



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Therapeutic Applications of Corn Silk, a Versatile Natural Medicine: A Comprehensive Review

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ARTICLE INFO

Received: 21 June 2024

Accepted: 23 June 2024

Published: 08 July 2024

Keywords:

corn silk, antimicrobial, antioxidant, anti-diabetic, anti-inflammatory, anti-hypertensive, anti-hyperlipidemic, diuretic, anti-cancer.

DOI:

10.5281/zenodo.12687174

ABSTRACT

Corn silk, is a by-product of the maize plant, and is known for its traditional medicinal applications since a long time. Corn silk contains various bioactive compounds such as steroids, alkaloids, saponins, carotenoids, tannins, flavonoids, anthocyanins, also some volatile and fixed oils, vitamins, proteins, carbohydrates, sodium, potassium, magnesium, and calcium salts, and steroids like sitosterol and stigmaterol. It has been widely used as a traditional medicine in countries such as China, Turkey, India, France, and the United States as an antidepressant, anti-fatigue, antioxidant, diuretic agent, anti-diabetic, and antimicrobial agent. Many studies on the safety profile of the corn silk have proved it safe and non-toxic. This article provides a comprehensive review on the various therapeutic applications of corn silk and the studies that support its safety profile as well as therapeutic potential in various diseases.

INTRODUCTION

Plants have been used for medicinal purpose since ancient times, even before the history was recorded. The mankind has been dependent on the natural resources for medicines since olden time which has revealed therapeutic potentials of many plants over the time, but the exact mechanism of many of the herbal drugs in curing a particular disease is yet to be explored. Throughout the history, humans have been developing and optimizing variety of formulations of herbal drugs

in order to improve their shelf life as well as to make them easy and compatible to ingest. Teas and decoctions are the oldest and simplest formulations of herbal drugs. Teas and decoctions are not only simple to prepare but also effective ways to extract beneficial compounds from herbs. In India, decoctions made with various herbs like tulsi, and spices like turmeric and ginger were commonly used by the Ayurvedic practitioners for a range of illnesses. Powdered herbs, alcohol-based extracts such as tinctures, syrups and elixers,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



capsules, tablets, ointments, poultices, etc. formulations have been developed by the time.

Corn silk (*Stigma maydis*) is a byproduct of *Zea mays* and is basically stigmas originated from the female flowers of corn and is generally either light green or yellow-brown in color.¹ Corn silk (CS) is widely been used conventionally for its various therapeutic uses in different countries including China, Turkey, India, France, and the United States as an antidepressant, anti-fatigue, antioxidant, diuretic agent, anti-diabetic, and antimicrobial agent.² Like many of the other traditional herbs, CS contains natural antioxidants, especially phenolic compounds. Other than phenolic compounds, it also contains volatile and fixed oils, vitamins, proteins, carbohydrates, sodium, potassium, magnesium, and calcium salts, steroids like sitosterol and stigmasterol, and several other bioactive compounds listed in the Fig. 1.³ Thus it has been widely reported to have various pharmacological activities including anti-inflammatory, anti-depressant, anti-hyperlipidemic, anti-diabetic, anti-fatigue, and antioxidant activities as well as neuroprotective, diuretic, and kaluretic effects and has also been linked to kidney stones, bedwetting and obesity.^{4,5} The result of a sub-chronic toxicity study of corn silk suggested that corn silk powder is safe to be used as food ingredient without concerning that it will decrease the blood glucose for healthy people, also the study observed that there were no toxicity estimated at the highest dose tested.⁶

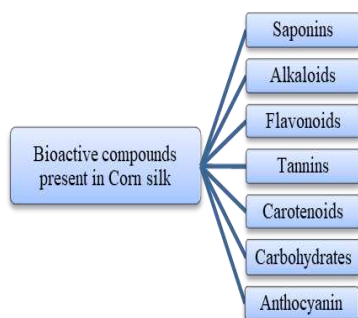


Fig. 1: Bioactive compounds present in corn silk

Herbal medicines are widely used for various treatment as well as diagnostic purposes due to the belief that, being natural, they are safe and harmless or having a very few side effects. A recent study⁷ evaluated the toxicity of corn silk extract administered to Wistar rats at 100, 200, and 400 mg/kg body weight for 28 days and found no haematological toxicity. And the LD50 of the corn silk extract was estimated to be above 2,000 mg/kg.⁸ These studies reported that consuming corn silk has no negative effects and it is safe for humans.

