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EXPLORING THE THERAPEUTIC AND NUTRACEUTICAL POTENTIAL OF *STIGMA MAYDIS*: A COMPREHENSIVE REVIEW

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ABSTRACT

Maize Silk (*Stigma maydis*) is a byproduct of *Zea mays* and is essentially a stigma that comes from the female maize blossoms. It is a member of the Poaceae family and is often either light green or golden brown in colour. Proteins, vitamins, polysaccharides, Ca, K, Mg, and Na salts, phenolic compounds, flavonoids, volatile and fixed oils and steroids like stigmasterol and sitosterol are all found in corn silk. The safest and best solvent for extracting the active components of corn silk is ethanol. As an anti-inflammatory, anti-depressant, anti-hyperlipidemic, anti-diabetic, anti-fatigue, anti-microbial and antioxidant as well as neuroprotective, diuretic, kaliuretic effects, kidney stones, urinary tract infection, bedwetting and obesity Corn silk (CS) has been widely used traditionally and medicinally for its many therapeutic uses in various countries. A thorough analysis of the literature revealed that the phytochemicals included in corn silk such as flavonoids, alkaloids, tannins and saponins are the constituents responsible for reducing blood glucose levels.

KEYWORDS: *Stigma maydis*, Phytochemical Constituents, Free Radical Scavenging Activity, Antioxidant, Anti-diabetic, Anti-hyperlipidaemic, Diuresis and Kaliuresis.

1. INTRODUCTION

Zea mays, the stigma that originates from the female corn blossoms and produces maize silk (*Stigma maydis*), which is typically light green or golden brown in hue. Proteins, vitamins, polysaccharides, Ca, K, Mg and Na salts as well as bioactive substances such as alkaloids, tannins, saponins, flavonoids and steroids are all found in corn silk. Mature corn silk had higher values for ash content (5.51 ± 0.24%), carbohydrate content (29.74 ± 1.26%) and total dietary fibers

(51.24 ± 1.50 g/100 g). While, immature corn silk had higher moisture content (89.31 ± 0.74%), crude lipid content (1.27 ± 0.16%) and crude protein (12.96 ± 0.38%).[1] *Zea mays* Linnaeus or Corn belongs to the family *Poaceae* or *Gramineae*. It originated in Mesoamerica and was domesticated in Mexico around 9,000 years ago before spreading over the continents of America. It is currently grown extensively worldwide. There are 10,000 species of native corn which are divided into 600–700 genera. This family includes rice, wheat, oats and barley.[2] In 2017, the global market for corn silk extract was divided into seven major geographical regions: North America, Latin America, Western Europe, Eastern Europe, Middle East & Africa (MEA), Asia Pacific Excluding Japan (APEJ) and Japan. When it comes to producing maize and corn silk, North America and Latin America lead the world followed by European nations.[3] Cystitis, Jaundice, Edema, Prostate diseases, Urinary tract infections, Hyperglycemia and Obesity have all been treated with corn silk which has been shown to have diuresis and detumescence properties as well as advantages for the liver and gallbladder.[4] In several nations including China, Turkey, India, France and the United States, Corn silk (CS) is extensively used traditionally for its many medicinal applications as an antidepressant, anti-fatigue, antioxidant, diuretic, anti-diabetic and antibacterial agent.[5] For medical use CS is harvested soon before pollination occurs and can be utilized in fresh or dry form.[6]

Figure 1.1: *Stigma maydis.*

Table 1.1: Taxonomical Classification of *Zea mays*.[7]

Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida
Order	Poales
Family	Poaceae
Genus	*Zea*
Species	*Z. mays*

