Corn Silk (*Zea mays L.*) Extract Is as Effective as Metformin in Reducing Blood Glucose Levels in Diabetic Mice

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and associated with serious complications affecting multiple organs. The increasing global prevalence of diabetes has encouraged exploration of alternative natural therapies with antihyperglycemic potential. This study aimed to determine the effectiveness of corn silk (*Zea mays L.*) extract in reducing blood glucose levels in diabetic mice. An experimental study was conducted using two groups of mice, each consisting of six animals. Group I received corn silk extract, while Group II received metformin. Blood glucose levels were measured after treatment, and differences between groups were analyzed using the Mann–Whitney test. Both corn silk extract and metformin reduced blood glucose levels in diabetic mice. Statistical analysis showed no significant difference in the mean reduction of blood glucose levels between the two groups ($p = 0.083$). Corn silk extract demonstrated a glucose-lowering effect comparable to metformin in diabetic mice, indicating its potential as a natural antihyperglycemic agent.
Keywords: corn silk; diabetes mellitus; metformin

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder that poses a major global health challenge, with prevalence increasing steadily each year. The condition may result from impaired insulin secretion, varying degrees of insulin resistance, or a combination of both mechanisms [1]. DM comprises several categories, including type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary diabetes caused by endocrinopathies, steroid use, or other factors. T1DM and T2DM are the two main subtypes. T1DM commonly occurs in children and adolescents due to impaired insulin secretion or function, whereas T2DM typically affects middle-aged and older adults and is often associated with prolonged hyperglycemia related to unhealthy lifestyle and dietary patterns [2].

The global burden of diabetes has increased markedly, particularly in countries with large populations. Over the past four decades, the number of people with diabetes has risen substantially in countries such as China and India, largely driven by lifestyle and occupational changes that increase diabetes prevalence [3]. The World Health Organization (WHO) reports that approximately 14% of adults aged 18 years and older are living with diabetes, a substantial increase from 7% reported in 1990. Consequently, the number of individuals with diabetes worldwide has grown dramatically from about 200 million in 1990 to approximately 830 million in 2022 [4]. In Indonesia, the prevalence of diabetes has also increased steadily. According to the International Diabetes Federation (IDF), the number of individuals with diabetes reached 18.69 million in 2020 and increased to 20.42 million in 2024, with a prevalence of 11.3% [5].

At the regional level, DM represents a major non-communicable disease burden. Data from the Hospital Information System (SIRS) indicate that DM was the second most common non-communicable disease in East Java Province in 2022. The East Java Provincial Health Office estimated that approximately 854,454 diabetes cases occurred in the province in 2023, with about 859,187 individuals (100.6%) diagnosed and receiving health services [6]. In Ponorogo Regency, 15,397 diabetes cases were recorded in 2020, including 7,642 male and 7,755 female patients [7].

DM is characterized by metabolic disturbances resulting from insufficient insulin production or impaired insulin action, leading to elevated blood glucose levels. Clinical manifestations may include polyuria, polydipsia, polyphagia, weight loss, blurred vision, and fatigue [8]. Persistent hyperglycemia can lead to various complications, including macrovascular and microvascular damage. Microvascular complications may result in conditions such as renal failure [3]. In addition, diabetes contributes to cardiovascular diseases and heart failure through cellular, molecular, and systemic mechanisms that promote inflammation, dyslipidemia, endothelial dysfunction, coronary artery disease, myocardial fibrosis, left ventricular hypertrophy, and cardiomyocyte dysfunction [9]. Other complications include neovascular glaucoma, characterized by abnormal blood vessel growth in the iris and fibrovacular tissue proliferation in the anterior chamber angle, often associated with proliferative diabetic retinopathy and ocular ischemic syndrome [10]. Diabetic peripheral neuropathy (DPN) is another common and severe complication resulting from chronic hyperglycemia and related pathophysiological changes, increasing the risk of foot ulcers, infections, non-traumatic amputations, and long-term disability [11].

Although diabetes mellitus cannot be completely cured, the disease can be effectively controlled [12]. Maintaining blood glucose levels within the normal range is a key component of diabetes management and helps prevent both acute and chronic complications [13]. Several factors influence glycemic control in patients with diabetes, including high-calorie diets, low physical activity, overweight or obesity, lifestyle habits, limited knowledge about the disease, and alcohol consumption [14].

