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Preliminary phytochemical screening and scientific validation of the anti-diabetic effect of the dried husk of *Zea mays L.* (Corn, Poaceae)

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Abstract

The dried husk of *Zea mays L.* (Poaceae) also known as corn husk (CH) has been used as traditional remedies in some cultures including Ghana for the management/treatment of Diabetes Mellitus (DM, Type 2). However, there is no evident documentation on the phytoconstituents of CH and the scientific validation of the antidiabetic properties of CH. Therefore, the methanolic and aqueous extracts of CH were phytochemically screened, and the decoction of CH was administered to human subjects (Type 2 diabetic patients with uncontrolled blood glucose level). The fasting blood glucose levels of subjects on regularly prescribed oral antidiabetic agents were determined over a period of three weeks. In addition to the regular oral antidiabetic medications, decoctions of CH were administered to the subjects for a further period of three weeks, and the fasting blood glucose levels were again determined. The fasting blood glucose level of the control group was however monitored continuously for a period of six weeks. The phytochemical analyses of the CH extracts revealed the presence of flavonoids, saponins, alkaloids and glycosides as common constituents of the aqueous and methanolic extracts, whereas tannins and phenols were found exclusively in the methanolic extract. The decoction of CH demonstrated a significant anti-diabetic property, attesting to the traditional use of CH as antidiabetic therapy.

Keywords: Corn Husk, Diabetes Mellitus, Fasting Blood Glucose Test, flavonoids, *Zea mays*.

1. Introduction

Diabetes Mellitus (DM) is a chronic metabolic disease that results from disorders in carbohydrate, lipid and protein metabolism [1]. The disease is characterized by chronic high blood glucose level (hyperglycaemia), oxidative stress and microvascular pathology of the renal glomeruli, retina and peripheral nerves [1,2]. Some of the main clinical symptoms of DM are polyuria, polydipsia, polyphagia, hyperglycaemia and weight loss [3, 4]. There are two main types of DM which are Type 1 and Type 2 DM [1]. The prevalence of Type 2 DM is higher than Type 1, with only 5 - 10 % of cases belonging to Type 1. In Type 2 DM, there are defects in insulin secretion or/and insulin action (insulin resistance) [5]. The insulin resistance leads to conditions such as amyloid deposits, hyperinsulinaemia and reduction of pancreatic beta cell mass through the inflammation of pancreatic beta cells [6].

The International Diabetes Federation has estimated 552 million diabetic patients worldwide by the year 2030 [7]. According to the World Health Organization (WHO), there will be 300 million adult DM patients globally by the year 2025 [8]. In Ghana, 266,200 cases of DM were reported in the year 2015 alone, with the patients aged between 20 to 79 yrs. [9]. In view of the economic burden, high risk of disabling conditions (e.g. hypertension, amputation, blindness, renal failure) and premature death

associated with Type 2 DM, the search for more antidiabetic remedies that are safe and effective remains important.

The current therapeutic options for the control of hyperglycaemia in Type 2 DM include the use of insulin secretagogues (e.g. sulfonylureas), insulin sensitizers (e.g. thiazolidinediones and biguanides) and carbohydrate digesting enzyme inhibitors (e.g. α-glucosidase inhibitors). However, side effects (e.g. abdominal pains, diarrhoea, hypoglycaemia, kidney and liver failure) [1] from some of the conventional antidiabetic agents do not promote the adherence of DM patients to prescribed therapeutic regimens. The sulfonylureas, for example, can lead to pancreatic beta cell death, and hypoglycaemia through insulin oversecretion [6]. Similarly, the α-glucosidase inhibitors such as acarbose and miglitol have been documented to exhibit diarrhoea and intestinal disturbances. These intestinal disturbances can result in bloating, flatulence, cramping and abdominal pain [7]. However, reports on secondary metabolites from plants as safe and effective remedies for diseases including DM are available [10, 11]. In view of the low cost, easy availability, perceived lesser side effects and cultural acceptability of medicines of plant origin, about 80 % of the people living in developing countries are reported to use medicines of plant origin for their health care needs. As a result, the WHO has recommended the inclusion of traditional medicines in the primary health care programmes of developing countries [10].

