

ZEA MAYS L. STIGMA (CORN SILK): ETHNOPHARMACOLOGICAL SIGNIFICANCE AND CONTEMPORARY PHARMACOLOGICAL EVIDENCE

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Abstract: *Background:* *Zea mays L. stigma*, commonly known as corn silk, has been utilized in traditional medicine systems across Asia, Europe, the Americas, and Africa for centuries, primarily for the management of urinary tract disorders, hypertension, hyperglycemia, and inflammatory conditions. Despite its longstanding ethnopharmacological use, a systematic synthesis of phytochemical profiles and experimentally validated pharmacological properties remains warranted for evidence-based clinical translation.

Objective: This review consolidates existing ethnobotanical records with contemporary pharmacological investigations to provide a comprehensive appraisal of the therapeutic relevance of *Zea mays L. stigma* and to identify priority areas for future clinical research.

Methods: A systematic literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar databases (1990–2024) using predefined Mesh terms and Boolean operators. Inclusion and exclusion criteria were applied following PRISMA 2020 guidelines. A total of 78 studies met the eligibility criteria and were subjected to qualitative synthesis.

Results: Corn silk is rich in flavonoids (maysin, apimaysin, luteolin), polyphenols (chlorogenic acid, caffeic acid), β -sitosterol, polysaccharides, vitamins C and K, and trace minerals. Pharmacological investigations confirm significant diuretic, antioxidant, anti-inflammatory, hypoglycemic, nephroprotective, hepatoprotective, and antimicrobial activities, supported by both *in vitro* and *in vivo* evidence. Several mechanistic pathways—including NF- κ B inhibition, AMPK activation, and free radical scavenging—have been elucidated.

Conclusions: The cumulative evidence positions *Zea mays L. stigma* as a pharmacologically promising natural product. Rigorous randomized controlled trials, standardized extraction protocols, and pharmacokinetic profiling are urgently

needed to facilitate the incorporation of corn silk-derived formulations into evidence-based therapeutic regimens.

Keywords: *Zea mays L. stigma; corn silk; ethnopharmacology; phytochemistry; diuretic; antioxidant; anti-inflammatory; nephroprotection; urinary tract; natural products*

1. Introduction

Natural products derived from medicinal plants continue to represent an indispensable resource in global healthcare, particularly in low- and middle-income countries where a significant proportion of the population relies on traditional medicine as a primary healthcare modality (WHO, 2019). Among the most accessible and widely distributed cereal crops worldwide, *Zea mays* L. (family Poaceae) occupies a unique position, not only as a staple food crop but also as a phytomedicinal resource of enduring significance.

The stigma of *Zea mays* L.—popularly designated as corn silk, maize silk, or in Uzbek as makkajo'xori popugi—constitutes the thread-like, yellowish-green pistillate structures extending from the ears of the plant. Although these structures are typically discarded as agricultural waste during grain processing, they have been systematically employed in traditional and folk medicine across diverse geographical and cultural contexts for more than two millennia (Ren et al., 2020).

In Traditional Chinese Medicine (TCM), corn silk—referred to as Yu Mi Xu—has been documented in classical pharmacopoeial texts as a treatment for edema, hepatitis, cholecystitis, and hyperglycemia. Pre-Columbian Mesoamerican civilizations similarly recorded its use for urinary retention, kidney stones, and febrile conditions. In Central Asian ethnomedicine, including Uzbek, Kazakh, and Tajik folk practices, corn silk infusions (decoctions or teas) are widely prescribed by hakims (traditional healers) for urinary tract infections, nephrolithiasis, and arterial hypertension (Tashmatov et al., 2020). European phytotherapy traditions, particularly those of Romania, Turkey, and Eastern European countries, incorporate corn silk into official herbal pharmacopoeias as a recognized diuretic agent.

Despite this extensive ethnopharmacological heritage, the scientific community has only recently commenced systematic investigation of corn silk's bioactive constituents and mechanistic pharmacology. Existing reviews are either narrowly focused on a single pharmacological activity or lack rigorous methodological appraisal of the underlying evidence. Furthermore, the translation of in vitro and animal study findings into clinical applications remains largely unaddressed. The present review was therefore undertaken to provide an integrated, evidence-based analysis spanning botanical characterization,

phytochemical composition, ethnopharmacological records, and contemporary pharmacological findings.

The specific objectives of this review are: (I) to document the global ethnopharmacological applications of *Zea mays* L. stigma; (II) to systematically describe its phytochemical composition; (III) to evaluate the pharmacological evidence for its principal therapeutic activities; (IV) to analyze relevant safety and toxicological data; and (V) to identify critical knowledge gaps warranting future investigation.

2. Materials and Methods

This review was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Page et al., 2021). A comprehensive, reproducible search strategy was developed and independently verified by two co-authors prior to database interrogation.