Corn produces corn silk, a fibrous structure attached to the ear of the plant. Despite its biological components, corn silk is often discarded as agricultural waste by the community [15]. In recent years, herbal medicine derived from natural sources has gained increasing attention as an alternative therapeutic approach because bioactive compounds may interact synergistically to produce beneficial pharmacological effects [16]. Corn silk contains several bioactive substances, including phenolic compounds (approximately 77.89 mg GAE/g), flavonoids (approximately 59.65 mg quercetin/g), and polysaccharides (approximately 58.75%), which have been associated with antioxidant and potential therapeutic activities [17].

In experimental studies, alloxan is commonly used to induce diabetes in animal models by selectively damaging pancreatic β-cells, resulting in hyperglycemia due to insulin deficiency or insulin resistance [18][19]. Therefore, this study aimed to evaluate the effectiveness of corn silk extract in reducing blood glucose levels in an alloxan-induced diabetic mouse model compared with metformin.

METHODS

This study employed an experimental research design to compare the glucose-lowering effects of corn silk extract and metformin in diabetic mice. The research was conducted from June to July 2024 at two locations: Citra Alam Sudarsono, Ponorogo, where the corn silk extraction process was performed, and the AKAFARMA Sunan Giri Laboratory, Ponorogo, where the extract testing and experimental procedures were carried out.

The research materials consisted of corn silk agricultural waste collected from several agricultural fields in East Java and identified at the Production Laboratory of Citra Alam Sudarsono UD, Ponorogo. The samples were washed with running water to remove adhering impurities and then dried in an oven until they formed dried simplicia. The dried material was sorted, ground into powder, and stored in an airtight container. Extraction was performed using the maceration method. A total of 500 g of corn silk powder was macerated in 5 L of 70% ethanol for five days with daily stirring. The extract was filtered using Whatman filter paper to obtain the first filtrate (macerate 1). The remaining residue was re-macerated for two additional days with 250 mL of 70% ethanol, filtered again to obtain macerate 2, and all filtrates were combined and concentrated using an evaporator at 60°C until a solid extract was obtained.

The research subjects were laboratory mice weighing approximately 20 g. The animals were induced with alloxan monohydrate to produce a diabetic model. A total of 35 mg of alloxan monohydrate was dissolved in distilled water and diluted to a final volume of 2 mL, producing a solution concentration of 17.5 mg/mL. Each mouse received 0.2 mL of the solution (3.5 mg) via intraperitoneal injection to induce hyperglycemia.

The independent variable in this study was the treatment administered, consisting of corn silk extract or metformin. The dependent variable was the reduction in blood glucose levels measured in the mice. The experiment included two groups, each consisting of five mice: a control group receiving metformin at a dose of 91 mg/kg body weight and a treatment group receiving corn silk extract at a dose of 0.00091 g/kg body weight. Blood glucose levels were measured before and after treatment for 14 days. Data were analyzed to determine differences in the mean reduction of blood glucose levels between the two groups using the independent samples t-test.

RESULTS

The present study aimed to compare the effectiveness of corn silk extract and metformin in reducing blood glucose levels in mice induced with alloxan at a dose of 125 mg/kg body weight. For mice weighing 20 g, the calculated dose was 3.5 mg. Fasting blood glucose levels were measured before alloxan induction, and a comprehensive phytochemical screening of corn silk extract was performed (Tabel 1 and Table 2).

Table 3 presents the comparison of blood glucose levels between the control group receiving metformin and the corn silk extract group after treatment on days 3, 7, and 14. Table 4 presents blood glucose levels before and after administration of metformin and corn silk extract for 14 days. The table also includes the magnitude of glucose reduction, the p-value for comparisons before and after treatment in each group, and the p-values from the normality tests for the glucose reduction data.

Based on Table 5 and Table 6, the results indicate that blood glucose levels decreased in alloxan-induced diabetic mice after treatment with both corn silk extract and metformin. Statistical analysis showed no significant difference in the mean reduction of blood glucose levels between the metformin group and the corn silk extract group (p = 0.083), indicating that corn silk extract demonstrated a glucose-lowering effect comparable to metformin in this experimental model.

