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Review Article

Antiuro lithiatic Potential of *Tagetes erecta*: A Review of Its Phytochemistry and Pharmacological Insights

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ABSTRACT

Urolithiasis, or urinary stones are a common illness with few treatment choices and a high recurrence rate. Traditionally used in a variety of ethnomedicinal systems, *Tagetes erecta*, a member of the Asteraceae family, is currently receiving attention for its possible antiuro lithiatic properties. The phytochemical components and pharmacological data that support *T. erecta*'s usage in urolithiasis prevention and management are highlighted in this review. Flavonoids (quercetagenin, quercetin), tannins, phenolic acid, saponins, and carotenoids (lutein and zeaxanthin) are all found in *T. erecta*, according to phytochemical investigations. These substances have diuretic, anti-inflammatory, and antioxidant qualities that are essential for preventing calcium oxalate crystals from forming and aggregating. *T. erecta* hydroalcoholic extracts lower urinary calcium, oxalate, and phosphate levels while enhancing renal antioxidant status and histological architecture, according to experimental research conducted on rats by using ethylene glycol and Na-oxalate-induced urolithiasis models. According to the data, *T. erecta* exhibits strong antiuro lithiatic action via a variety of pathways. However, more research is needed with an emphasis on clinical validation, bioactive separation, and molecular pathways. The therapeutic potential of *T. erecta* as a herbal treatment for urolithiasis is supported by this review.

INTRODUCTION

Kidney stone disease, also known as urolithiasis, is a common urological condition marked by the development of calculi in the urinary tract. Urolithiasis has been becoming more common worldwide; research shows that its lifetime

frequency in Western nations ranges from 3% to 5% for females and from 8% to 19% for males ^[1]. Approximately 1 out of 11 people in the US are impacted, which results in high medical costs and more than a million-emergency room visits each year ^[2]. The pathophysiology of urolithiasis is complex and includes crystal nucleation,

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development, aggregation, retention in the kidneys, and supersaturation of urine with components that cause stones. Stone formation is affected by various factors, such as metabolic disorders, genetic susceptibility, dietary habits, and dehydration [3]. The most prevalent kinds of stones include cystine, struvite, uric acid, calcium phosphate, and calcium oxalate [4].

Epidemiology and Socioeconomic Burden

Urolithiasis is a common condition that is becoming more common in many parts of the world. Despite a minor drop in age-adjusted incidence rates, the Global Burden of Disease Study, according to the 2019 Disease Study, there were 115.55 million annual cases in 2019 compared to 77.78 million in 1990 [5]. Its prevalence is largely caused by hot weather and inadequate fluid intake in regions like the Middle East and South Asia. About 8.4% of people in the US are impacted, and men are more vulnerable [6]. A significant financial burden is also imposed by urolithiasis because of recurrent episodes, numerous hospital stays, and surgical procedures, all of which raise direct and indirect medical expenses [7].

Etiology and Risk Factors

Urolithiasis is caused by a confluence of various factors such as environmental, metabolic, & hereditary. Urinary excretion of chemicals that create stones is increased by conditions such as cystinuria and hyperoxaluria [8]. Metabolic disorders including hypocitraturia and hypercalciuria also contribute to the development of stones by upsetting the equilibrium between inhibitors and promoters of crystallization [9]. Excessive ingestion of animal protein, sodium, and oxalate, along with dehydration, obesity, and alcohol use, are external risk factors that raise urine concentrations or acidity, which promotes the development of stones [10].

Types and Composition of Urinary Stones

The classification of urinary stones is based on their chemical makeup, which influences how they develop, are diagnosed, and are treated. Approximately 75–85% of cases are calcium stones, which are the most prevalent type. These mostly consist of calcium oxalate stones, which are associated with metabolic problems and arise in urine that is supersaturated with calcium and oxalate. Usually, these stones form in alkaline urine [11]. Gout, metabolic syndrome, and excessive purine intake are linked to uric acid stones, which make up 5–10% of all stones and develop in acidic urine [12]. Urease-producing bacteria cause struvite stones, also known as infection stones, to form in alkaline urine. These stones frequently form huge staghorn calculi that need to be surgically removed [13]. Cystinuria, a hereditary condition that causes excessive cystine excretion and repeated stone formation, is the cause of rare cystine stones [14].

