

CASSIA FISTULA L. IN UROLITHIASIS: PHYTOCHEMISTRY, BIOACTIVE CONSTITUENTS AND EXPERIMENTAL EVIDENCE OF ANTIUROLITHIATIC POTENTIAL

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ABSTRACT

Cassia fistula L. (Fabaceae), commonly known as Amaltas or the Golden Shower Tree, has been used in traditional medicine for the treatment of various ailments and has received considerable attention for its diverse phytochemical and pharmacological properties. However, information connecting its phytochemical constituents with its possible role in urolithiasis is still scattered. This review brings together the available information on the phytochemistry, isolation and characterization of bioactive constituents, pharmacological activities, and experimental evidence related to the antiurolithiatic potential of *Cassia fistula*. Different parts of the plant have been reported to contain anthraquinones, flavonoids, phenolic compounds, tannins, terpenoids, glycosides, and other secondary metabolites. These constituents have been investigated using analytical techniques including HPTLC, HPLC, LC–MS/MS, GC–MS, FTIR, and NMR spectroscopy.

Studies on the plant have also reported antioxidant, anti-inflammatory, nephroprotective, diuretic, analgesic, and antibacterial activities, some of which may be relevant to the processes involved in urinary stone formation. Direct evidence for antiurolithiatic activity is limited but includes inhibition of calcium oxalate crystal nucleation and aggregation in vitro and reduction of crystal deposition in experimental models. However, the constituents

responsible for these effects and the mechanisms involved have not yet been clearly established. Further work involving standardized extracts, isolation of active constituents, mechanistic studies, safety evaluation, and clinical investigation is needed to determine the actual therapeutic value of *Cassia fistula* in urolithiasis.

KEYWORDS: *Cassia fistula*; urolithiasis; antiurolithiatic activity; HPTLC; LC–MS/MS; nephrolithiasis.

1. INTRODUCTION

Urolithiasis, commonly known as kidney stone disease, is one of the most prevalent disorders affecting the urinary tract and continues to pose a substantial healthcare challenge worldwide. Its incidence has increased steadily over recent decades because of changes in lifestyle, dietary habits, metabolic disorders, and environmental factors. Stone formation is a complex process initiated when urine becomes supersaturated with lithogenic substances, resulting in crystal nucleation, growth, aggregation, and eventual retention within the renal collecting system. Calcium oxalate constitutes the principal component of most urinary calculi, while obesity, diabetes mellitus, hypertension, inadequate fluid intake, and metabolic syndrome are recognized as important risk factors that contribute to both disease development and recurrence. Although advances in minimally invasive procedures have improved stone removal, recurrence remains frequent, highlighting the need for safe preventive strategies and alternative therapeutic approaches capable of targeting the underlying mechanisms of lithogenesis.^[1]

The development of urinary stones is influenced by a combination of physicochemical, metabolic, and biological factors rather than a single pathological event. Crystal formation begins when lithogenic substances in urine exceed their solubility limits, leading to nucleation, crystal growth, aggregation, and subsequent retention within the kidneys. In addition to urinary supersaturation, oxidative stress, renal epithelial injury, and inflammatory responses have been recognized as important contributors to crystal adherence and persistence. Current management includes increased fluid intake, dietary modification, pharmacotherapy, extracorporeal shock wave lithotripsy, ureteroscopy, and percutaneous nephrolithotomy. Although these approaches are generally effective for stone removal, they do not completely eliminate the risk of recurrence and may be associated with adverse effects or high treatment costs. Consequently, there is growing interest in identifying plant-derived

therapeutic agents capable of preventing stone formation while simultaneously protecting renal tissue from crystal-induced damage.^[2]

The increasing recurrence of urolithiasis and the limitations associated with existing therapeutic approaches have encouraged researchers to explore medicinal plants as potential sources of safer and more effective antiurolithiatic agents. Traditional systems of medicine have long utilized numerous plant species for the management of urinary disorders, and many of these remedies are now being scientifically investigated for their ability to inhibit crystal formation and protect renal function. Their therapeutic effects are often attributed to the presence of bioactive secondary metabolites such as flavonoids, phenolic compounds, saponins, alkaloids, terpenoids, and glycosides, which exhibit antioxidant, anti-inflammatory, diuretic, and nephroprotective activities. Unlike single-target synthetic drugs, these phytoconstituents may influence multiple stages of lithogenesis simultaneously, making medicinal plants attractive candidates for the prevention and management of urinary stone disease.^[3]

Among medicinal plants explored for the prevention and management of urolithiasis, *Cassia fistula* L. has attracted increasing scientific interest because of its chemically diverse secondary metabolites and experimentally validated biological activities. Phytochemical investigations have identified anthraquinones, flavonoids, phenolic compounds, tannins, glycosides, and several other constituents from different parts of the plant, while advanced analytical techniques such as HPTLC, HPLC, LC–MS/MS, GC–MS, FTIR, and NMR spectroscopy have improved their identification and structural characterization. In addition to phytochemical studies, experimental investigations have demonstrated antioxidant, anti-inflammatory, nephroprotective, and antiurolithiatic properties, highlighting the potential of *Cassia fistula* as a source of bioactive molecules for kidney stone research. Although these findings are encouraging, the available evidence remains scattered across studies focusing on different aspects of the plant. The present review brings together the existing literature on its phytochemistry, isolation and characterization of bioactive compounds, pharmacological activities, experimental evidence related to urolithiasis, and future directions for research. The major stages involved in urinary stone formation are illustrated in Fig. 1.