Electronic databases searched included PubMed/MEDLINE, Scopus, Web of Science (Core Collection), Cochrane Library, Google Scholar, and EMBASE. The search was conducted for publications in the English language from January 1990 to December 2024. The following MeSH terms and keywords were employed in combination with Boolean operators (AND/OR): «*Zea mays*», «corn silk», «maize silk», «stigma maydis», «cornsilk extract», «phytochemistry», «ethnopharmacology», «diuretic», «antioxidant», «anti-inflammatory», «nephroprotective», «hepatoprotective», «hypoglycemic», «antimicrobial», «traditional medicine», «folk medicine».

Additional literature was identified through manual screening of reference lists of eligible studies and consultation of grey literature sources including WHO monographs, European Medicines Agency (EMA) assessments, and ESCOP monographs.

Studies were included if they: (I) utilized *Zea mays* L. stigma or its extracts as the principal study material; (II) employed in vitro, in vivo (animal), or clinical experimental designs; (III) reported quantitative or qualitative pharmacological or phytochemical outcomes; and (IV) were published in peer-reviewed journals or official regulatory documents. Studies were excluded if they: (I) used *Zea mays* grain, husk, or leaf as the primary material; (II) were duplicated reports from the same dataset; (III) were case reports without reproducible methodology; or (IV) were written in languages other than English without available translations.

Methodological quality of in vivo studies was assessed using the ARRIVE 2.0 checklist. The quality of in vitro studies was evaluated according to the criteria of

the Good Laboratory Practice (GLP) standards. Risk of bias was assessed using the SYRCLE Risk of Bias tool for animal studies. The evidence was graded using a modified Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence framework.

3. Results

Zea mays L. (syn. *Zea mays* subsp. *mays*) belongs to the family Poaceae (Gramineae), tribe Andropogoneae. It is an annual monoecious grass with a robust erect stem (culm) reaching 1.5–4.0 m in height. The stigmas emerge as long, silky, thread-like structures (5–30 cm) from the ears, serving as receptive surfaces for pollen capture. Botanically, each silk strand represents a single elongated style-stigma unit, one per kernel on the cob. The color transitions from pale yellow-green to reddish-brown with maturation. The optimal collection period for medicinal purposes is the fresh, pre-pollination stage, when bioactive constituent concentration is highest (Hu et al., 2017).

In Central Asia specifically, corn silk decoctions are among the most commonly prescribed plant-based remedies by traditional healers, with an ethnopharmacological use value (UV) index of 0.82—among the highest recorded for urinary tract remedies in the region. Across Uzbek folk medicine, the standard preparation involves boiling 2–3 tablespoons of dried stigmas in 500 mL of water for 10–15 minutes, with the resulting decoction consumed 3 times daily.

Phytochemical investigations employing HPLC-DAD, GC-MS, LC-MS/MS, and NMR spectroscopy have identified over 60 bioactive constituents in *Zea mays* L. stigma. The major compound classes and key representatives, together with their documented biological activities, are presented in Table 1.

Table 1. Major phytochemical constituents of *Zea mays* L. stigma and their biological activities

Compound Class	Key Compounds	Biological Activity	References
Flavonoids	Maysin, Apimaysin, Luteolin	Antioxidant, Anti-inflammatory	Ren et al., 2020
Polyphenols	Chlorogenic acid, Caffeic acid	Hepatoprotective, Antioxidant	Ebrahimzadeh et al., 2019
Sterols	β -Sitosterol, Stigmasterol	Anti-inflammatory, Diuretic	Hu et al., 2017
Terpenes	α -Terpineol, Limonene	Antimicrobial, Antifungal	Habtemariam, 2018
Vitamins & Minerals	Vit C, Vit K, Potassium, Selenium	Antioxidant, Diuretic support	FAO/WHO, 2016
Polysaccharides	β -Glucans, Arabinoxylans	Immunomodulatory, Hypoglycemic	Zhang et al., 2022

Among flavonoids, maysin (2'-O- α -L-rhamnosyl-6-C-(6-deoxy-4-O-(E)-p-coumaroyl-glucosyl)luteolin) has emerged as a marker compound characteristic of corn silk, demonstrating potent free-radical scavenging, antibacterial, and insecticidal properties. Chlorogenic acids account for up to 34% of total polyphenol content in aqueous extracts. The phytosterol fraction, dominated by β -sitosterol, contributes significantly to anti-inflammatory and membrane-stabilizing effects.

A total of 66 experimental studies (in vitro and in vivo) provided quantitative pharmacological data. Principal findings are summarized in Table 2.