Pathophysiology of Urolithiasis

Calcium oxalate is the most common type of kidney stone, and it forms along the surfaces of renal papillaries at Randall's plaque. Urinary stone components undergo a complex procedure of creation that includes physicochemical processes such as supersaturation, nucleation, aggregation, and retention inside tubular cells. These processes are impacted when the factors that promote or inhibit urine crystallization are out of balance. Furthermore, cellular injury has been demonstrated to promote particle retention on renal papillary surfaces [15]. In renal epithelial cells, exposure to oxalate sets off a series of signals that ultimately cause apoptosis through p38 MAP-kinase channels. There is currently no effective drug for treating kidney stones or prevent them from occurring in the future. Therefore, a better knowledge of the process underlying kidney stone



formation is one field that is being studied for curing urolithiasis with new drugs. Therefore, the purpose of this study was to provide an extensive overview of the state of knowledge about kidney stone origin, pathophysiology, and prevention

techniques. When lithogenic ions including Ca^{2+} , oxalate, phosphate, and uric acid are supersaturated in urine, their solubility is exceeded and crystallization is allowed, which starts the formation of stones [16].

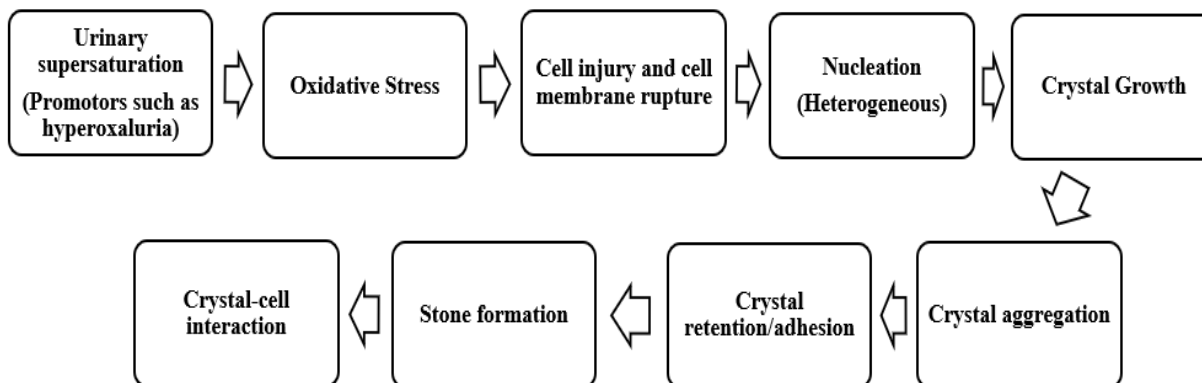


Figure 1: Pathophysiology of Urolithiasis

Limitations of Current Therapies

Surgical and conservative methods are used to treat urolithiasis, depending on the patient's unique circumstances, the size and placement of the stone, and other considerations. Conservative treatment involves dietary changes like cutting back on sodium and animal protein, increasing fluid intake to keep urine output above 2.5 liters per day, and using medications like potassium citrate, thiazide diuretics, or allopurinol to help correct metabolic abnormalities and stop recurrence [17]. Surgical options are taken into consideration when the stones are big, symptomatic, or obstructive. Percutaneous nephrolithotomy (PCNL) is appropriate for big or complex renal calculi, ureteroscopy (URS) works well for mid-to-distal ureteral stones, and extracorporeal shock wave lithotripsy (ESWL) is recommended for renal stones smaller than 2 cm [18]. Treatment-associated problems, recurrence risk, and inconsistent clinical standards are among the issues that persist despite technological advancements.

Potential of Medicinal Plants in Urolithiasis

The investigation of medicinal plants for the treatment of urolithiasis has attracted interest because of their diverse therapeutic qualities and minimal adverse impact profiles. Numerous facets of stone development and advancement can be addressed by phytotherapeutic substances' anti-inflammatory, antioxidant, diuretic, and litholytic properties [19]. In experimental models, a number of plants, including *Coriandrum sativum* (coriander) and *Spinacia oleracea* (spinach), have shown antiurolithiatic properties. These plants work through processes such as diuresis augmentation, urinary pH regulation, and suppression of crystal aggregation. Such herbal therapies could provide accessible and economical alternatives for the prevention treatment of urolithiasis if they are incorporated into clinical practice [20].