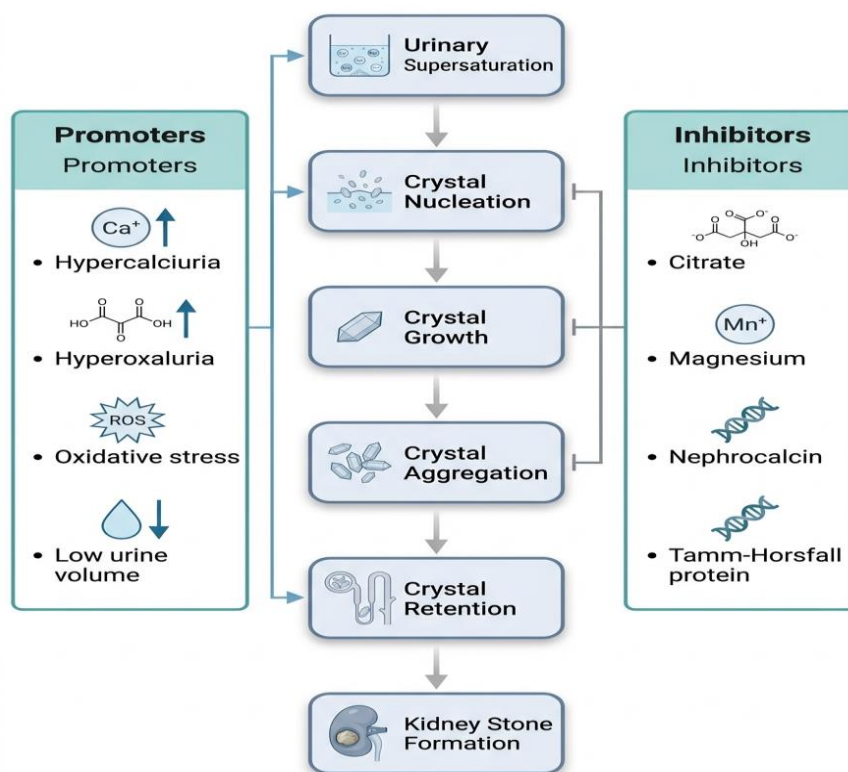


Figure 1: Pathogenesis of urolithiasis illustrating urinary supersaturation, crystal nucleation, crystal growth, aggregation, retention and kidney stone formation.

2. BOTANICAL DESCRIPTION AND ETHNOMEDICINAL IMPORTANCE

Cassia fistula L., popularly known as the Golden Shower Tree or Amaltas, is a medicinal tree belonging to the family Fabaceae (subfamily Caesalpinioideae). Native to the Indian subcontinent, it is widely cultivated and naturally distributed across many tropical and subtropical regions, including India, Sri Lanka, Bangladesh, Myanmar, Thailand, and Malaysia. The species has been valued for centuries in traditional systems of medicine, particularly Ayurveda, where different parts of the plant have been prescribed for the treatment of a variety of ailments. Leaves, flowers, fruits, bark, roots, pods, and seeds are traditionally used for managing constipation, skin disorders, fever, inflammatory conditions, diabetes, liver diseases, microbial infections, and urinary tract disorders. The continued medicinal importance of *Cassia fistula* has stimulated extensive scientific investigations into its phytochemical composition and therapeutic properties, supporting several of its traditional applications. ^[4]

The plant is a medium-sized deciduous tree that commonly reaches 10–20 m in height and is easily recognized by its striking pendulous clusters of bright yellow flowers. It possesses a straight trunk with smooth greyish-brown bark, whereas the leaves are alternate and pinnately

compound, consisting of opposite ovate to elliptic leaflets with entire margins. Mature fruits are long, cylindrical pods that gradually change from green to dark brown or black and contain numerous flattened seeds embedded in a dark, sticky pulp. Such morphological characteristics are useful not only for botanical identification but also for the selection and authentication of plant material intended for phytochemical and pharmacological investigations.^[4]

Scientific investigations have shown that the chemical composition and biological activities of *Cassia fistula* vary among different plant parts. Leaves have been widely investigated for phytochemical screening and antiurolithiatic evaluation, whereas fruits, bark, roots, and pods have received greater attention for the isolation of bioactive compounds and the assessment of diverse pharmacological properties. These variations highlight the importance of selecting appropriate plant material according to the intended analytical or biological study. Collectively, the available evidence demonstrates that each plant part contributes unique phytoconstituents, reinforcing the medicinal significance of *Cassia fistula* and supporting its continued exploration as a valuable source of natural therapeutic agents.^[4] The main botanical features of *Cassia fistula* are shown in Fig. 2.