Antimicrobial activity of corn silk:

Bacterial infections and fungal infections are common infections across the world. Among various bacterial infections, respiratory infections, skin infections, gastrointestinal infections, and urinary tract infections and among various fungal infections, oral thrush, vaginal yeast infection, skin and nail fungal infections, and respiratory fungal infections are most common. Bacteria such as *Enterococcus faecalis*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Staphylococcus saprophyticus* and *Escherichia coli*, are the primary cause of Urinary tract infections (UTIs)⁹, which afflict 150 million individuals annually globally¹⁰. But, of these microorganisms, majority of UTI cases are caused by *Escherichia coli* (*E. coli*).^{11,12,13}

Common symptoms of UTI may include burning sensation or pain while urinating (dysuria), fever or chills may indicate a sign that infection has reached the kidneys, pain or pressure in the back or lower abdomen, and dark, cloudy, bloody urine (haematuria), tiredness, pelvic pain in women, especially in the centre of the pelvis and around the area of pubic bone, a frequent need and sudden urge to urinate (urgency), and bladder spasms.¹⁴ Urinary tract infections (UTIs), although being widely studied for hundreds of years, are still the most prevalent infectious disease in women, a major driver of morbidity and health-related spending, a contributor to decreased quality of life,

and a significant social burden.¹⁵ Among numerous approaches, use of probiotics, bioactive natural foods, antibiotics, and good personal hygiene are few of the many methods used to treat and prevent chronic and recurrent UTI. However, solution to these issues has not yet been found. Due to the widespread resistance that the typical UTI microorganisms exhibit to previously used treatments, it has been demonstrated that the selection of medications for the treatment of UTI is currently rather limited. Since bacteria typically cause UTIs, antibiotics are typically used to treat them. Adhesion of the pathogen to host cells or

tissue is the first step during bacterial infection. Alternatively, colonization of pathogens takes place further invading host cells. Fig. 2 shows formation of UTI due to adhesion of *E. coli* to the urinary tract wall leading to inflammation of the cells. Colonization and subsequent internalization facilitate delivery of toxin and virulence factors to the host cell and helps the bacteria maintain their position, fending off the host immunity.¹⁶ Thus, anti-adhesion therapy emerges as an important way for the prevention or treatment of bacterial infections.

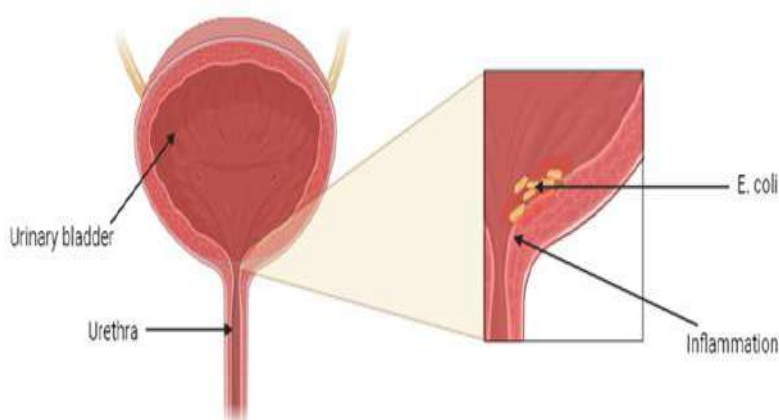


Fig. 2: Urinary tract having bacterial infection due to bacterial adhesion (UTI)

Antibiotics used for UTI have a variety of unpleasant side effects, including headache, dizziness, indigestion, nausea, vomiting, rash, and appetite loss. According to one study on the antibiotic sensitivity pattern in UTI, cotrimoxazole and amoxicillin were essentially worthless against the uropathogens that cause UTI, since they were effective against only 18% and 22% of all isolated organisms, respectively. Minocycline and Amoxiclav performed marginally better, showing action in 35% and 53% of instances, respectively. Because uropathogens are more susceptible to minocycline, which is likely due to the drug's effective activity against *E. coli*, which was also shown in the investigation where *E. coli* isolates demonstrated 75% sensitivity, some studies particularly point to an increase in the usage of oral

minocycline over the past five years.¹⁷ The increasing incidence of resistance to antibiotics among bacterial pathogens necessitates herbal medicines as an alternate therapy in the management of UTI.¹⁸