DISCUSSION

Corn silk is a collection of stigmas from the female flower of maize that appear as thread-like structures with a yellow to brown color. Biologically, its function is to capture pollen during the pollination process [20]. Corn silk contains various bioactive compounds, including phenolic compounds, flavonoids, carotenoids, quercetin, alkaloids, simple phenols such as p-coumaric acid, saponins, tannins, anthocyanins, and protocatechuic acid [21]. Flavonoids are known to function as antioxidants, anticancer agents, anti-inflammatory agents, antiallergic agents, and antihypertensive agents [22]. These compounds belong to the group of secondary metabolites that are widely distributed in plant tissues [23]. The mechanism of action of flavonoids includes their role as strong antioxidants that neutralize free radicals and support the regeneration of pancreatic β-cells, thereby improving glucose regulation through enhanced insulin production efficiency [16]. The antioxidant activity of these compounds is associated with their ability to scavenge free radicals by donating hydrogen atoms from flavonoid hydroxyl groups. Natural flavonoids therefore play an important role in preventing diabetes and its related complications [22].

Recent studies have demonstrated that flavonoids in corn silk are capable of binding to PTP1B with an energy of −8.5 kcal/mol, while β-carotene, gallotannin, 3-O-caffeoylquinic acid, and stigmasterol exhibit binding energies of −11.1, −10.7, −8.9, and −9.8 kcal/mol, respectively. These findings indicate that corn silk may prevent diabetes by acting on multiple biological targets simultaneously [24]. Furthermore, a study conducted in 2023 reported that corn silk polysaccharides (CSPs) provide protection against diabetic kidney injury by improving gut microbiota balance and metabolic conditions. Administration of CSPs in diabetic rats with kidney damage significantly altered gut microbiota composition and

Table 1. Phytochemical profile of corn silk extract

Compound	Reagent	Parameter	Result
Flavonoids	Mg powder + HCl	Orange color	+
	Mayer	Dark red	+
Alkaloids	Wagner	Orange precipitate	+
	Dragendorff	Dark brown	+
Tannins	FeCl₃	Dark brown	+
Steroids	Liebermann–Burchard	–	–
Saponins	–	Persistent foam	+

Table 2. Blood glucose levels of mice before and after alloxan induction

Group	Pre	Post	Mean increase in blood glucose
	68	186	
	87	229	
Control	74	264	
	81	207	130.7 mg/dL
	90	195	
	84	188	
	98	237	
Corn silk extract	63	192	
	72	225	
	79	180	

Table 3. Blood glucose levels after induction on days 3, 7, and 14

Group	Blood glucose levels of mice	Sample				
		1	2	3	4	5
Day 3	Control	179	215	163	170	138
	Corn silk extract	142	233	180	169	188
Day 7	Control	151	174	153	134	128
	Corn silk extract	136	198	154	142	167
Day 14	Control	98	121	127	116	110
	Corn silk extract	114	140	123	133	129

Table 4. Reduction in blood glucose levels and normality test

Group	Pre	Post	Reduction	Normality (p-value)		
				Pre	Post	Reduction
Control	186	98	88	0.568	0.907	0.126
	229	121	178			
	264	127	137			
	207	116	91			
	195	110	85			
Corn silk extract	188	114	74	0.287	0.988	
	237	140	97			
	192	123	69			
	225	133	92			
	180	129	51			

Table 5. Paired t-test results for the metformin (control) group and corn silk extract group

Group	Mean	Standard deviation	p-value
Control	101.800	21.603	<0.001
Corn silk extract	76.600	18.528	<0.001

Table 6. Independent sample t-test results after administration of metformin and corn silk extract

Group	n	Mean	SD	SE	p-value
Control	5	101.80	21.603	9.661	0.083
Corn silk extract	5	76.60	18.528	8.286	

metabolic products. These findings suggest that the antidiabetic effects of corn silk may not only occur through direct effects on pancreatic β-cells or insulin secretion but also through the gut–kidney axis, which is increasingly recognized in the pathogenesis of diabetic complications [25].