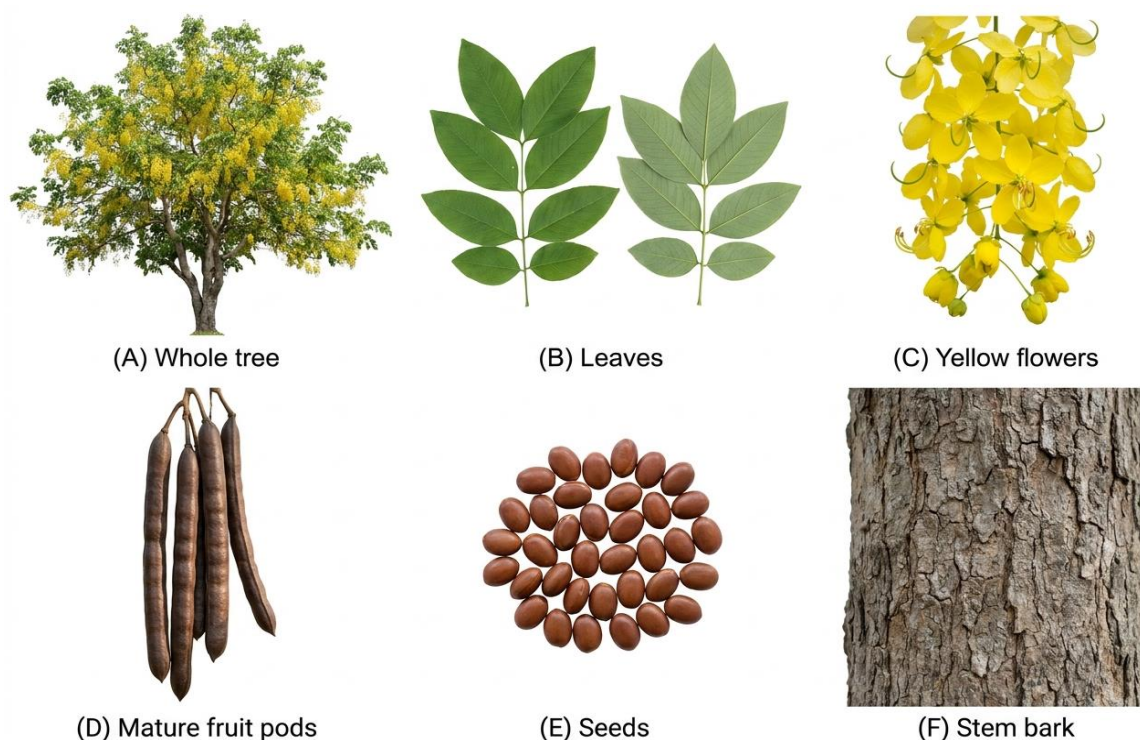


Figure 2: Botanical profile of *Cassia fistula* L. showing whole tree, leaves, flowers, mature fruit pods, seeds and stem bark.

3. PHYTOCHEMICAL INVESTIGATION OF *CASSIA FISTULA* L.

Phytochemical evaluation forms the basis for understanding the medicinal potential of plant species by revealing the diversity of secondary metabolites associated with their biological activities. Investigations on *Cassia fistula* have demonstrated that its chemical composition is influenced by factors such as the plant part selected, extraction solvent, and extraction procedure. Qualitative screening of methanolic leaf extracts has identified flavonoids, phenolic compounds, tannins, saponins, alkaloids, glycosides, carbohydrates, proteins, steroids, terpenoids, and anthraquinones, indicating the presence of multiple classes of bioactive constituents. The observed variation among extracts highlights the importance of optimizing extraction conditions to obtain reproducible phytochemical profiles and ensure reliable biological evaluation.^[5]

Chromatographic fingerprinting has become an essential tool for the authentication and quality assessment of herbal materials. In *Cassia fistula*, HPTLC analysis of leaf extracts prepared using solvents of varying polarity produced characteristic chromatographic profiles with several well-resolved bands, reflecting differences in the distribution of phytochemicals among the extracts. These reproducible fingerprints provide valuable information for plant authentication, quality control, and batch-to-batch consistency, making HPTLC a practical analytical approach for the standardization of *Cassia fistula*-based herbal preparations.^[6]