Due to their benign makeup, long history of use, and comparatively less toxicity, herbal medicines are receiving lot of attention nowadays. D-mannose, uva ursi, cranberry, garlic, and green tea are famous options for natural UTI therapy and prevention despite the shortage of data on their efficacy. Many herbs having antibacterial activity are preferred over the antibiotics because of their tolerance issues. Corn silk is a reported natural remedy to be useful in treating urinary tract infections.¹⁹ A clinical study by Ahmed Salih Sahib et al.³ has added another proof for the

potential of corn silk in the treatment of UTI. The study results showed significant reduction of UTI symptoms. The time course incidence of UTI symptoms and the time course change in the UTI

symptoms score after aqueous corn silk extract treatment were observed as per given in the Table 1

Table 1: Time course change in UTI symptoms score

Time (days)	Time course incidence of UTI symptoms				Time course change in UTI symptoms score			
	0	5	10	20	0	5	10	20
Suprapubic pain	33	5	1	0	3.12	0.47	0.095	0
Urgency	35	10	2	0	3.32	0.95	0.19	0
Frequency	35	11	3	1	3.32	1.04	0.28	0.095
Dysuria	32	6	2	1	3.04	0.57	0.19	0.095
Total			-		12.8	3.03*	0.73*	0.19*

* Significant change ≤ 0.05

These observations stated that administration of corn silk extract (CSE) to UTI patients resulted in significant ($P \leq 0.05$) decrease in the symptoms of UTI after 5 days, 10 days and 20 days as compared to the 0th day symptoms score.

This study supports the antimicrobial potential of corn silk and suggests that there is more scope and need of study on the antimicrobial properties of corn silk.

Antioxidant activity of corn silk:

Imbalance between the production of reactive oxygen species (ROS) which results in oxidative stress (OS) that may cause lethal damages to the biomolecules such as proteins, lipids, and DNA. Persistent oxidative stress may even result in cell death and can trigger many diseases including cancer, diabetes mellitus, kidney diseases, aging, etc.^{20, 21, 22} Fig. 3 shows a diagrammatic representation of cell proliferation due to ROS attack.

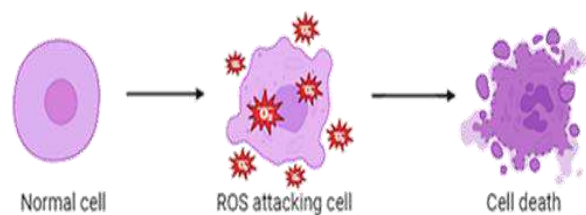


Fig. 3: Cell proliferation due to oxidation

Corn silk contains different phytochemicals including polyphenols, phenolic acids, flavonoids, anthocyanins, carotenoids, glycosides, and polysaccharides etc. which possess remarkable antioxidant activity that help reducing oxidative

stress and thus treat consequences arising due to it.²³ Flavonoids are phenolic compounds, generally soluble in polar solvents and are powerful antioxidants that protect cells from free radicals damage and oxidative stress. Maysin is one of the predominant phenolic compounds found in corn silk has found to possess 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, primarily through the glycosylation of two sugar moieties i.e., rhamnose and keto-fructose. Eman, A. Alam stated that upper parts of corn silk were found to possess the highest total antioxidant capacity and DPPH scavenging activity.²⁴ The results of a research study by Qinglan Hu and Zhi-hong Deng²⁵ showed that flavonoids contained in the corn silk were able to elevate exercise tolerance of mice, and provide protection against oxidative stress occurred by exhaustive exercise in mice. The mechanism of this antioxidant action of corn silk was found to be inhibition of lipid peroxidation and increase in the levels of anti-oxidant enzymes. A study from 2014²⁶ says that maysin was found to be the most abundant corn silk flavonoid and 5 μ g/ml, 10 μ g/ml, 25 μ g/ml and 50 μ g/ml concentrations of it significantly reduced intracellular ROS accumulation dose-dependently by 21.01%, 25.82%, 28.71% and 31.42%, and enhanced intracellular antioxidant enzymes expression in H₂O₂-induced SK-N-MC cells in 0, 5, 10, 25, 50

µg/ml concentration in dose dependent manner by 2.49 fold (α-amylase), 2.42 fold (glutathione peroxidase-1), 2.40 fold (superoxide dismutase-1), 3.15 fold (superoxide dismutase-2), 14.75 fold (heme oxygenase-1) respectively.