Tagetes Erecta

Tagetes erecta, a blooming plant in the Asteraceae family, is also referred to as marigold. Its therapeutic qualities have historically been utilized in many cultures to treat infections, inflammation, and digestive issues [21]. Phytochemical studies

have revealed bioactive compounds such as flavonoids, carotenoids, and essential oils, that increases the plant's potential for medicinal application [22]. *T. erecta* extracts have been shown in recent research to have diuretic and natriuretic actions in animal models, indicating a possible function in encouraging urine evacuation and avoiding the formation of stones. In light of its pharmacological characteristics and historical application in treating renal conditions, *T. erecta* shows promise as a subject for additional research in the treatment of urolithiasis [23].

Botanical Description

The aromatic herb *T. erecta* can reach a height of 120 cm and is erect and branching. It has big, solitary flower heads made of ray and disc florets, as well as pinnately split leaves with serrated edges. The inflorescences might be rich orange or golden yellow in hue. An achene is the fruit, and the essential oil in the plant gives it a powerful aroma. Mostly found in tropical and subtropical areas, it can flourish in a range of soil types and climates and is spread by seeds [24].



Character	Description
Habit	Erect, annual, herbaceous plant
Height	Typically, 30–100 cm
Stem	Erect, cylindrical, branched, and grooved; glabrous or sparsely pubescent
Leaves	Pinnately divided, aromatic, dark green; leaflets are lanceolate with serrated margins
Flowers	Large, solitary or clustered; colours range from bright yellow to deep orange; composite inflorescence (capitulum) composed of ray and disc florets
Fruit	Achenes, oblong, dark brown to black with a pappus of two to three scales
Root	Taproot system

Figure 2: *Tagetes erecta* plant and its botanical description

Geographical Distribution

Originally indigenous to Mexico and Central America, *T. erecta* is now grown all over the world, particularly in the southern United States, China, India, and Africa. It is an essential part of these areas' traditional medicinal systems as well as commercial agriculture [25].

Traditional and Medicinal Uses

Tagetes erecta has been used traditionally for therapeutic purposes in many cultures, according to ethnopharmacological archives. Because of its remarkable antibacterial and wound-healing qualities, plant has been used extensively to treat wounds and skin infections. Additionally, it has

long been used to treat eye conditions, especially conjunctivitis. *T. erecta* has been used in the field of gastrointestinal health to treat conditions like diarrhea [26].

Phytochemical Investigations of *Tagetes erecta*

The therapeutic benefits of *Tagetes erecta* are attributed to its abundance of various bioactive substances. One of *T. erecta*'s most prevalent secondary metabolites are flavonoids, which are especially prevalent in the petals. Patuletin, kaempferol, isorhamnetin, quercetagenin, and its glycosides have all been found using sophisticated analytical methods including LC-MS and HPLC-DAD [27]. Total flavonoid concentration has been observed to vary between 15 and 25 mg QE/g dry

extract, depending upon the solvent used and the maturation stage of the plant. These flavonoids have a substantial role in both pigmentation as well as antioxidant activity^[28,29]. Reverse-phase HPLC is used to quantify the presence of phenolic acids, such as gallic acid, chlorogenic acids, caffeic acid, ellagic acid, and syringic acid, at about 8–12 mg GAE/g dry extract. The DPPH and ABTS tests show that these substances improve the plant's ability to scavenge free radicals^[30,31]. Using GC-MS, terpenoids and phytosterols like stigmasterol, erythrodiol, lupeol, and β -amyirin have been found. The leaves and stems are very rich in these; the total terpenoid content is estimated to be 20–30 mg/g, and GC-FID is used to quantify specific sterols, such as stigmasterol, between 0.5 and 1.2 mg/g^[32]. Petal chromoplasts have been shown to include carotenoids such as lutein (15mg/100g), zeaxanthin (5-8mg/100g), violaxanthin, and β -carotene (in negligible levels) that are important for colour and eye health. Their concentrations are

affected by environmental elements including light exposure and reach their maximum during full bloom^[33]. Mono- and sesquiterpenes make up the majority of *T. erecta*'s essential oil makeup, according to GC-MS analysis. The main components are limonene (6–10%), (E)-ocimenone (5–7%), β -caryophyllene (3–5%), dihydrotageton (12–15%), (Z)- β -ocimene (35–42%), and (Z)-tageton (7–8%). Fresh leaves and flowers can generate 0.3–0.6% essential oil (w/w) using hydrodistillation. These six volatile chemicals consistently make up more than 80% of the overall oil content, according to studies conducted in different geographical areas^[26]. The traditional and contemporary therapeutic usage of *Tagetes erecta* is justified by the combination of these phytochemicals, which support a wide variety of pharmacological potentials, especially anti-inflammatory, antioxidant, hepatoprotective, diuretic, antibacterial, and antiurolithiatic characteristics.