Quantitative HPTLC analysis has also been used to assess rhein as a marker compound in *Cassia fistula*. Shailajan et al. developed and validated an HPTLC method for the estimation of rhein in different plant parts and in fruit-pulp samples collected from different geographical regions. The study showed noticeable variation in rhein content among the fruit-pulp samples, indicating that geographical origin can influence the concentration of marker compounds. The validated method was considered suitable for routine estimation of rhein and quality assessment of *Cassia fistula*-based herbal materials.^[7]

The use of high-resolution analytical techniques has considerably advanced the characterization of phytochemicals present in *Cassia fistula*. HPLC coupled with UHPLC/LTQ-Orbitrap mass spectrometry enabled detailed profiling of fruit extracts and facilitated the identification of characteristic marker compounds with high sensitivity and mass accuracy. The structural information generated through this analytical platform not only supports qualitative phytochemical profiling but also contributes to the selection of suitable markers for quality assurance and standardization of plant-derived materials.^[8]

Further expansion of the phytochemical profile has been achieved through GC–MS analysis of stem bark extracts. This approach enabled the detection of numerous volatile and semi-volatile metabolites, including fatty acid derivatives, hydrocarbons, phenolic constituents, and several other compounds of pharmacological interest. In addition to broadening the chemical database of *Cassia fistula*, GC–MS investigations provide valuable preliminary information for selecting candidate molecules that may be explored in future pharmacological studies and natural product-based drug discovery.^[9]

Comparative chemical profiling of the stem bark and small branches has provided additional information on the distribution of marker compounds in different parts of *Cassia fistula*. Meena et al. examined these plant materials using HPLC, LC–MS and GC–MS and found broadly similar chromatographic profiles between the stem bark and small branches. Rhein was quantified by HPLC, with mean contents of 0.0084% in the stem bark and 0.0257% in the small branches. The study also reported several compounds common to both plant parts, along with additional compounds detected in the small branches, highlighting the influence of plant part on the chemical profile of the species.^[10]

Collectively, these phytochemical investigations demonstrate that *Cassia fistula* possesses considerable chemical diversity that can be explored using complementary analytical techniques. Conventional screening provides preliminary information on the major classes of secondary metabolites, while chromatographic and mass spectrometric methods allow more detailed profiling, marker estimation and identification of characteristic constituents. The observed variation among plant parts and geographical samples also highlights the importance of appropriate authentication and standardization of plant material before pharmacological evaluation.

Table 1: Major phytochemicals identified from different analytical techniques.

Analytical technique	Plant part	Major compounds identified	Significance	Reference
Preliminary phytochemical screening	Leaves	Flavonoids, tannins, saponins, alkaloids, glycosides	Initial qualitative screening	[5]
HPTLC fingerprinting	Leaves	characteristic fingerprint bands	Authentication and standardization	[6]
HPTLC	Leaves/fruit pulp	Rhein	Marker estimation and quality control	[7]
HPLC/UHPLC-LTQ-Orbitrap MS	Fruits	Marker compounds reported in the study	Comprehensive metabolite profiling	[8]

GC-MS	Stem bark	Volatile and semi-volatile phytochemicals reported in the study	Chemical profiling	[9]
HPLC, LC-MS and GC-MS	Stem bark/Small branches	Rhein and other detected constituents	Comparative chemical profiling	[10]

4. ISOLATION AND CHARACTERIZATION OF BIOACTIVE CONSTITUENTS FROM *CASSIA FISTULA* L.

Preliminary phytochemical screening provides useful information regarding the classes of metabolites present in a medicinal plant; however, it cannot identify the individual compounds responsible for specific biological activities. Consequently, the isolation of pure phytoconstituents followed by detailed structural characterization is essential for establishing chemical identity, ensuring quality control, and understanding the relationship between chemical structure and pharmacological activity. Research on *Cassia fistula* has gradually progressed from qualitative phytochemical investigations to the purification and characterization of individual constituents using chromatographic separation techniques in combination with modern spectroscopic methods. These studies have revealed a wide range of chemically distinct metabolites, particularly anthraquinones, flavonoids, phenolic compounds, and glycosides, thereby expanding the phytochemical knowledge of this medicinal species.

One of the notable achievements in the phytochemical investigation of *Cassia fistula* was the successful isolation of fistulic acid, followed by its structural confirmation using complementary spectroscopic techniques. The isolated compound was initially examined by UV spectroscopy to determine its characteristic absorption profile, whereas FTIR analysis was employed to identify the functional groups present within the molecule. Definitive structural confirmation was subsequently obtained through both ^1H and ^{13}C NMR spectroscopy, providing reliable evidence for its molecular identity. The combined use of these analytical techniques established a systematic approach for characterizing phytoconstituents and generated valuable reference information for future investigations involving *Cassia fistula*.^[11]