2. An Overview of the Phytoconstituents of *Zea Mays* Silk Extracts

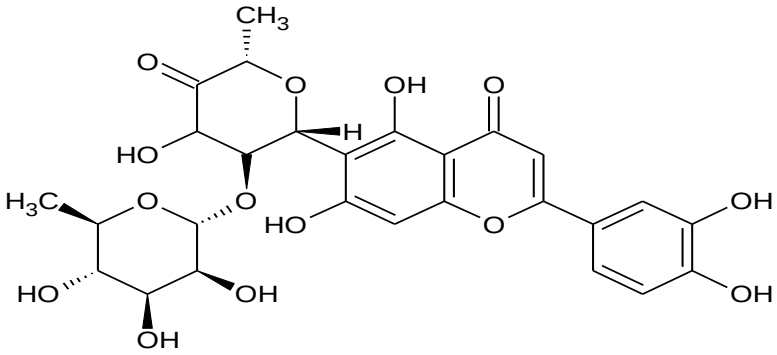
The compositions of CS extracts are vital to assess their biological activities which are mostly attributable to their flavonoids concentration. Flavonoids are a broad class of phenolic chemicals found in plants that have antioxidant properties.[6] From the CS of several corn inbreeds, a flavonoid 3'-methoxymaysin and reduced derivatives of maysin have been discovered. 2"-O-α-L-rhamnosyl-6-C-quinovosylluteolin, 2"-O-α-L-rhamnosyl-6-C-fucosylluteolin and 2"-O-α-L-rhamnosyl-6-C-fucosyl-3'-methoxyluteolin are among the chemicals that were identified.[8] Five other flavonoid derivatives were isolated from CS ethanol extract (80%) and identified as 2"-O-α-L-rhamnosyl-6-C-3"-deoxyglucosyl-3'-methoxyluteolin, 6,4'-dihydroxy-3'-methoxyflavone-7-O-glucosides, ax-5"-methane-3'-methoxymaysin, ax-4"-OH-3'-methoxymaysin and 7,4'-dihidroxy-3'-methoxyflavone-2"-O-α-L-rhamnosyl-6-C-fucoside.[9] Besides maysin,

additional flavonoid molecules identified from CS methanol extract (100%) were c-glycosylflavones.[10] CS 95% ethanol extract included two flavone glycosides: isoorientin-2-2''-O-α-L-rhamnoside and 3'-methoxymaysin.[11]

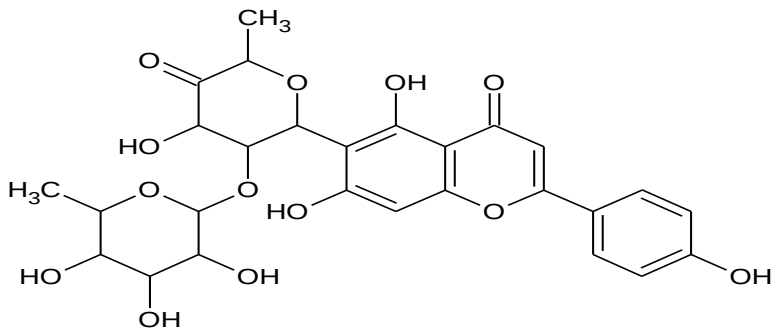
Terpenoids accounted for over 99% of the extract's volatile chemicals with cis-α-terpinol (24.22%), citronellol (16.18%), 6,11-oxidoacor-4-ene (18.06%), trans-pinocamphone (5.86%), eugenol (4.37%), neo-iso-3-thujanol (2.59%) and cis-sabinene hydrate (2.28%). These substances are frequently used for flavouring and fragrance in a variety of goods including cosmetics, home goods and soaps. Furthermore, the CS was rich in minerals including sodium (0.05%), potassium (15%), iron (0.0082%), zinc (0.016%) and chloride (0.25%)[12] as well as cinnamic derivatives, glucose and rhamnose. The proximate compositions of corn silk demonstrate presence of 9.65% moisture, 3.91% ash, 0.29% crude fat, 17.6% crude protein and 40% crude fiber.[13]

Table 1.2: Biochemical Constituents of Corn Silk Extract.[14]