It is estimated that more than 200 pure phytochemicals with antihyperglycaemic properties have been discovered [12]. The maize plant (*Zea mays* L., Poaceae) for instance, has been one of the sources of traditional antidiabetic principles. Previous studies have shown that the maize kernel contains anthocyanins, phenolic acids (e.g. *p*-coumaric acid, vanillic acid and procatechuic acid) and flavonoids (e.g. quercetin and hesperidin) [13]. It has been reported in the literature that phenolics of the maize kernel have OH radical scavenging and α-glucosidase inhibition activities [14]. The flavonoids of the maize kernel, on the other hand, have been found to inhibit aldose reductase activity, and consequently delay cataractogenesis as a complication of DM [15]. Other studies have shown that the anthocyanins protect the pancreatic β-cells [6] and reduce insulin resistance and hyperlipidaemia in rodent models of obesity and DM [16]. Therefore, the ethno pharmacological importance of *Zea mays* L. in the treatment and management of DM cannot be overemphasized.

Considering the other plant parts of *Zea mays* L., several studies have indicated that phenolics (*p*-coumaric acid, protocatechuic acid and vanillic acid), anthocyanins, maizenic acid, maysin, rutin, flavon-4-ols and derivatives of quercetin and hesperidin are present in the corn silk (style and stigma of the corn fruit) [17]. Thus, the corn silk (CS) extract has been found to decrease blood glucose levels and concentrations of glycohaemoglobin (HbA1c) in alloxan-induced DM mice [10]. Additional beneficial effects of the CS extract reported include promotion of partial recovery of damaged pancreatic ß-cells, increase in insulin secretion and reduction in serum lipid concentration [17]. Although corn husk (CH), the outer leafy covering of an ear of *Zea mays* L. is gaining much attention in Ghana for the folklore treatment of Type 2 DM, a lot is yet to be learnt about the phytochemical constituents of CH and the scientific basis for the perceived hypoglycaemic effect. Therefore, this study was designed to provide preliminary phytochemical information of the dried husk of *Zea mays* L., scientific validation of the antidiabetic properties of CH in human subjects, and possible correlation of phytoconstituents of CH with antidiabetic effect. Since CH is readily available as farm waste in several geographical locations in Ghana, the phytochemical understanding and scientific development of CH dosage forms will contribute immensely to the availability of treatment options for, and improvement in quality of life of DM patients.

2. Experimental

2.1 Materials

The dried CH was purchased from the Ayeduase market, a suburb of Kumasi in the Ashanti-Region of the Republic of Ghana. The materials were identified at the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana. The specimen voucher reference number deposited at the herbarium of the Department of Pharmacognosy is KNUST/HMI/2015/L033. The collected plant material was further air dried, coarsely milled and stored at room temperature in a dry place.

2.2. Methods

2.2.1 Preparation of CH extract and phytochemical screening

In order to prepare the CH extract, 300 g of the powdered CH was macerated at room temperature (28 ^{o}C) for 48 h in methanol (2 L). The mother liquor was decanted, filtered, dried under reduced pressure and stored at 8 ^{o}C. A decoction of CH was also prepared and concentrated to obtain an aqueous extract. The standard procedures described by Tiwari *et al* [18] were adopted for the phytochemical screen of the methanolic and aqueous extracts.

