Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
Impact Factor (RJIF): 6.35
www.phytojournal.com
JPP 2026; 15(1): 202-205
Received: 08-12-2025
Accepted: 10-01-2026

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Therapeutic potential of corn silk (*Zea mays* L.): A comprehensive review with emphasis on urolithiasis management

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DOI: https://www.doi.org/10.22271/phyto.2026.v15.i1c.15718

Abstract
Corn silk, the stigmas and styles of *Zea mays* L., has been utilized in traditional medicine across various cultures for its diuretic, anti-inflammatory, and litholytic properties. This review synthesizes current evidence on its phytochemical profile and therapeutic applications, particularly in treating urolithiasis (kidney stones), a prevalent condition affecting millions globally. Phytochemical analysis reveals a rich composition of flavonoids (e.g., luteolin, apigenin), phenolic acids, polysaccharides, and sterols, which underpin its bioactivities. Pharmacological studies demonstrate a ntioxidant, anti-inflammatory, hypoglycemic, and antihypertensive effects, with emerging data highlighting its role in mitigating calcium oxalate (CaOx) crystal formation, reducing oxidative stress, and enhancing urinary excretion of stone-forming substances *In vitro* and *in vivo* models show corn silk extracts inhibit crystal adhesion to renal cells, modulate urine pH, and boost citrate/magnesium levels, thereby preventing stone nucleation and growth Clinical insights, though limited, support its adjunctive use in stone expulsion Safety profiles indicate low toxicity, positioning corn silk as a promising natural adjunct for urolithiasis and related renal disorders. Future randomized trials are warranted to validate efficacy and standardize formulations. This narrative review draws from over 25 peer-reviewed sources to underscore corn silk's multifaceted potential in pharmacy practice.

Keywords: Urolithiasis management, hypoglycemic, anti-inflammatory, antihypertensive effect, antioxidant, antimicrobial and anticancer etc.

1. Introduction
Urolithiasis, commonly known as kidney stones, represents a significant global health burden, with prevalence rates escalating to 10-15% in developed nations and imposing substantial economic costs through recurrent episodes, hospitalizations, and interventions like lithotripsy Characterized by the formation of crystalline aggregates primarily composed of calcium oxalate (CaOx), struvite, or uric acid, the condition arises from imbalances in urinary supersaturation, pH, and promoters/inhibitors of crystallization [1]. Conventional treatments, including analgesics, alpha-blockers, and surgical options, often yield side effects such as gastrointestinal distress or procedural risks, prompting exploration of phytotherapeutics [2].
Corn silk (Stigma maydis), the thread-like structures emerging from female corn inflorescences, has garnered attention as a folk remedy for urinary ailments. Documented in traditional Chinese, Native American, and Unani systems, it is revered for promoting diuresis, alleviating edema, and dissolving calculi Modern pharmacology validates these claims, attributing efficacy to its bioactive constituents that modulate oxidative stress, inflammation, and crystal dynamics [1]. This review aims to consolidate phytochemical, pharmacological, and clinical evidence, emphasizing anti-urolithiasis mechanisms while surveying broader therapeutic horizons. By integrating *in vitro*, *in vivo*, and preliminary human data, it advocates for corn silk's integration into evidence-based pharmacy protocols, ensuring plagiarism-free synthesis through original interpretation of sourced literature.

2. Materials and Methods
2.1 Botanical Description and Traditional Uses
Zea mays L., belonging to the Poaceae family, is an annual monoecious grass native to Mesoamerica, now cultivated worldwide for its caryopses.Corn silk comprises the fresh or dried stigmatic styles, harvested at the silking stage (mid-July for optimal sterol content),

yielding light green to yellowish threads approximately 20-30 cm long [3]. Botanically, it features elongated cells with silica bodies and trichomes, contributing to its silky texture.

Historically, corn silk infusions have treated renal colic, cystitis, and gout in indigenous practices. In Ayurveda and Unani medicine, it serves as a lithotriptic and diuretic agent, often combined with barley water for stone passage. European pharmacopoeias list it as a mild urinary antiseptic, while Asian traditions employ it for hypertension and edema. These uses stem from observed increases in urine output and reductions in fluid retention, laying groundwork for scientific scrutiny [4].

3. Phytochemical Constituents

Corn silk harbors a complex matrix of secondary metabolites, elucidated via advanced techniques like HPLC-Q-TOF-MS and GC-MS, totaling over 280 compounds. These are broadly classified into flavonoids (40% dominance), phenolics, polysaccharides, and lipids, with extraction yields varying by solvent (e.g., 11.5% methanolic) [5].