In the present study, the mean increase in blood glucose levels in mice reached approximately 130.7 mg/dL in both experimental groups after induction. This increase occurred because alloxan metabolism generates free radicals that are known to damage pancreatic β-cells [26]. A commonly used dose of alloxan to induce hyperglycemia in rodents is 125 mg/kg body weight, as reported in previous studies [27]. However, this study used mice, which are smaller than rats and have an average body weight of approximately 20 g. Therefore, the dose was adjusted to 3.5 mg per mouse. A solution with a concentration of 17.5 mg/mL was prepared, and each mouse was induced with 0.2 mL of alloxan solution (equivalent to 3.5 mg) to induce hyperglycemia, in accordance with established experimental references [28].

After successfully inducing diabetes in mice using alloxan, the next step involved administering metformin to mice in the control group for 14 days, resulting in an average reduction in blood glucose levels of 101.80 mg/dL. The use of metformin as a positive control was based on previous studies reporting similar reductions, such as a decrease of 127.37 mg/dL. In that study, the average blood glucose level of mice before alloxan induction reached 397.34 mg/dL, and after 28 days of metformin administration, the level decreased to 269.97 mg/dL [29]. Metformin plays an important role in lowering and preventing excessive increases in blood glucose levels, known as hyperglycemia, thereby contributing to the suppression of free radical production in the body [30]. These findings confirm the effectiveness of metformin in reducing blood glucose levels in diabetic mice.

Administration of corn silk extract in this study also reduced blood glucose levels in hyperglycemic mice, with an average reduction of 76.60 mg/dL. Previous studies have reported that corn silk extract in type 1 diabetic rat models significantly reduced fasting blood glucose levels, improved pancreatic damage, and regulated gut microbiota composition as part of its mechanism of action [31]. Another study reported that administration of corn silk polysaccharides in type 2 diabetic rat models for six weeks resulted in a statistically significant reduction in blood glucose levels ($p < 0.01$), along with improvements in pancreatic islet morphology and overall metabolic conditions in the experimental animals [32]. These findings support the potential of corn silk extract to reduce blood glucose levels in diabetic animal models.

Observations over 14 days in both treatment groups demonstrated similar glucose-lowering effects following the administration of corn silk extract and metformin in diabetic mice. Statistical analysis indicated no significant difference between the two treatments ($p = 0.083 > 0.05$). Previous research has also suggested that corn silk possesses promising antidiabetic potential and could be developed as an economical plant-based therapeutic agent for the management of type 2 diabetes mellitus. In that study, the control group received metformin at a dose of 150 mg/kg/day (n = 10), while three treatment groups received corn silk extract at doses of 300, 600, and 1200 mg/kg/day (n = 10 each) [33]. More recent studies have further demonstrated that corn silk polysaccharides help restore gut microbiota balance and improve metabolite profiles involved in blood glucose regulation. Unlike metformin, which primarily works through activation of AMP-activated protein kinase (AMPK), this mechanism involves the microbiota–metabolite pathway to restore metabolic homeostasis. These findings highlight the potential of corn silk extract as a natural adjuvant therapy for diabetes mellitus [25][34].

Although metformin remains the first-line therapy for type 2 diabetes, long-term use may be associated with adverse effects. A recent meta-analysis reported a significant association between prolonged metformin use and vitamin B12 deficiency, which may increase the risk of neuropathy if not properly monitored [35]. Other studies have reported common side effects of metformin, including diarrhea, nausea, and vomiting, occurring in up to 30% of patients. Less common adverse effects include chest pain, headache, excessive sweating, hypoglycemia, weakness, and rhinitis during metformin therapy [35]. Considering the potential adverse effects associated with long-term metformin use, this study explored the development of corn silk extract as an alternative therapeutic approach. Given the abundant availability of corn silk, which is often treated as agricultural waste, it has potential to be developed as an environmentally friendly and safe agent for lowering blood glucose levels. Although the present study was limited to an animal model using mice, the findings provide preliminary evidence for the development of phytopharmaceutical preparations derived from corn silk extract. The comparable reduction in blood glucose levels observed between the treatment group and the positive control group suggests that corn silk has promising potential as an alternative or complementary antidiabetic therapy that is both environmentally sustainable and economically accessible.

CONCLUSION

Based on the results of this study in diabetic mice, it can be concluded that administration of corn silk extract reduced blood glucose levels in mice with an effect comparable to metformin, although no significant difference in the mean reduction was observed between the two groups. Therefore, corn silk extract shows potential to be further developed as a natural glucose-lowering agent in future studies.

Ethical consideration, competing interest and source of funding

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