Antidiabetic property of corn silk:

Sedentary life style is one of the major causes of overweight issues in many people; overweight and lack of physical movements are one of the remarkable causes of type-2 diabetes mellitus (T2DM). Diabetic patients are characterized by high blood glucose levels. The condition is termed as hyperglycemia. Oxidative stress is also considered as one of the factors causing diabetes. Excess production of ROS as a result of high OS on mitochondria induced through non-enzymatic protein glycation and glucose auto-oxidation due to prolonged exposure to high glucose levels leads to dysfunction of β-cells of pancreas. This makes β-cells unable to produce insulin alternately causing T2DM.²⁷ Also, digestion of carbohydrates by α-amylase and α-glucosidase by hydrolysis of 1,4-glycosidic linkages of polysaccharides to disaccharides and disaccharides to monosaccharides respectively, leads to postprandial hyperglycemia.^{28, 29}

Among the available treatments of diabetes mellitus, insulin and oral anti-diabetic chemical compounds such as glucosidase inhibitors, biguanides, insulin sensitizers, and sulfonylurea are common. But many of them show some unpleasant side effects including lactic acidosis, hypoglycemia, diarrhea, and hepatotoxicity and kidney failure, which can be hard to handle.^{30, 31} This suggests a need for novel compounds with improved efficacy and less toxicity as anti-diabetic medications for DM patients which can shield patients from these harmful effects of synthetic medicines. As cited by Liu et al., the World Health Organization (WHO) recognizes traditional herbal medicines as valuable resources for primary

healthcare, and this has stimulated research into alternative therapies derived from them.³²

One of the effective and non-toxic herbal remedies over hyperglycemia is corn silk extract consumption. Many studies have confirmed the antidiabetic potential of corn silk. Corn silk is traditionally being used as an effective aid for diabetes mellitus since long. Corn silk tea is widely consumed as a supplement for various benefits including for its anti-hyperglycemic activity. Guo et al. experimented effectiveness of corn silk extract in alloxan-induced diabetic mice and found that corn silk extract markedly reduced hyperglycemia through elevating insulin level as well as recovery of damaged β-cells.¹ Kai-Jin Wang, Jin-Liang Zhao (2018) in their study evaluated antioxidant capacity of corn silk and investigated its antioxidant linked properties relevant to the treatment of DM and diabetic nephropathy (DN) in in-vitro models. Where, DN is a common complication of diabetes mellitus. The study results showed that ethyl acetate fraction (ECS) and n-butanol fraction (BCS) of ethanolic corn silk extract contained the highest antioxidant activity, reducing power, and highest DPPH scavenging and hydroxyl radical scavenging activities, while ECS showed highest α-amylase and α-glucosidase inhibition, inhibition of advance glycation end products (AGEs) formation in BSA-glucose model, as well as highest potential against DN in comparison with BCS, petroleum ether fraction (PCS), and water fraction (WCS).³³ Many other studies have been done recently to assess the therapeutic potential of CS including its anti-diabetic property, opening a crate of new potential information about therapeutic evidences of CS.

Diuretic activity of corn silk:

Diuretics are medicines that increase fluid (urine) outflow from the body. Diuretics help kidney remove salt and water from the body through increased urine outflow. Kidney stones are the