Subsequent studies further enriched the phytochemical profile of *Cassia fistula* by isolating several anthraquinone derivatives from the roots. These compounds represent one of the characteristic classes of secondary metabolites associated with the genus and are known for a

variety of biological properties, including antioxidant, antimicrobial, and anti-inflammatory activities. Following chromatographic purification, their structures were confirmed using spectroscopic methods such as FTIR and NMR, demonstrating both structural integrity and chemical purity. In addition to their pharmacological relevance, these anthraquinone derivatives contribute to the chemotaxonomic characterization of *Cassia* species and provide promising candidates for future biological evaluation.^[12]

Beyond the isolation of individual compounds, quantitative determination of marker constituents has become an essential aspect of herbal standardization. HPTLC has been successfully utilized to quantify anthraquinone derivatives while simultaneously generating reproducible chromatographic fingerprints for *Cassia fistula*. Such analytical data are valuable for authentication, quality assurance, and maintaining consistency between different batches of herbal materials. Reliable quantification of marker compounds also facilitates compliance with regulatory expectations and improves the reproducibility of phytochemical investigations performed across different laboratories.^[13]

The available studies clearly demonstrate that phytochemical research on *Cassia fistula* has advanced from basic screening procedures to sophisticated isolation and structural characterization of individual bioactive molecules. The integration of chromatographic purification with modern spectroscopic techniques has considerably strengthened the understanding of its chemical composition and established a scientific platform for future structure–activity investigations. Nevertheless, only a limited number of isolated constituents have been evaluated individually for their pharmacological properties. Future research should therefore focus on bioactivity-guided fractionation together with detailed biological assessment to identify the compounds primarily responsible for the reported antiurolithiatic activity.

4.1. Critical Evaluation

Despite the growing number of phytochemical studies on *Cassia fistula*, research focusing on the isolation of pharmacologically active constituents remains comparatively limited when evaluated from a bioactivity-guided perspective. Most published investigations have primarily emphasized preliminary phytochemical screening, chromatographic fingerprinting, or analytical profiling, whereas only a limited number have successfully isolated and structurally characterized individual bioactive compounds. Consequently, the specific constituents responsible for the experimentally observed antiurolithiatic activity remain

largely unidentified. Future investigations should integrate advanced metabolomic techniques with bioactivity-guided fractionation to establish clear relationships between individual phytoconstituents and their therapeutic potential against urolithiasis.

5. PHARMACOLOGICAL ACTIVITIES RELEVANT TO ANTIUROLITHIATIC POTENTIAL

5.1 antioxidant activity

Antioxidant activity is considered one of the most extensively investigated pharmacological properties of *Cassia fistula*. Comparative studies using different extraction solvents demonstrated that the free radical scavenging capacity of the plant is influenced by both solvent polarity and phytochemical composition. Among the extracts evaluated, the methanolic fraction showed the strongest antioxidant activity, which was associated with its higher concentration of phenolic compounds and flavonoids. These observations indicate that optimization of the extraction process is essential for obtaining extracts with improved antioxidant potential and may influence their subsequent pharmacological performance.^[14]

Hydroalcoholic extract prepared from the fruit pulp has also demonstrated appreciable antioxidant activity in established in vitro models. The study attributed this effect to naturally occurring polyphenols and flavonoids present in the extract. Considering that oxidative stress contributes to renal epithelial injury during calcium oxalate stone formation, maintenance of cellular antioxidant defenses may represent one mechanism through which *Cassia fistula* protects renal tissue against crystal-induced damage.^[15]

Further evidence supporting the antioxidant potential of *Cassia fistula* was provided by Ilavarasan et al., who investigated aqueous and methanolic bark extracts using multiple in vitro antioxidant models. The methanolic extract consistently produced superior scavenging of DPPH, nitric oxide, and hydroxyl radicals while effectively reducing lipid peroxidation. Acute toxicity studies further indicated a favorable safety profile at the investigated dose levels. Collectively, these findings reinforce the role of *Cassia fistula* as a promising natural source of antioxidant phytoconstituents with potential applications in renal protection.^[16]

5.2 anti-inflammatory activity

Inflammatory processes play an important role in crystal-induced renal injury and contribute to the progression of calcium oxalate nephrolithiasis. Experimental evaluation of *Cassia fistula* bark extracts demonstrated significant inhibition of both acute and chronic

inflammatory responses in carrageenan-induced paw oedema and cotton pellet granuloma models. Greater activity was consistently observed with the methanolic extract, suggesting that extraction solvent influences the recovery of anti-inflammatory constituents. Since inflammation enhances renal epithelial damage and promotes crystal retention, suppression of inflammatory responses may represent an additional mechanism supporting the antiurolithiatic potential of *Cassia fistula*.^[16]

5.3 analgesic activity

Renal colic associated with urinary stone disease is often severe and remains one of the principal reasons for seeking medical attention. Investigation of the methanolic pod extract of *Cassia fistula* demonstrated significant analgesic activity in experimental animal models, including hot plate, tail clip, and acetic acid-induced writhing tests. The extract produced dose-dependent increases in pain threshold and reduced chemically induced nociceptive responses, indicating both central and peripheral analgesic effects. Although analgesic activity does not directly prevent stone formation, it may provide supportive symptomatic relief when used alongside therapies intended to control or prevent urolithiasis.^[17]