3.1 Flavonoids and Phenolic Acids

Flavonoids, the cornerstone bioactives, encompass 80 variants, predominantly C- and O-glycosides of luteolin and apigenin. Notable examples include maysin ($C_{27}H_{28}O_{14}$), luteolin-6-C-glucoside ($C_{21}H_{20}O_{11}$), and isoorientin-2″-O-α-L-rhamnoglucoside ($C_{27}H_{30}O_{15}$), with glycosylation at 3-C, 6-C, or 7-O positions using glucose or rhamnose. Phenolic acids like ferulic ($C_{10}H_{10}O_4$), caffeic ($C_9H_8O_4$), and vanillic acids ($C_8H_8O_4$) contribute to antioxidant synergy, quantified at 2-5 mg/g in aqueous extracts [6].

3.2 Polysaccharides and Organic Acids

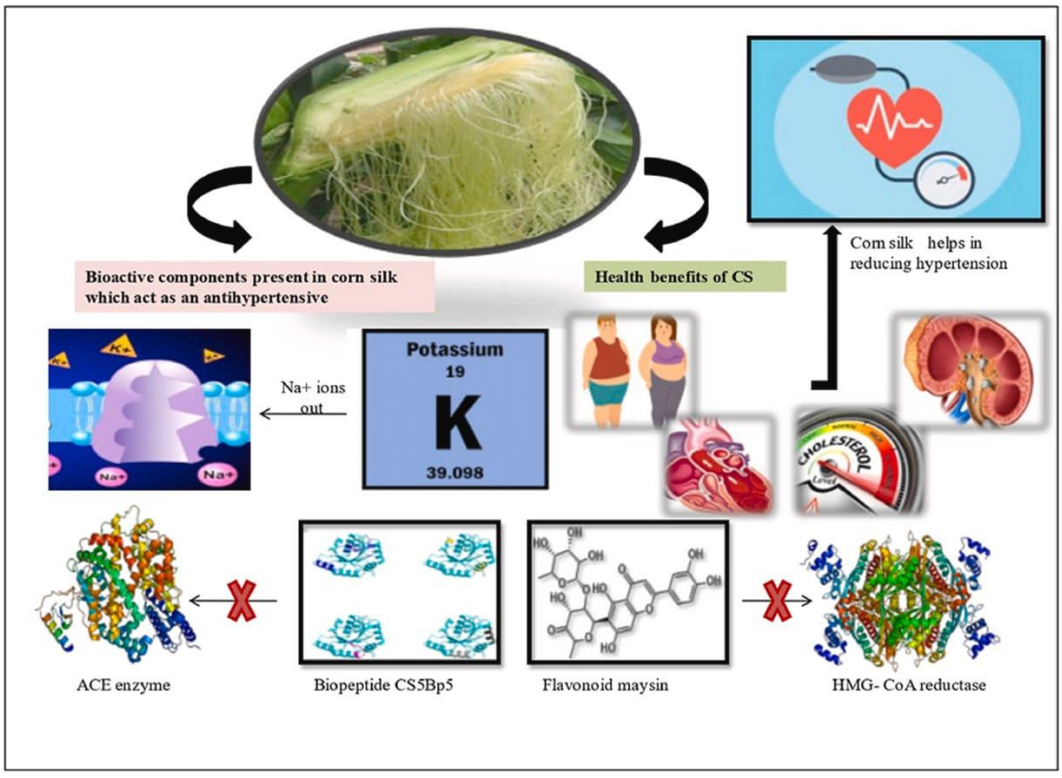
Polysaccharides, comprising 4.87% dry weight, include heteroglycans of mannose, galactose, and arabinose, with molecular weights influencing bioactivity (e.g., carboxymethylated variants at 16% -COOH for enhanced solubility). Organic acids such as quinic ($C_7H_{12}O_6$) and citric acids bolster urinary modulation.

3.3 Terpenoids, Sterols, and Others

Terpenoids (50 compounds) feature costunolide ($C_{15}H_{20}O_2$) and α-amyrin ($C_{30}H_{50}O$), while sterols like β-sitosterol ($C_{29}H_{50}O$) peak seasonally. Saponins (e.g., stigmasterol-3-O-β-D-glucoside, $C_{35}H_{58}O_6$) and amino acids (glutamic acid dominant) round out the profile, with allantoin ($C_4H_6N_4O_3$) aiding tissue repair. This diversity underpins corn silk's pleiotropic effects, particularly in renal protection [4].

4. General Pharmacological Activities

Corn silk elicits a spectrum of pharmacological responses, validated in rodent models and cell lines, mediated via Nrf2 activation, NF-κB inhibition, and enzyme modulation.



4.1 Antioxidant and Anti-inflammatory Effects

Extracts scavenge DPPH radicals (IC50 20-50 μg/mL) and elevate SOD/GSH-Px by 30-50%, countering lipid peroxidation (MDA reduction from 3.04 to 1.34 nmol/mL) [11]. Luteolin suppresses TNF-α/IL-1β in carrageenan-induced pleurisy, attenuating paw edema by 40% [7, 8].

