	√	√	CT	√	√	√	√	09
68	Onaran et al., 2016	√	√	√	√	√	CT	√	√	√	√	09
69	Pauzi et al., 2019	√	√	√	√	√	CT	√	√	√	√	09
70	Raj et al., 2024	√	√	√	√	√	CT	√	√	√	√	09
71	Saha and Verma, 2013	√	√	√	√	√	CT	√	√	√	√	09
72	Saleh et al., 2013	√	√	√	√	√	CT	√	√	√	√	09
73	Siddiqui et al., 2018	√	√	√	CT	√	√	√	√	√	√	09
74	William et al., 2025	√	√	√	CT	√	√	√	√	√	√	09
75	Zarei and Rhmani, 2015	√	√	√	√	√	CT	√	√	√	√	09
76	Atmani and Khan, 2000	√	√	√	CT	√	CT	√	√	√	√	08
77	Chaudhary et al., 2010	√	**CT**	√	CT	√	√	√	√	√	√	08
78	Coşkun et al., 2022	√	√	√	CT	√	**CT**	√	√	√	√	08
79	Niharika et al., 2018	√	√	√	CT	√	CT	√	√	√	√	08
80	Ranaweera et al., 2023	√	√	CT	CT	√	√	√	√	√	√	08
81	Sairi et al., 2019	√	√	CT	CT	√	√	√	√	√	√	08

The 10 questions are: Q1: Was there a clear statement of the aims of the research? **Q2:** Is a qualitative methodology appropriate? **Q3:** Was the research design appropriate to address the aims of the research? **Q4:** Was the recruitment strategy appropriate to the aims of the research? **Q5:** Was the data collected in a way that addressed the research issue? **Q6:** Has the relationship between the researcher and participants been adequately considered? **Q7:** Have ethical issues been taken into consideration? **Q8:** Was the data analysis sufficiently rigorous? **Q9:** Is there a clear statement of findings? **Q10:** How valuable is the research? **"(√) = Yes", "(x) = No", "CT" = Cannot tell"**.