5.4 nephroprotective activity

Protection of renal tissue is an important consideration during the management of urolithiasis because crystal deposition frequently results in tubular injury and impaired renal function. Hydroalcoholic fruit extract of *Cassia fistula* has demonstrated significant nephroprotective activity in bromobenzene-induced nephrotoxicity. Treatment improved serum creatinine and blood urea nitrogen levels while reducing histopathological evidence of tubular degeneration. Preservation of normal renal architecture suggests that the plant may help limit tissue damage and maintain renal function during pathological conditions involving oxidative injury. Such nephroprotective effects further support the therapeutic relevance of *Cassia fistula* in disorders affecting the kidney.^[18]

5.5 diuretic activity

Adequate urine output is a key factor in preventing urinary stone formation because increased urinary flow reduces supersaturation of lithogenic salts and facilitates crystal elimination. Evaluation of aqueous and ethanolic pod extracts of *Cassia fistula* using the Lipschitz model demonstrated significant diuretic activity, accompanied by increased excretion of sodium, potassium, and chloride ions. The ethanolic extract exhibited comparatively greater efficacy, indicating that extraction conditions influence the recovery of diuretic constituents.

Enhancement of urine volume may reduce crystal aggregation and promote the removal of microscopic crystals before clinically significant calculi develop, thereby supporting the proposed antiurolithiatic potential of the plant.^[19]

5.6 antibacterial activity

Although antibacterial activity is not directly associated with calcium oxalate crystallization, it may contribute to maintaining urinary tract health and reducing complications arising from bacterial infections. Successive leaf extracts of *Cassia fistula* have demonstrated activity against both Gram-positive and Gram-negative bacteria, with ethanol and methanol extracts producing the lowest minimum inhibitory concentrations. Bioautographic analysis further confirmed the presence of antibacterial constituents within the active fractions. The antimicrobial effect was attributed to the combined contribution of several phytochemical classes rather than a single compound. While primarily relevant to infectious disorders, this property may indirectly support the prevention of infection-associated urinary complications.^[20]

6. EXPERIMENTAL EVIDENCE OF THE ANTIUROLITHIATIC POTENTIAL OF *CASSIA FISTULA* L.

Although *Cassia fistula* has been extensively investigated for several pharmacological properties, experimental studies specifically evaluating its antiurolithiatic activity remain limited. The currently available evidence is primarily derived from preclinical investigations employing methanolic leaf extracts in both in vitro and in vivo models of urolithiasis. Despite the limited number of studies, the reported findings indicate that the plant possesses the ability to influence multiple stages of stone formation, including crystal nucleation, aggregation, renal crystal deposition, and crystal-induced tissue injury. These preliminary observations provide a scientific basis for further phytochemical and pharmacological investigations aimed at identifying the bioactive constituents responsible for these protective effects.^[21]

6.1 in vitro antiurolithiatic activity

The inhibitory effect of *Cassia fistula* on calcium oxalate crystallization was assessed using an in vitro crystallization model with methanolic leaf extract. The extract produced concentration-dependent inhibition of both crystal nucleation and aggregation, suggesting interference with the earliest physicochemical events involved in urinary stone formation. Because nucleation and aggregation are essential steps in the development of calcium oxalate

calculi, suppression of these processes may reduce crystal growth and limit subsequent stone formation. Although the active phytoconstituents responsible for this activity were not identified, the findings indicate that the extract contains constituents capable of modifying crystal formation under experimental conditions.^[21]

6.2 *in vivo* antiurolithiatic activity

The protective effect of *Cassia fistula* was further demonstrated in an ethylene glycol- and ammonium chloride-induced model of experimental urolithiasis. Oral administration of the methanolic leaf extract resulted in significant improvement of renal biochemical parameters compared with untreated animals, including reductions in urinary calcium, phosphate, serum creatinine, blood urea nitrogen, and uric acid levels. Histopathological examination also revealed reduced crystal deposition together with preservation of normal renal tissue architecture, particularly at higher extract doses. These observations indicate that the extract not only suppresses stone formation but also protects renal tissue from crystal-associated damage, thereby supporting both antiurolithiatic and renoprotective activities.^[21]

6.3 limitations of the available evidence

Despite the encouraging experimental findings, the available evidence is still limited and does not allow definitive conclusions regarding the therapeutic potential of *Cassia fistula* in urolithiasis. The reported antiurolithiatic effects have mainly been demonstrated using crude methanolic leaf extracts, and the specific constituents responsible for inhibition of calcium oxalate crystallization and renal protection have not yet been established. Differences in plant material, extraction procedures, and the absence of detailed phytochemical standardization also make it difficult to compare results across studies. Furthermore, the molecular mechanisms underlying the observed effects remain insufficiently investigated, while pharmacokinetic, long-term safety, and clinical data are currently lacking.^[21]