calcium oxalate crystals formed at Randall's plaque on the renal papillary surfaces by a complex process involving several physicochemical events including supersaturation, nucleation, growth, aggregation, and retention of urinary stone constituents within tubular cells.³⁴ Among the four stages of kidney stone, nephrolithiasis is the condition when the stones are formed within the kidneys and urolithiasis is the condition when these stones exit the renal pelvis and move into the ureters, bladder, and urethra. Obesity, hyperlipidemia, and type 2 diabetes mellitus have a strong association with calcium oxalate and uric acid stones. Also, there is more risk of the kidney stone development in the patients with medical conditions such as kidney disease, hypertension, gout, diabetes mellitus, hyperlipidemia, obesity, endocrine, and malignancies.³⁵ Conventional diuretics such as carbonic anhydrase inhibitors, osmotic diuretics, loop diuretics, thiazide and related diuretics, potassium-sparing diuretics are available. But these medications show side effects such as hyponatremia, hypokalemia and hyperkalemia, hypomagnesemia, metabolic alkalosis, hyperuricemia, metabolic abnormalities such as hyperglycemia, and hyperlipidemia. Thiazide and thiazide-like diuretics show adverse effects on male sexual functions such as decreased libido, erectile dysfunction, and difficult ejaculation. Also, other side effects shown by diuretics include drug allergies such as photosensitivity dermatitis due to thiazide or furosemide therapy, severe necrotizing pancreatitis due to thiazide therapy, acute allergic interstitial nephritis with fever, rash, and eosinophilia, and carcinogenesis.³⁶ As cited before,^{3, 4} corn silk show therapeutic applications against many of the above mentioned medical conditions which ensure that corn silk can be effective as a diuretic.

Shamkhy A et al. in their study, have confirmed that corn silk stood effective against kidney stone

by increasing the contraction of smooth muscles leading to increase in the urinary outflow and not by the decomposition of kidney stones.³⁷ A study by Hussein S Gumaih defines the possible mechanism of prevention of calcium oxalate (CaOx) crystals deposition by corn silk methanol extract; corn silk possesses high amount of antioxidants and phenolic content that help in the reduction of the lipid peroxidation level thus preventing CaOx crystals attachment and subsequent development of kidney stones. The author has also cited that the diuretic effect of corn silk may be due to the inhibition of the Angiotensin Converting Enzyme and Aldosterone.³⁸

Anti-hypertensive activity of corn silk:

Hypertension is one of the most common but serious chronic health problems worldwide and is also a major risk factor for the development of devastating disorders such as stroke, heart failure, coronary artery disease and renal failure.³⁹ In the past few years, lot of research has been done to explore herbal remedies for the problem of hypertension as herbal medicines are considered to have less toxicities and side effects as compared to the conventional synthetic medicines available. Majority of the world population nowadays use herbal medicines, especially in developing countries, for primary health care because of their better acceptability with human body and lesser side effects.⁴⁰

Use of corn silk extract as an anti-hypertensive agent has been done for years. A very recent study on angiotensin converting enzyme (ACE) inhibitory activity of CS in spontaneously hypertensive rats by Tin-Yun Ho et al. identified a novel Angiotensin Converting Enzyme (ACE) inhibitory peptide CSBp5 in the corn silk extract that showed significant inhibition of ACE activity and decrease in the systolic blood pressure in a dose dependent manner. With this study, the author concluded that corn silk extract exhibited anti-hypertensive property in spontaneously



hypertensive rats via the inhibition of ACE which has been proved to be the target of most anti-hypertensive drugs.⁴¹ According to an article on WebMD, taking corn silk with medications to reduce blood pressure helps to control blood pressure more than taking the medications without corn silk.

Anti-inflammatory activity of corn silk:

Inflammation is one of the body's natural defence mechanisms against an injury to the cell or tissue. The cell or tissue damage may occur due to trauma, microbial invasion, or noxious compounds. According to the severity and lasting time, inflammation is classified as acute inflammation (short lasting) and chronic (long lasting) inflammation. The World Health Organization (WHO) ranks chronic diseases as the greatest threat to human health as these are the most remarkable cause of death worldwide; worldwide, 3 of 5 people die due to chronic inflammatory diseases like chronic respiratory diseases, heart disorders, stroke, diabetes, cancer, and obesity.⁴² Steroidal anti-inflammatory drugs such as corticosteroids and non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen, diclofenac, aceclofenac, celecoxib, indomethacin, aspirin, etc. are common treatment options for different inflammatory diseases such as nephritis, myocarditis, rheumatoid arthritis, multiple sclerosis, and inflammation due to physical injury. Although, NSAIDs show some unpleasant side effects, they are mostly preferred over steroidal drugs because of the risk of serious side effects such as depression, stomach ulcer, osteoporosis, hypertension, hyperglycemia, cataract, dermatitis, adrenal suppression and crisis, impaired wound healing, worsening of previously acquired medical conditions, and fluid retention edema.^{43, 44}