2.2.2 Preparation of CH decoction (Traditional dosage form) and design of the anti-diabetic assay

A decoction of CH was prepared by boiling 65 g of CH in water (2.5 L) for an hour. The decoction was then allowed to cool, decanted, filtered, packaged in plastic bottles, labelled and stored at room temperature (28 ^{o}C). Only clinically diagnosed Type 2 diabetic patients with uncontrolled blood glucose levels were included in the study. Healthy volunteers were excluded from the study. The volunteers were adequately informed about the details of the study, and were given Participant Information Leaflets and Consent Forms. Volunteers were included in the study after assessment of responses to administered questionnaires. Ethical clearance was obtained from the Committee on Human Research Publications and Ethics (CHRPE) of the School of Medical Sciences, KNUST, and the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana. Eighteen (18) subjects (males and females) aged between 45 – 65 years with an average body weight of 76.6 ± 5 kg were selected. The basal fasting blood glucose levels of twelve (12) subjects on their orthodox diabetic medications were determined weekly over a period of three (3) weeks using the OneTouch® glucometer. After the first three weeks, the CH decoction was administered orally (100 mL every 8 h for 21 d) to the subjects for an additional period of three weeks. The subjects took the CH decoction after meals alongside their orthodox anti-diabetic medications. Blood glucose levels were determined after the completion of the weekly dosage regimen. Six (6) other subjects selected served as a control group for the study. The fasting blood glucose levels of this cohort still on oral anti-diabetic medications without simultaneous administration of the CH decoction were determined every week for a duration of six weeks.

3. Results

3.1. Phytochemical Screen

The aqueous and methanolic crude extracts of the corn husk were screened for the presence of secondary metabolites (phytochemicals) and the results is as shown in Table 1 below.

Table 1: Phytochemical screen of the methanolic and aqueous extracts of dried corn husk

Test	Methanolic extract	Aqueous extract
Tannins	+	–
Saponins	+	+
Alkaloids	+	+
Flavonoids	+	+
Steroids	–	–
Cardiac glycosides	–	–
Phenols	+	–
Terpenoids	–	–
Glycosides	+	+

3.2 Anti-diabetic assay

This assay with corn husk tea was carried out to provide evidence for its glucose reduction ability and obtain a scientific data on the anti-diabetic activity of the corn husk tea. The results are as shown in Figure 1 below.

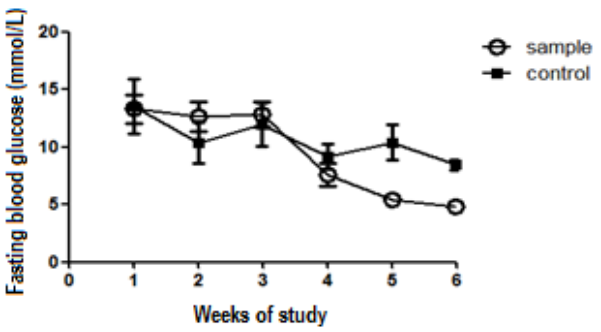

Figure 1: The hypoglycaemic effect of decoction of corn husk (CH) in human subjects.

The treated subjects took regularly prescribed oral antidiabetic agents for three weeks before the addition of the decoction of CH to the therapy for another three weeks. The control cohort took only the prescribed antidiabetic agents for six weeks.

4. Discussion

4.1. Phytochemical Screen

The phytochemical profile of medicinal plants is usually the source of bioactive principles for the prevention, management and treatment of diseases. Therefore, it is imperative to obtain reasonably comprehensive information on the qualitative phytoconstituents of plants or plant parts in folklore use. Subsequent quantitative data on relevant phytochemical compounds, together with some toxicological screen can lead to the development of standardized dosage forms for traditional applications. Common secondary metabolites identified in both aqueous and methanolic extracts of CH were alkaloids, saponins, flavonoids and glycosides. However, phenols and tannins were identified exclusively in the methanolic extract of CH. Generally, a number of beneficial biological activities associated with alkaloids (anti-inflammatory), saponins (anti-inflammatory, cholesterol reducing properties), glycosides (antifungal, antibacterial), phenols and flavonoids (antioxidant, antibacterial, anti-diabetic) are well documented [19]. Therefore, the phytochemical compounds of the CH extract can provide knowledge about the scope of potential therapeutic usefulness of CH extract in folklore medicine.

4.2 Anti-diabetic assay

In order to demonstrate and provide further insights into the hypoglycaemic effect of corn husk (CH), decoction of CH (traditional dosage form) was administered to diabetic patients with uncontrolled blood glucose levels.