Future research should therefore focus on linking the observed biological activity with specific phytoconstituents through bioactivity-guided fractionation and appropriate analytical characterization using techniques such as HPTLC, LC–MS/MS, FTIR, and NMR spectroscopy. Studies using chemically standardized extracts and isolated compounds, supported by well-defined experimental models, could help clarify their effects on crystal nucleation, aggregation, renal crystal deposition, and tissue injury. Further mechanistic, pharmacokinetic, and toxicity investigations are also needed before the findings can be considered for clinical translation. Ultimately, well-designed clinical studies will be

necessary to determine whether *Cassia fistula* has a meaningful role in the prevention or management of urolithiasis.^[21]

Table 2: Summary of experimental studies evaluating the antiurolithiatic potential of *Cassia fistula* L.

Study	Plant part	Extract	Experimental model	Major findings	Limitations
[21]	Leaves	Methanolic extract	In vitro: Calcium oxalate crystallization assay	Inhibited crystal nucleation and aggregation	Crude extract; no bioactive compound identified
[21]	Leaves	Methanolic extract	In vivo: Ethylene glycol + ammonium chloride-induced urolithiasis in rats	Improved renal biochemical parameters, reduced crystal deposition, preserved renal histology	Single study; no detailed phytochemical standardization

7. POSSIBLE MECHANISMS UNDERLYING THE ANTIUROLITHIATIC POTENTIAL OF *CASSIA FISTULA* L.

The protective effects of medicinal plants against urolithiasis are generally associated with their ability to influence several stages of stone formation while preserving normal renal function. Rather than acting through a single molecular target, *Cassia fistula* appears to exhibit a multitarget pharmacological profile arising from its diverse phytochemical composition. Although the exact mechanisms responsible for its antiurolithiatic activity have not yet been completely defined, the available evidence indicates that antioxidant, anti-inflammatory, nephroprotective, diuretic, and crystal-modulating properties may act together to reduce calcium oxalate crystal formation and limit crystal-induced renal injury. This complementary mode of action makes *Cassia fistula* an attractive candidate for further investigation as a phytotherapeutic agent for urolithiasis.

7.1 antioxidant-mediated protection

Among the various mechanisms proposed, antioxidant activity appears to be one of the principal contributors to the renoprotective effects of *Cassia fistula*. Excessive production of reactive oxygen species during calcium oxalate nephrolithiasis damages renal tubular epithelial cells, creating favourable sites for crystal adhesion and retention. Experimental studies have demonstrated that methanolic bark extracts possess greater antioxidant activity than aqueous extracts by effectively scavenging free radicals, reducing lipid peroxidation,

and preserving endogenous antioxidant defenses. Maintenance of epithelial integrity through these antioxidant effects may therefore reduce crystal attachment and interrupt an important stage in stone development.^[16]

7.2 regulation of inflammatory responses

Inflammation represents another important event in the progression of crystal-induced renal injury. Calcium oxalate crystals stimulate inflammatory cell infiltration and the release of mediators that aggravate tissue damage and facilitate crystal persistence within the kidney. Experimental evaluation of *Cassia fistula* bark extracts demonstrated marked suppression of both acute and chronic inflammatory responses, with methanolic extracts exhibiting superior activity. Because antioxidant and anti-inflammatory actions occur simultaneously, these pharmacological effects are likely to complement each other in reducing renal injury associated with crystal deposition, although the precise molecular pathways remain to be clarified.^[16]

7.3 contribution of phytochemical constituents

The broad spectrum of phytochemicals identified in *Cassia fistula* provides a plausible explanation for its multitarget pharmacological behaviour. Anthraquinones, flavonoids, phenolic compounds, tannins, terpenoids, and related secondary metabolites have been detected in different plant parts and are known to possess antioxidant, membrane-protective, and nephroprotective properties. Rather than acting independently, these constituents may exert additive or synergistic effects that collectively contribute to the reduction of crystal-induced renal damage. However, because most investigations have evaluated crude extracts, the individual contribution of each phytochemical to the observed antiurolithiatic activity remains to be established.^[5]

7.4 integrated mechanism of antiurolithiatic action

Experimental evidence further supports these proposed mechanisms by demonstrating inhibition of calcium oxalate crystallization together with improvement of biochemical markers and preservation of renal histology in experimental models of urolithiasis. Although the molecular targets responsible for these protective effects have not yet been identified, the observed reduction in crystal deposition is consistent with mechanisms involving antioxidant defense, modulation of crystal nucleation and aggregation, suppression of inflammatory responses, and protection of renal tissue. Future studies integrating bioactivity-guided fractionation with molecular docking, metabolomics, transcriptomics, proteomics, and

mechanistic pharmacology are expected to provide a clearer understanding of the phytoconstituents responsible for these activities.^[21] A proposed integrated mechanism underlying the antiurolithiatic potential of *Cassia fistula* is presented in Fig. 3.