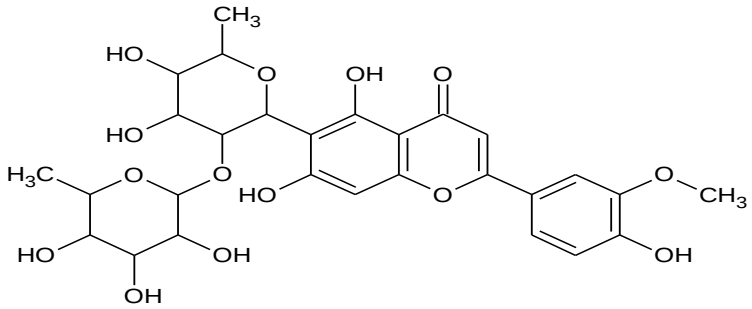
Chemical Constituents	Concentration
Sodium	3654.21 ± 2.97 µg/g
Magnesium	1169.05 ± 12.94 µg/g
Calcium	1338.13 ± 14.23 µg/g
Potassium	1135.78 ± 6.3 µg/g
Manganese	11.10 ± 2.15 µg/g
Copper	11.91 ± 1.15 µg/g
Iron	41.77 ± 2.67 µg/g
Zinc	83.75 ± 1.80 µg/g
Total Phenolic Content	94.10 ± 0.26 mg GAE/g
Total Flavonoid Content	163.93 ± 0.83 mg QE/ 100g
Phenols	34.67mg/g
Tannins	77.05 mg/g
Alkaloids	0.27%
Saponins	2.0%



Maysin ($C_{27}H_{28}O_{14}$)



Apimaysin ($C_{28}H_{32}O_{14}$)



3'-methoxymaysin ($C_{28}H_{32}O_{14}$)

Figure 1.2 Structure of Flavonoids in corn silk.[15]

3. An Overview of the Reported Activities of Corn Silk

3.1 Antioxidant Activity

Numerous illnesses including atherosclerosis, neurological disorders, cancer, diabetes, inflammation and aging can be brought on by oxidation. Natural antioxidants extract from fruits, teas, vegetables, cereals and medicinal plants have been investigated extensively due to their effectiveness in eliminating free radical and claimed to be less toxic than synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT).[16] In comparison to other CS fractions, the n-butanol fraction (100 µg/mL) had the highest total phenolic (164.1 µg GAE/g DCS) and total flavonoid content (69.4 µg RE/g DCS) which demonstrated the strongest antioxidant activity. BF at 100 µg/mL had the highest total antioxidant (0.789) and reducing power (1.242). In contrast, BF at 120 µg/mL had the radical scavenging activity 72.93% and iron-chelating activity 62.06%. These antioxidant levels were comparable with vitamin C (positive control) and ethylenediaminetetraacetic acid (EDTA). At doses of 0.8 and 1.6 mg/mL, CS ethanol extract had a strong reducing power and the outcomes were similar to those of vitamin C ($p > 0.05$).[17] By acting as an electron donor, the extract stops the chain reactions caused by free radicals. Additional research has shown that CS ethanol extract (400 µg/mL) exhibited potent antioxidant activity by preventing β-carotene bleaching (75%) and free radical scavenging activity (84%).[18] The polyphenol content of CS contributes to its antioxidant activity and total polyphenol, tannin, proanthocyanidin and flavonoid levels are linearly correlated with Ferric Reducing/Antioxidant Power (FRAP) values.[19] Total antioxidant capacity and DPPH assays were used to assess the antioxidant activities of the upper (dark brown, exposed to the air) and bottom (light yellow, not exposed to the air) portions of CS ethanolic extract.[20] The maximum DPPH scavenging activity (IC50 = 0.704 mg/mL) and overall antioxidant capacity (2.735 mg/g GA equivalents) were reported in the top portions. Since, the higher portions of CS are more exposed to the Sun than the bottom portions, flavonoids and other phenolic chemicals have accumulated there to shield maize DNA from UV damage.[21] At 200 µg/mL, Z. mays var. intendata EtOH extract showed 25% SO scavenging efficacy. At 500, 1000, and 2000 µg/mL, Z. mays var. indurata EtOH extract had the greatest iron chelating capacity (63%).[22] According to the study, flavonoids from CS (FCS) extract shielded mice against oxidative damage brought on by strenuous exercise.[23]