The assay was carried out using fasting blood glucose test. The fasting blood glucose test was adopted because the test clearly indicates the effectiveness of different antidiabetic medications administered to subjects, since the subject by the end of the fasting period, would not have eaten any meal or taken any hypoglycaemic agent [20]. As shown in Figure 1, although the control subjects were regularly on their prescribed allopathic antidiabetic medications and maintained a healthy lifestyle over the six-week duration of the study, the fasting blood glucose (FBG) levels were consistently higher (8.5 – 13.5 mmol/L, Figure 1) than normal FBG levels (3.9 – 5.5 mmol/L) [20]. In the test subjects, FBG levels within the first three weeks of exclusive allopathic antidiabetic medication were also higher (13.3 – 12.8 mmol/L, Figure 1) than the normal FBG levels reported in the literature [20]. However, during the following three weeks of the study, where the test subjects administered the decoctions of CH in addition to the conventional antidiabetic medications, an appreciable reduction nearly to normal FBG levels were observed (7.6 – 4.9 mmol/L, Figure 1). FBG levels of 7.6 ± 4 mmol/L and 4.9 ± 1 mmol/L were determined at the end of the first and third weeks respectively, after CH decoction, as an adjunct therapy, was administered to the test subjects. The observed reduction in FBG levels in the treated group before and after the administration of the decoction of CH was statistically significant ($p < 0.0001$) at 95 % confidence interval (4.420 – 9.513 mmol/L). Thus, the reduction in the FBG levels of the treated group was due to the CH decoction. The antidiabetic property of CH was therefore scientifically demonstrated, and to the best of our knowledge, reported for the first time.

Several studies have indicated the antidiabetic, antioxidant, antibacterial, antiproliferative, immunomodulatory, cholesterol reducing and anti-inflammatory potential of phytochemicals such as alkaloids, saponins, glycosides and flavonoids [19, 21, 22]. The antioxidant, antidiabetic, antiproliferative and antidiuretic activities of several flavonoids are also well reported [1, 23, 24]. Since diabetes mellitus (DM) does not only involve hyperglycaemia, but also oxidative stress and lipid metabolism disorders [1], an antidiabetic remedy with bioactive principles to address diverse DM disorders is worth exploring. Hence, the application of CH extract containing these relevant phytocompounds (Table 1) in the management of DM could be a very useful therapy. The additional presence of saponins and glycosides in the CH extract may provide anti-inflammatory, antibacterial and antifungal activities in patients with diabetic foot ulcers.

Among the various phytochemicals already described to exhibit antidiabetic activities, flavonoids are reported as the principal compounds responsible for antidiabetic effects [1]. In this regard, flavonoids isolated from corn silk have been demonstrated to elicit antidiabetic actions [23]. Consequently, we concluded that the flavonoids present in CH could be mainly responsible for the observed antihyperglycaemic effect in this preliminary study. Since anthocyanins are a class of flavonoids soluble in water [14], the decoction of CH administered to the subjects was perceived to be rich in anthocyanins. In the literature, purple corn anthocyanin is reported to have shown insulin secretion, hypoglycaemic and HbA1c reduction activities [6]. Therefore, although we do not at the moment understand the mechanism by which hypoglycaemia is obtained by the administration of the decoction of CH, we hypothesized that anthocyanins contained in the CH decoction led mainly to the observed antihyperglycaemic effect. It is however evident that over a period of three weeks, the decoction of CH, at least, served as a very good adjunct antidiabetic therapy for diabetic patients on antidiabetic agents (biguanides and sulfonyl ureas) in this baseline study. The decoction of CH therefore holds a great potential for glycaemic control upon a longer period of administration. Further antihyperglycaemic effect of CH will be explored in alloxan or streptozotocin-induced diabetic rats in a follow-up study.

The importance of polyphenols and other non-water soluble flavonoids as antioxidant, antiradical and insulin secretion agents cannot be overemphasized [6, 13]. The methanolic extract of CH as shown in Table 1 contains phenols and flavonoids. The flavonoids in the methanolic extract of CH could consist of non-water soluble derivatives due to differences in polarity of methanol and water as solvents. In order to harness the full antidiabetic potential of the phenols and flavonoids of CH, it was inferred from Table 1 that hydroalcoholic or alcoholic extract of CH could be investigated in subsequent studies to obtain quantitative phytochemical, antioxidant, biochemical and metabolic data to aid in the further development of CH extract as an antidiabetic therapy in evidence-based traditional medicine.