Phytochemical Class	Major Compounds Identified	Analytical Method	Quantitative Data	Localization
Flavonoids	Quercetagenin, Quercetin, Kaempferol, Isorhamnetin, Patuletin	HPLC-DAD, LC-MS	15–25 mg QE/g dry extract	Concentrated in petals; antioxidant & pigment roles
Phenolic Acids	Gallic acid, Chlorogenic acid, Caffeic acid, Ellagic acid, Syringic acid	Reverse-phase HPLC	8–12 mg GAE/g dry extract	Contribute to antioxidant activity in DPPH and ABTS assays
Terpenoids & Sterols	Lupeol, Erythrodiol, β -Amyrin, Stigmasterol	GC-MS, GC-FID	Terpenoids: 20–30 mg/g; Sterols: 0.5–1.2 mg/g	Enriched in leaves & stems; anti-inflammatory, hepatoprotective properties
Carotenoids & Pigments	Lutein, Zeaxanthin, Violaxanthin, β -Carotene	HPLC-UV	Lutein: up to 15 mg/100 g; Zeaxanthin: 5–8 mg/100 g	Located in petal chromoplasts; varies with light and season
Essential Oils / Volatiles	(Z)- β -Ocimene, Dihydrotagetone, (Z)-Tagetone, Limonene, (E)-Ocimenone, β -Caryophyllene	GC-MS	Oil yield: 0.3–0.6% w/w (fresh); 80% from 6 compounds	Found in fresh leaves and flowers; antimicrobial, diuretic, and antiurolithiatic

Figure 3: Phytochemical Profile of *Tagetes erecta*

Pharmacological Properties of *Tagetes erecta*

Antioxidant Activity

Tagetes erecta's high concentration of phenolics and flavonoids, including quercetagenin and patulitrin, gives it potent antioxidant qualities. Because oxidative stress is a major contributor to many degenerative diseases, these bioactive chemicals help the plant scavenge free radicals and lessen it. The strong antioxidant capacity of *T. erecta* extracts was confirmed by a recent investigation that showed significant DPPH and ABTS radical scavenging activities [24]. Additionally, it has been demonstrated that the antioxidant-rich extract stabilizes oils against oxidation, confirming its usefulness in

pharmaceutical and food preservation applications [27].

Anti-inflammatory Activity

Studies conducted in vitro and in vivo shown that *T. erecta* has anti-inflammatory properties. According to one study, the plant's extract effectively decreased inflammation by modifying important inflammatory indicators and reducing neutrophil migration²¹. Furthermore, in a rat model of ulcerative colitis *T. erecta* extract enhanced with lutein dramatically decreased inflammatory cytokine levels while simultaneously enhancing indicators for oxidative stress. These results bolster its possible application in the treatment of inflammatory conditions [28].

Antimicrobial Activity



Broad-spectrum antibacterial activity has been demonstrated by *T. erecta* extracts. Ethanolic floral extracts demonstrated efficacy against a number of bacterial and fungal species, such as *Candida albicans*, *Staphylococcus aureus*, and *E. coli*, in a preliminary study³⁴. When combined with traditional antibiotics, solvent-based extracts showed synergistic action, according to another study assessing them³⁵. This demonstrates its potential for creating substitute antibacterial agents.

Diuretic and Natriuretic Effects

Recent pharmacological studies have substantiated the traditional usage of *T. erecta* as a diuretic. Both hypertension and normotensive rats' sodium excretion and urine volume were markedly elevated by a hydroethanolic floral extract. Bioactive substances may interact with muscarinic acetylcholine receptors to enhance renal fluid excretion and provide this diuretic action²³.

Antidiabetic Activity

T. erecta has shown to have antidiabetic properties through α -glucosidase inhibition, which helps regulate blood glucose levels after meals. Flower extracts were found to strongly block enzymes that hydrolyze carbohydrates in one research³⁶. Furthermore, in diabetic mice administered *T. erecta* extract, an in vivo investigation showed decreased blood glucose and enhanced insulin sensitivity³⁷.