Oral gavage of FCS (100 and 400 mg/kg body weight) for 28 days prior to treadmill activity was used to examine the protective effect. Exhausted mice were then anesthetized to death to remove skeletal muscle tissue for MDA and antioxidant enzyme superoxide dismutase (SOD) and glutathione peroxidase (GPX) assays. When compared to the control group, the FCS-treated groups running times rose by 41.52% (100 mg/kg body weight) and 72.32% (400 mg/kg body weight) ($p < 0.05$). MDA levels were considerably lowered by FCS at concentrations of 100 mg/kg body weight

and 400 mg/kg body weight by 26.46% and 37.91%. The results demonstrated that FCS protects skeletal muscle from oxidative damage caused by acute exercise. By considerably raising SOD and GPX levels in comparison to the control group ($p < 0.05$), the exercise improved the activities of antioxidative enzymes and offered defense against reactive oxygen species (ROS). Peripheral blood cells and bone marrow membrane lipids can be destroyed by radiation-induced ROS. Consequently, it inhibits creation of blood cells and increases blood cell destruction which leads to the loss of blood cell mass and lowered production of Nrf2 expression dramatically. In the same study, CS extract administration enhanced the protein expression of Nrf2 (dose-dependently) and detoxifying antioxidant enzymes such as glutathione reductase (GR) and superoxide dismutase (SOD). Nrf2 is a transcription factor that attaches itself to the antioxidant response element in many target genes that encode few of these enzymes including SOD and GR.[24] Therefore, controlling antioxidants is crucial for controlling oxidative stress. Many researches established that the CS extract play a key function in regulating the oxidative stress.

3.2 Diuresis and Kaliuresis Effect

Diuresis is a discharge of urine in a significant amount whereas kaliuresis is the secretion of potassium in a large amount in urine.[11] The CS aqueous extract in Wistar rats demonstrated kaliuresis effects (K^+ urine excretion) at dosages of 350 mg/kg body weight (100.42 µEq/5 h/100g body wt) and 500 mg/kg body weight (94.97 µEq/5 h/100g body wt). In contrast to the water control, an increase in diuresis (urinary volume) was noted at a dosage of 500 mg/kg body weight (1.98 mL/5 h/100 g body wt) ($p < 0.05$). At a dosage of 500 mg/kg body weight of CS extract, the effects of urine volume, salt, potassium, uric acid excretions, glomerular and proximal tubular function via creatinine and lithium clearance were examined. The potassium excretion is considerably enhanced (0.2289 µEq/min/100g body wt).

However, urine volume, sodium, lithium and uric acid excretions remain unchanged. Glomerular function evaluated by creatinine varied from 295 to 241 µL/min/100 g body weight and the sodium filtered load from 41.9 to 34.3 revealed a decrease in activity while there is no change in proximal tubular function measured by lithium and sodium excretion.[25]

3.3 Hyperglycaemia Reduction

An extremely high blood glucose level is known as hyperglycemia[23]. Utilizing Xiaoke tablets, a Chinese diabetic medication as a positive control and saline as a control, the effects of CS aqueous extract (0.5, 1.0, 2.0, and 4.0 g/kg body weight) on glycemic metabolism utilizing an alloxan-induced hyperglycemia in mice model were investigated.