Wang et al. in their study results have pointed the anti-inflammatory activity of the extract of corn silk in acute inflammatory conditions stating that corn silk extract could effectively inhibit the

inflammatory exudate and leukocyte migration promoted by carrageenan in rat pleurisy test.⁴⁵ Corn silk also proved its anti-inflammatory activity by reducing the prostatic inflammation in prostatitis. A study on the potential of corn silk extract in improving benign prostatic hyperplasia (BPH) in male Wistar rats confirmed the reduction in prostate weight and inhibition of prostate tissue hypertrophy due to the administration of a high-maysin corn silk extract. The study concluded that treatment with high-maysin corn silk extract could inhibit prostate cell proliferation in prostate cells of BPH rats by regulating the mRNA expression of PCNA and the mRNA expression of 5 α -R2.⁴⁶ Including these studies, results of many recent pharmacological investigations have proved the anti-inflammatory potential of corn silk. Also, considering safety profile and non-toxic nature of corn silk, it is suggested that more study should be done on more possible therapeutic uses of corn silk.

Anticancer activity of corn silk:

Cancer is one of the most prevalent, complex and devastating diseases worldwide. As per WHO, cancer accounted for nearly 10 million deaths in 2022. The ratio was stated as 1 in 6 deaths was due to cancer. The WHO also listed the most common types cancer that were marked as one of the major causes of death in 2020⁴⁷;

- Lung cancer (1.80 million deaths)
- Colon and rectum cancer (916000 deaths)
- Liver cancer (830000 deaths)
- Stomach cancer (769000 deaths)
- Breast cancer (685000 deaths).

Common treatment methods of cancer include surgery, chemotherapy, and radiotherapy, although all of these treatment methods cannot be always useful for cancer. Although chemotherapy and radiotherapy are considered as highly effective methods, these exert several severe side effects. Some of the serious concerns of cancer treatments are the development of chemotherapy resistance

and serious long term side effects due to radiotherapy which presents a significant challenge.^{48, 49} Unlike the conventional treatments of cancer, herbal drugs are considered to have low toxicity profile, potential of reducing side effects, and potential benefits for quality of life.⁵⁰

Several studies have confirmed anti-cancerous property of corn silk (CS). Recent studies have found that CS slows down proliferation of normal cells, also the results of some studies showed that corn silk extract decreased the cancer cell viability and increased cell apoptosis in human breast cancer cells via the ROS-mediated mitochondrial pathway in dose dependent manner.^{51, 52} Of the various cancer types, pancreatic cancer is considered as highly lethal disease. Pancreatic cancer is highly drug resistant and immunosuppressive. Therefore, the treatment strategies such as surgery, chemotherapy, radiotherapy, and immunotherapy rarely show any effect.⁵³ Researchers have found that the flavonoids present in CS play an important role in anti-cancer activity. Maysin is the major flavonoid found in CS and is reported to be a potential phytochemical showing anti-cancer activity. A study by Yong Il Park et al. (2014) on the anti-cancer activity of maysin in prostate cancer (PC) found that maysin reduced the PC-3 prostate cancer cell viability in a dose-dependent manner as well as significantly induced apoptotic cell death. The study results also showed that a combination of maysin with other known anticancer agents such as etoposide, 5-FU, cisplatin, or camptothecin synergistically enhanced PC-3 cell death.⁵⁴

CONCLUSION

Many studies have confirmed the potential of corn silk as a therapeutic agent for various diseases. Pharmacological studies have confirmed its antidepressant, anti-fatigue, antioxidant, diuretic agent, anti-diabetic, and antimicrobial properties. Being herbal medicine, corn silk is less prone to

show adverse effects and any toxicity as compared to the conventional medicines. Some new studies have also supported the earlier findings confirming its safety profile and non-toxic nature. Based on the study results and claims by different studies on the therapeutic potential of corn silk, it is sure that CS could be a potential alternative to conventional medicines. For this, it is important to further study and investigate possible medicinal uses of corn silk.

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HOW TO CITE: Amey Dongaonkar*, Dadaso Mane, Gajanan Sormare, Milind Umekar, Nishant Awandekar, Therapeutic Applications of Corn Silk, a Versatile Natural Medicine: A Comprehensive Review, *Int. J. of Pharm. Sci.*, 2024, Vol 2, Issue 7, 551-562.
<https://doi.org/10.5281/zenodo.12687174>