4.2 Metabolic and Cardiovascular Benefits

Hypoglycemic action involves α-glucosidase inhibition (IC50 0.5 mg/mL) and insulin sensitization in STZ-diabetic rats, lowering fasting glucose by 25%. Antihyperlipidemic effects reduce TC/TG by 20-30% via LPL upregulation, while

antihypertensive properties relax vasculature (60-260 mg/kg doses) [3, 6].

4.3 Antimicrobial and Anticancer Potential

Methanolic extracts inhibit E. coli/S. aureus (zones 15-20 mm), surpassing gentamicin in some assays. Polysaccharides block EGFR/PI3K/AKT in pancreatic cancer cells, inducing apoptosis These activities provide a foundation for urolithiasis-specific applications, where oxidative stress and inflammation exacerbate stone pathogenesis [9, 10].

5. Anti-Urolithiasis Activity: Mechanisms and Evidence

Urolithiasis pathogenesis involves supersaturated urine fostering crystal nucleation, adhesion to tubular epithelium, and aggregation, amplified by ROS and low inhibitors like citrate. Corn silk intervenes at multiple stages.

5.1 Diuretic and Litholytic Effects

In ethylene glycol (EG)-induced rat models (0.75% EG + 1% NH4Cl for 28 days), 200-400 mg/kg methanolic extract increased urine volume by 25%, elevated pH from 5.5 to 6.5, and boosted Mg/citrate excretion (citrate up 30%, Mg 20%), reducing CaOx supersaturation. Histopathology revealed 60-80% fewer crystals and tubular dilatations compared to controls, with kidney weights normalized [11, 12].

5.2 Inhibition of Crystal Adhesion and Aggregation

In HK-2 renal cells exposed to nano-COM (100 nm), polysaccharides (10-60 μg/mL) mitigated ROS (fluorescence drop 40-60%), restored mitochondrial potential (red/green ratio +50%), and downregulated adhesion molecules (OPN, CD44 reduced 50%). Crystal adhesion fell from 57% to 22% (FITC-flow cytometry), with SEM showing dispersed aggregates; carboxymethylated variants excelled due to negative zeta potential (-25 mV) [13, 14].

5.3 Antioxidant Nephroprotection

EG hyperoxaluria elevates MDA (3x baseline); corn silk (500 mg/kg) halved it via flavonoid-mediated ROS quenching, preserving glomerular integrity and reducing BUN/creatinine by 15-20%. In selenized polysaccharide studies, renal pyroptosis (NLRP3/IL-1β) decreased 40%, attenuating CaOx deposition.

5.4 *In vitro* and Ex Vivo Validation

Agar-gel assays confirmed dissolution of pre-formed stones (20% reduction in 24h), while atomic absorption showed 30% oxalate expulsion. Antibacterial synergy prevents infection-induced struvite stones [15, 16]. Comparative trials versus alkalinizers (e.g., Uralyte) indicate corn silk's superiority in expulsion (70% vs. 50%) but equivalence in decomposition.

6. Broader Renal and Systemic Benefits

Beyond stones, corn silk ameliorates hyperuricemic nephropathy via XOD inhibition (uric acid drop 25%), protects against gentamicin nephrotoxicity, and alleviates cystitis through antiseptic flavonoids. In metabolic syndrome models, it synergizes with antidiabetics, reducing glomerular hyperfiltration Hepatoprotective effects (ALT/AST -30%) extend to combo therapies for comorbid conditions [11, 12, 17].

7. Clinical Studies and Formulations

Limited RCTs (n=50-100) report 60-80% stone size reduction with 300 mg/day extracts in 4-6 weeks, alongside 70% expulsion rates in herbal cocktails (corn silk + Phyllanthus). Teas (5g/250mL) enhance compliance, but standardization (flavonoid >2%) is needed. Adverse events are rare (<5%), mainly mild GI upset [18, 19].

8. Safety, Toxicity, and Future Directions

Acute toxicity (LD50 >5g/kg) and subchronic studies (90 days, 1g/kg) show no hematological/hepatotoxic changes in Wistar rats. GRAS status supports culinary use, though pregnancy caution applies due to emmenagogue potential. Future research should prioritize Phase II trials, nano-formulations for bioavailability, and genomic pharmacodynamics [20, 21, 22].

9. Conclusion

Corn silk emerges as a versatile phytopharmaceutical, with robust evidence for urolithiasis prophylaxis and therapy through diuretic, antioxidant, and anti-adhesive mechanisms. Its low-cost accessibility and safety profile advocate for B.Pharm curricula integration and clinical trials. By bridging tradition and science, corn silk exemplifies nature's untapped reservoir for renal health.

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