Alloxan (a diabetogenic substance) is utilized for the production of diabetes in experimental animals. It specifically reduces glucose-induced insulin secretion by targeted inhibition of glucokinase. It also reduces the glucose sensor of the β-cell and causes a state of insulin-dependent diabetes through selective necrosis of β-cells in type 1 and 2 diabetes mellitus. The results demonstrated that the body weight of the Xiaoke pill and CS treated groups grew steadily after 20 days. This demonstrates that CS may function as a supplemental nutrition for the mice. Meanwhile, the blood glucose levels from hyperglycemic mice were dropped to 15.6 mmol/L and 11.5 mmol/L following the consumption of CS extract at 2.0 and 4.0 g/kg compared to control (21.2 mmol/L) respectively. At a dosage of 4.0 g/kg, the blood insulin level was increased to 9.8 µU/mL, while the control group was 3.8 µU/mL. 15 days later, cell damage was not seen in the CS-treated animals. The injured pancreatic β-cells of the mice given 4.0 g/kg CS extract largely healed.[26]

3.4 Anti-depressant Activity

Extract concentration of 1500 mg/kg demonstrated similar action as the positive standard imipramine (10 mg/kg) with immobility duration of 57.6 seconds in Forced Swim Test. However, there is no mortality recorded upto 4000 mg/kg dose and this data revealed that the CS extract might be an important natural anti-depressant. Recent investigations further validated that CS demonstrated an anti-depressant action towards streptozotocin-induced diabetic rats.[27]

3.5 Anti-fatigue Activity

Mice given 100 and 400 mg/kg of flavonoids CS (FCS) orally for 14 days were used to test the anti-fatigue properties of CS through swimming exercises. During the exercise, hepatic glycogen concentration of the FCS treatment group was enhanced by 261% at 100 mg/kg and 281% at 400 mg/kg concentration compared to the control.[28]

3.6 Anti-diabetic and Anti-hyperlipidaemic activity

Triglycerides (TG), total cholesterol (TC), cholesterol esters and phospholipids are examples of plasma lipids that are elevated in hyperlipidemia.[29] Twenty-six bio-actives were docked against five different targets i.e. PTPN1B, GLUT1, DPP4, α-glucosidase and α-amylase from which flavones were found to possess the highest binding affinity towards PTPN1B with a binding energy of -8.5 kcal/mol. β-carotene, gallotannins, 3-O-caffeoylquinic acid and stigmasterol were predicted to possess the highest binding affinity towards GLUT1, DPP4, α-glucosidase and α-amylase with binding energy -11.1 kcal/mol, -10.7 kcal/mol, -8.9 kcal/mol and -9.8 kcal/mol respectively. This work tested the anti-diabetes ability of 26 bioactives against five distinct diabetic proteins suggesting that maize silk bioactives may have anti-diabetic potential.[30] The AB-8 resin was selected for the purification of crude flavonoids because of the higher absorption and desorption rate. Flavonoids with content of 68.3% was obtained with a flavonoid recovery of 93.7% after purification. Flavonoids from corn silk had notable anti-hyperlipidaemic activities by reducing the concentration of serum TC, TG and LDL-C and increasing the concentration of HDL-C.[31]

4. Toxicity Studies of Corn Silk Extract

7.5 g/kg (single administration), 15.0 g/kg (twice in 12 hours) and 20.0 g/kg (three times in 24 hours) were given to the mice. During the trial, there were no notable anomalies in body weight increase or food intake nor were there any animal deaths or behavioural abnormalities.[32]

5. CONCLUSION

Stigma maydis has been traditionally used for its vast medicinal uses. It can be concluded that the extract of corn silk contains alkaloids, glycosides, tannins, maysin, luteolin, quercetin, rutin, apigenin, kaempferol 2"-*O*-α-L-rhamnosyl-6-C-3"-deoxyglucosyl-3'-methoxyluteolin, 6,4'-dihydroxy-3'-methoxyflavone-7-*O*-glucosides, ax-5"-methane-3'-methoxymaysin, ax-4"-OH-3'-methoxymaysin, 7,4'-dihidroxy-3'-methoxyflavone-2"-*O*-α-L-rhamnosyl-6-C-fucoside, c-glycosylflavones and phenolic compounds. Because of the presence of these essential phytoconstituents, Corn silk exhibited multiple pharmacological actions like antioxidant, Diuresis and kaliuretic effect, anti-depressant, anti-fatigue, anti-diabetic, anti-hyperlipidaemic and many other effects.

Author Contributions

All the authors contributed to the manuscript equally.

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