Antiurolithiatic Mechanism of *Cassia fistula* via Antioxidant and Nephroprotective Effects

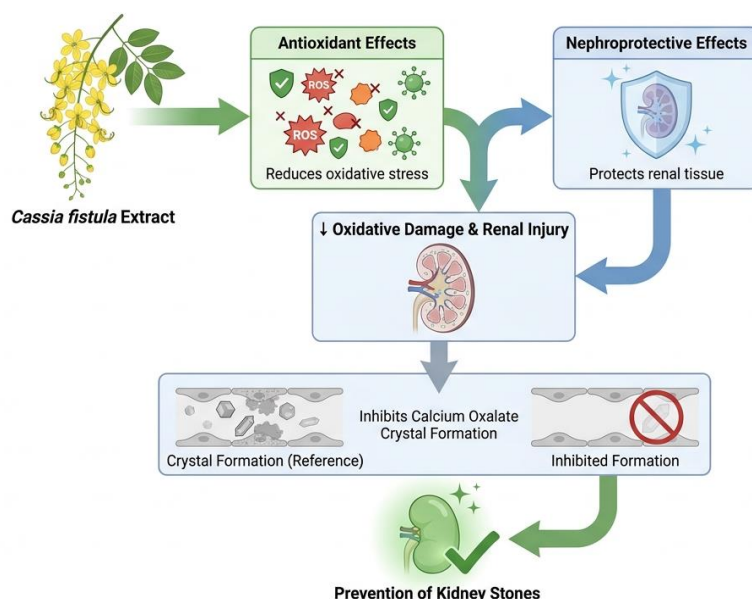


Figure 3: Proposed mechanism of the antiurolithiatic activity of *Cassia fistula* L.

8. RESEARCH GAPS AND FUTURE PERSPECTIVES

Although considerable information is available on the phytochemistry and pharmacological properties of *Cassia fistula*, direct evidence for its antiurolithiatic activity remains limited. Most studies have used crude extracts and a small number of experimental models, while differences in plant parts, extraction methods, and phytochemical composition make comparison between studies difficult. Standardized extraction procedures and reproducible experimental protocols are therefore needed to strengthen the evidence base.^[21]

Another important gap is the limited investigation of individual phytoconstituents. Compounds such as fistulic acid and anthraquinone derivatives have been isolated and characterized, but their specific antiurolithiatic activities have not been adequately studied. Bioactivity-guided fractionation combined with validated crystallization assays, modern analytical techniques, and appropriate experimental models could help identify active constituents and clarify their possible mechanisms of action.^[11]

Future research should also address the standardization, safety, pharmacokinetic properties, and formulation of *Cassia fistula*-based preparations. Further studies are needed to clarify how its reported antioxidant, anti-inflammatory, nephroprotective, and diuretic properties may contribute to protection against stone formation and renal injury. Well-designed preclinical studies followed by controlled clinical investigations will be essential for determining the applicability of standardized *Cassia fistula* preparations in urolithiasis.

9. CONCLUSION

The findings summarized in this review demonstrate that *Cassia fistula* is a chemically rich medicinal plant with significant potential for antiurolithiatic research. Investigations conducted over the past several years have revealed the presence of diverse classes of phytoconstituents, including anthraquinones, flavonoids, phenolic compounds, tannins, terpenoids, and glycosides, many of which have been identified and characterized using modern analytical techniques such as HPTLC, HPLC, LC–MS/MS, GC–MS, FTIR, and NMR spectroscopy. The combined application of these analytical approaches has considerably improved the understanding of the plant's chemical composition and established a reliable foundation for future phytochemical investigations.

Available experimental studies indicate that *Cassia fistula* possesses multiple pharmacological properties relevant to the prevention of urinary stone disease. In addition to inhibiting calcium oxalate crystallization, the plant has demonstrated antioxidant, anti-inflammatory, nephroprotective, diuretic, analgesic, and antibacterial activities that may collectively reduce crystal-induced renal injury and support urinary tract health. However, these findings are derived mainly from preclinical studies employing crude extracts, and the specific phytoconstituents responsible for the observed biological effects have not yet been conclusively identified.

Taken together, the current evidence supports continued investigation of *Cassia fistula* as a promising source of bioactive molecules for antiurolithiatic drug discovery. Future progress will depend on the isolation of active constituents, preparation of standardized extracts, detailed mechanistic evaluation, and carefully designed clinical studies to establish efficacy and safety. Integrating phytochemistry, pharmacology, and advanced analytical technologies will be essential for translating the experimental potential of *Cassia fistula* into scientifically validated phytotherapeutic interventions for the prevention and management of urolithiasis.

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