Table 2. Summary of key pharmacological activities of *Zea mays* L. stigma — selected experimental evidence

Pharmacological Effect	Model/Study Type	Key Findings	Authors (Year)
Diuretic	Rat model, in vivo	Urine output $\uparrow$ 45%; Na/K excretion $\uparrow$	Asghari et al. (2018)
Antioxidant	DPPH, FRAP assays	IC ₅₀ = 38.4 μ g/mL; FRAP = 2.14 mM Fe ²⁺ /g	Deng et al. (2020)
Anti-inflammatory	LPS-induced macrophage	TNF- α $\downarrow$ 62%; IL-6 $\downarrow$ 55%	Hu et al. (2017)
Hypoglycemic	STZ-diabetic rats	Blood glucose $\downarrow$ 31% vs. control	Zhao et al. (2019)
Nephroprotective	Cisplatin nephrotoxicity model	Creatinine $\downarrow$; GFR restoration	Sahin et al. (2021)
Hepatoprotective	CCl ₄ -induced rat model	ALT/AST normalization; oxidative stress $\downarrow$	Ebrahim et al. (2019)
Antimicrobial	MIC assay (<i>E. coli</i> , <i>S. aureus</i>)	MIC 0.25–1 mg/mL	Velazquez et al. (2021)

The diuretic effect of corn silk is among its most consistently validated pharmacological properties. In a controlled rat model, intraperitoneal administration of an aqueous corn silk extract (200 mg/kg) produced a 45% increase in 24-hour urine output compared to vehicle controls, with concomitant enhancement of sodium and potassium excretion, comparable in magnitude to furosemide at sub-maximal doses (Asghari et al., 2018). The mechanism involves inhibition of renal tubular sodium reabsorption and modulation of aquaporin-2 expression.

Multiple assay systems (DPPH, ABTS, FRAP, ORAC) consistently demonstrate moderate-to-high antioxidant potency of corn silk extracts. Ethanol extracts generally exhibit superior radical-scavenging capacity (IC₅₀ DPPH: 38.4 μ g/mL) compared to aqueous preparations, attributable to higher recovery of polyphenolic

compounds. The antioxidant activity is positively correlated with total flavonoid content ($r = 0.91$, $p < 0.001$).

In lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages, corn silk ethanol extract (100 $\mu\text{g/mL}$) reduced TNF- α secretion by 62% and IL-6 by 55% relative to untreated controls (Hu et al., 2017). In vivo, carrageenan-induced paw edema was reduced by 38–52% following oral administration of corn silk extract (250–500 mg/kg). Mechanistic studies implicate NF- κB pathway inhibition and downregulation of COX-2 expression as primary anti-inflammatory mechanisms.

In streptozotocin (STZ)-induced diabetic rat models, oral administration of corn silk extract (400 mg/kg/day for 28 days) resulted in a 31% reduction in fasting blood glucose levels and significant improvement in insulin sensitivity indices. AMPK (AMP-activated protein kinase) activation, inhibition of α -glucosidase and pancreatic lipase, and enhancement of hepatic glycogen synthesis have been proposed as plausible antidiabetic mechanisms (Zhao et al., 2019).

Corn silk extract demonstrated significant protective effects against cisplatin-induced nephrotoxicity in rats, as evidenced by restoration of glomerular filtration rate, normalization of serum creatinine and blood urea nitrogen (BUN) levels, and reduction of renal tubular oxidative damage markers (MDA, 8-OHdG). Histopathological examination confirmed preservation of tubular architecture in extract-treated animals (Sahin et al., 2021).

In CCl_4 -induced hepatotoxicity models, corn silk extract treatment normalized serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities, reduced hepatic lipid peroxidation, and enhanced superoxide dismutase and catalase activities. Protective effects were equivalent to 64–73% of the hepatoprotection observed with silymarin (positive control) (Ebrahimzadeh et al., 2019).

Ethanollic and methanolic corn silk extracts exhibited inhibitory activity against both Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*) and Gram-negative (*Escherichia coli*, *Klebsiella pneumoniae*) pathogens, with minimum inhibitory concentrations (MIC) ranging from 0.25 to 1.0 mg/mL. The antimicrobial activity is partially attributable to maysin and other flavonoid constituents disrupting bacterial membrane integrity.

Acute toxicity studies in rodents have established oral LD_{50} values exceeding 5 g/kg for standardized corn silk extracts, classifying them as practically non-toxic by OECD criteria. Sub-chronic (90-day) administration of 1,000 mg/kg/day produced no observable adverse effects on hematological, biochemical, or histopathological parameters in Wistar rats. Corn silk has been assigned GRAS (Generally Recognized

as Safe) status in the United States by the FDA. No clinically significant herb-drug interactions have been confirmed, though theoretical interactions with antidiabetic and antihypertensive medications warrant monitoring in clinical settings.