Hepatoprotective Activity

It is also well known that *T. erecta* has hepatoprotective properties. In models of hepatotoxicity caused by CCl_4 , the extract restored liver histology, strengthened antioxidant defenses, and dramatically decreased liver enzyme levels. An additional investigation employing ethanol-

induced liver damage validated the plant's ability to restore biochemical markers and hepatic architecture³⁸.

Mechanistic Relevance to Urolithiasis

Oxidative Stress role in Urolithiasis

The pathophysiology of urolithiasis is significantly influenced by oxidative stress. One important step in the growth of kidney stones is the adhesion and retention of calcium oxalate crystals, which might be facilitated by reactive oxygen species (ROS) and free radicals damaging renal tubular epithelial cells. Additionally, oxidative injury raises inflammation and lipid peroxidation, which encourages crystal aggregation and the formation of stones²⁴. Strong antioxidants like phenolic acids, carotenoids (lutein, zeaxanthin), & flavonoids (quercetagenin, patuletin) are abundant in *Tagetes erecta*. These substances may shield renal tissues from damage brought on by crystals by reducing oxidative stress and neutralizing ROS. Through tests like DPPH and ABTS, research has confirmed the antioxidant potential of *T. erecta* extracts, thereby bolstering their application in conditions like urolithiasis that are linked to oxidative stress³⁹.

Anti-inflammatory Effects and Renal Protection

Inflammation aggravates kidney damage caused by crystals. Further epithelium damage and fibrosis result from calcium oxalate crystals activating NLRP3 inflammasomes and stimulating the production of inflammatory cytokines such IL- 1β , TNF- α , and IL-6. By inhibiting inflammatory mediators, *Tagetes erecta* demonstrates potent anti-inflammatory properties. The plant's flavonoids inhibit the release of pro-inflammatory cytokines, COX-2 expression, and NF- κ B activation. These exercises can lessen renal

inflammation brought on by crystals, preventing tissue damage and delaying the course of urolithiasis^[40].

Diuresis and Urinary Stone Prevention

By diluting urine and lowering the supersaturation of lithogenic salts like calcium and oxalate, diuresis is a basic treatment approach for preventing kidney stones^[41]. Aqueous and hydroalcoholic *Tagetes erecta* extracts have been demonstrated in numerous investigations to enhance electrolyte excretion and urine production. Because its flavonoids and essential oils alter renal tubular transit, they are thought to have a diuretic impact. In order to reduce the danger of stone formation, increased urine flow which can help in the removal of tiny crystals and lessen their aggregation^[23].

Synergistic Action of Bioactive Compounds

Tagetes erecta's diverse defensive benefits are the result of the complex phytochemical profile's synergistic activity rather than a single molecule. Collectively, flavonoids, phenolic acids, carotenoids, and essential oils have the following effects: they have antioxidant properties by neutralizing free radicals; they have anti-inflammatory properties by suppressing inflammatory pathways; and they have a diuretic effect by encouraging urine production and solute excretion. Its status as a viable antiurolithiatic option is greatly enhanced by this combination. Studies indicate that plant-based remedies with several active ingredients frequently provide better protective outcomes, mostly as a result of the elements' additive or synergistic interactions^[42].

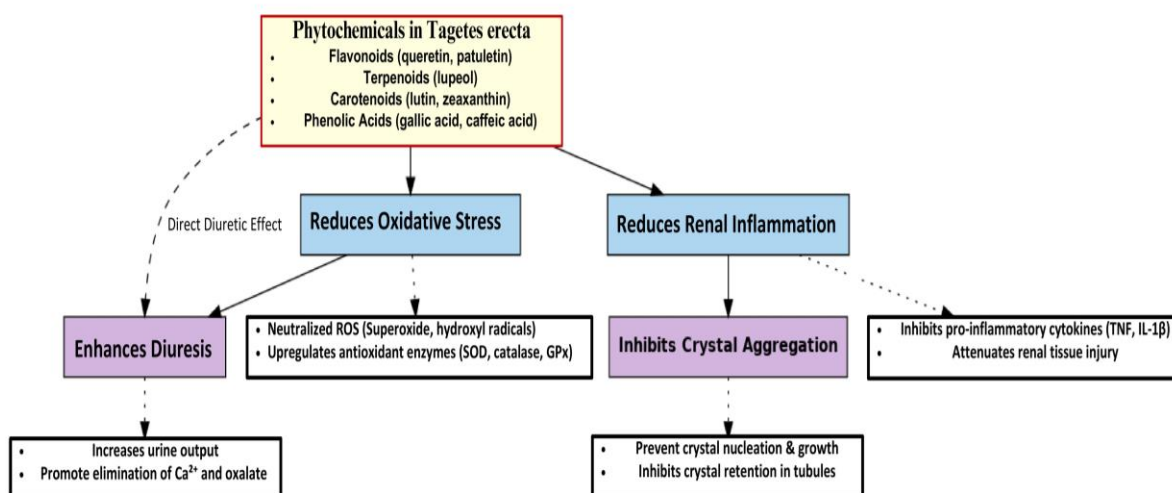


Figure 4: Proposed Mechanisms of Antiurolithiatic Action of *Tagetes erecta*.

Rationale for Investigating *Tagetes erecta* in Urolithiasis

Justification Based on Existing Pharmacology

Tagetes erecta (marigold) has a variety of phytochemical elements, such as flavonoids, carotenoids, and phenolic acids, which make it a

promising treatment for urolithiasis. Its potent antioxidant, anti-inflammatory, and diuretic properties—all of which are intimately related to preventing kidney stones—are attributed to these bioactive substances. Because it damages renal tubular cells and encourages crystal aggregation, oxidative stress is a major factor in urolithiasis. *T. erecta* extracts have shown strong free radical

scavenging activity, which lessens this damage [43]. Further supporting kidney protection are its anti-inflammatory properties, which are mediated by suppression of pro-inflammatory cytokines such as TNF- α and IL-6²¹. Additionally, the plant has calcium-sparing and diuretic qualities that help lower the concentration of urine solutes and prevent the crystallization of calcium oxalate [23]. Experimental investigations and traditional use of *T. erecta* for kidney diseases in Mesoamerican medicine highlight the plant's potential as a natural antiurolithiatic agent [44].

Gaps in Research and Scope for Novel Investigation

Tagetes erecta has a long history of traditional use and a promising pharmacological profile, but its clinical translation in the treatment of urolithiasis is hampered by a number of important research gaps. The majority of existing research is restricted to preclinical models, underscoring the pressing necessity for carefully planned clinical trials to validate its effectiveness and safety in human beings [45]. Furthermore, it is still mostly unclear how exactly *T. erecta* produces its possible antiurolithiatic properties. To comprehend the cellular and molecular pathways involved, in-depth mechanistic investigations are necessary. The absence of standardization for *T. erecta* extracts is another major drawback, since variations in phytochemical content might have a big impact on treatment results. Future applications would be more consistent and reliable if standardized procedures were established and bioactive markers were found. Furthermore, *T. erecta*'s ethnopharmacological significance—specifically, its application in traditional Mayan medicine for kidney problems—provides a solid basis that demands additional scientific verification. Closing these gaps could help facilitate the incorporation of *T. erecta* into

evidence-based phytotherapy and greatly accelerate the development of *T. erecta*-based therapies for urolithiasis [46,47].

CONCLUSION:

Tagetes erecta holds significant potential as a natural antiurolithiatic agent due to its rich phytochemical profile, which includes terpenoids, flavonoids, carotenoids, and phenolic acids, all of which contribute to its complex pharmacological effects. The strong diuretic, anti-inflammatory, antibacterial, and antioxidant qualities of these bioactive substances are all mechanistically related to the treatment and prevention of urolithiasis. While anti-inflammatory components aid in reducing renal inflammation frequently linked to stone formation, antioxidant elements may shield renal tissues from oxidative damage caused by oxalate. Its diuretic actions also boost urine production, which helps diluting and removal of lithogenic chemicals. These medicinal potentials are supported by preliminary experimental data and ethnopharmacological research. Nevertheless, *T. erecta*'s unique antiurolithiatic action has not been extensively investigated despite these encouraging characteristics. The conversion of traditional use into evidence-based medicines is hampered by critical gaps such as a lack of rigorous clinical studies, standardized extract preparations, and mechanistic understanding. Therefore, *Tagetes erecta* may become a useful natural agent for the alternative or adjunctive treatment of kidney stone disease with thorough phytochemical standardization and targeted multidisciplinary research.

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