Nine clinical studies were identified; however, methodological quality was generally limited (small sample sizes, lack of randomization or blinding). A prospective observational study in 45 patients with uncomplicated lower urinary tract infections reported symptomatic improvement in 71% of subjects following 14-day corn silk tea supplementation as adjunct therapy. A double-blind pilot trial (n = 60) demonstrated significant reduction in 24-hour urine oxalate and calcium excretion after 4 weeks of standardized corn silk extract (400 mg BID), suggesting utility in nephrolithiasis prevention (Lee et al., 2022). Definitive evidence from adequately powered RCTs is currently lacking.

4. Discussion

The convergence of ethnopharmacological records from geographically and culturally disparate populations regarding the utility of corn silk in urinary, metabolic, and hepatic disorders constitutes a compelling signal warranting scientific investigation—a principle central to the reverse pharmacology approach. The present synthesis corroborates ethnobotanical traditions with mechanistic experimental evidence, lending scientific legitimacy to decades of empirical use. Particularly noteworthy is the high ethnopharmacological consensus for diuretic and antilithiatic applications, which is now supported by multiple independent experimental studies.

The pharmacological versatility of corn silk is attributable to its complex polyphenolic matrix. Maysin, the characteristic flavone C-glycoside, demonstrates multi-target bioactivity encompassing antioxidant, antimicrobial, and cytotoxic properties. The high polyphenol-flavonoid synergy in corn silk extracts likely explains the superior anti-inflammatory effects observed relative to isolated constituents. Standardization of corn silk preparations based on maysin and chlorogenic acid content emerges as a priority for quality-controlled product development.

The emerging mechanistic picture positions corn silk as a pleiotropic modulator acting on multiple interconnected pathways: NF- κ B-mediated inflammation suppression, AMPK-regulated glucose and lipid metabolism, Nrf2-HO-1 antioxidant axis activation, and renal ion transport modulation. This polypharmacological profile aligns with contemporary interest in multi-target natural product therapeutics, particularly for complex chronic conditions such as metabolic syndrome, diabetic nephropathy, and chronic kidney disease, where single-target pharmacotherapy often proves insufficient.

Corn silk's pharmacological profile compares favorably with established herbal diuretics and nephroprotective agents. Its diuretic efficacy approaches that of hydrochlorothiazide at comparable doses in animal models, with a superior safety margin. The nephroprotective potency, while less well-characterized than that of silymarin for hepatoprotection, shows promising results that warrant systematic comparison in head-to-head studies. Importantly, the multifunctional nature of corn silk—simultaneously addressing oxidative stress, inflammation, and metabolic dysregulation—may confer therapeutic advantages over single-mechanism synthetic agents in complex disease contexts.

Several important limitations temper the enthusiasm generated by accumulated preclinical data. Firstly, the majority of pharmacological studies employed crude or semi-purified extracts of variable composition, impeding direct comparability across studies. Secondly, dose-response relationships and pharmacokinetic parameters (absorption, distribution, metabolism, excretion) of key bioactive constituents following oral administration in humans remain largely uncharacterized. Thirdly, the paucity of adequately powered, randomized, double-blind clinical trials represents the most critical gap precluding definitive efficacy and safety conclusions.

Priority areas for future investigation include: (I) development of standardized, well-characterized corn silk extracts and phytopharmaceutical formulations meeting Good Manufacturing Practice (GMP) requirements; (II) rigorous pharmacokinetic and bioavailability studies in humans; (III) multicenter, adequately powered RCTs evaluating efficacy in urinary tract infections, nephrolithiasis prevention, and diabetic nephropathy; (IV) investigation of synergistic interactions between corn silk phytoconstituents and established pharmaceutical agents; and (V) exploration of novel delivery systems (nanoparticle encapsulation, standardized softgels) to enhance bioavailability. The Central Asian region, including Uzbekistan, represents an important geographical context for clinical trials given the high prevalence of endemic nephrolithiasis and the strong cultural familiarity with corn silk-based preparations.

5. Conclusions

Zea mays L. stigma represents a phytomedicinal resource of considerable pharmacological promise, supported by a convergent body of ethnopharmacological evidence and increasingly mechanistic experimental data. Its rich phytochemical composition—encompassing flavonoids, polyphenols, phytosterols, polysaccharides, and essential micronutrients—underpins a broad spectrum of documented bioactivities including diuretic, antioxidant, anti-inflammatory, hypoglycemic, nephroprotective, hepatoprotective, and antimicrobial effects. The outstanding

safety profile and widespread cultural acceptance further support its potential as an integrative therapeutic agent.

However, translation from empirical use and preclinical evidence to evidence-based clinical application requires the systematic execution of standardization, pharmacokinetic, and well-designed clinical trial programs. The present review provides a consolidated reference foundation for researchers, clinicians, and pharmaceutical scientists pursuing the evidence-based development of corn silk-derived therapeutic products.

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