5. Conclusion

The decoction of CH has shown high antidiabetic potential. The CH extract has indicated diverse phytoconstituents including alkaloids, glycosides, flavonoids and saponins. The flavonoids could be responsible for the main antidiabetic properties of CH extract. In addition to the potential antioxidant and antiproliferative effects of the flavonoids of CH extract, the saponins and glycosides of CH extract could offer additional antibacterial, antifungal and anti-inflammatory

activities. Thus, the CH extract could serve as a potential one-pot remedy for the management of DM and some of the associated complications. Therefore, the development of hydroalcoholic/alcoholic extract of CH into standardized folklore antidiabetic therapy will provide cost-effective management/treatment options for DM patients in developing/low-middle income countries.

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References

[1] Zhang Y, Wu L, Ma Z, Cheng J, Liu J. Anti-Diabetic, anti-oxidant and anti-hyperlipidemic activities of flavonoids from Corn Silk on STZ-induced diabetic mice. *Molecules*. 2015; 21(1): 1 - 11.

[2] Van Roozendaal BW, I. Krass I. Development of an evidence-based checklist for the detection of drug related problems in type 2 diabetes. *Pharm. World Sci.* 2009; 31(5): 580–95.

[3] Aladag I, Eyibilen A, Güven M, Atiş O, Erkokmaz U. Role of oxidative stress in hearing impairment in patients with type two diabetes mellitus. *J. Laryngol. Otol*. 2009; 123: 957–63.

[4] Dierckx N., Horvath G, van Gils C, Vertommen J, van de Vliet J, De Leeuw I, Manuel-y-Keenoy B. Oxidative stress status in patients with diabetes mellitus: relationship to diet. *Eur. J. Clin. Nutr.* 2003; 5 (8): 999–1008.

[5] Goldstein, BJ. Insulin resistance as the core defect in type 2 diabetes mellitus. *Am. J. Cardiol.* 2002; 90: 3 - 10.

[6] Hong SH, Heo JI, Kim JH, Kwon SO, Yeo KM, Bakowska-Barczak AM, Kolodziejczyk P, Ryu OH, Choi MK, Kang YH, Lim SS, Suh HW, Huh SO, Lee JY. Antidiabetic and beta cell-protection activities of purple corn anthocyanins. *Biomol. Ther*. 2013; 21(4): 284–9.

[7] Ibrahim MA, Islam MS. Anti-diabetic effects of the acetone fraction of *Senna singueana* stem bark in a type 2 diabetes rat model. *J. Ethnopharmacol.* 2014; 153: 392–9.

[8] Kumanyika S, Jeffery RW, Morabia A, Ritenbaugh C, Antipatis VJ. Obesity prevention: the case for action. *Int. J. Obes. Relat. Metab. Disord.* 2002; 26(3): 425–36.

[9] www.idf.org/membership/afr/ghana

[10] Shafi S, Tabassum N. Survey on anti-diabetic plants in Kashmir [India]. *Journal of Advanced Pharmacy Education & Research.* 2013; 3(4): 306 - 318.

[11] Venkateshwarlu E, Sharavana Bhava BS, Achyuth Bharadwaj S, Shiva Kumar R, Umasankar K, Venkateshwar Rao J. Evaluation of diuretic and antidiabetic activities of esculin in wistar rats. *Int J Pharm Bio Sci.* 2015; 5(2): 267-276.

[12] Huang B, Wang Z, Park JH, Ryu OH, Choi MK, Lee JY, Kang YH, Soon Sung Lim SS. Anti-diabetic effect of purple corn extract on C57BL/KsJ db/db mice. *Nutr Res Pract*. 2015; 9(1): 22-9.

[13] Thiraphatthanavong P, Wattanathorn J, Muchimapura S, Thukham-mee W, Wannanon P, Tong-un T, Suriharn B, Lertrat K. Preventive effect of *Zea mays* L. (Purple Waxy Corn) on experimental diabetic cataract. *BioMed Res. Int*. 2014; 2014: 1-8.

[14] Nile SH, Park SW. Antioxidant, α-Glucosidase and Xanthine Oxidase inhibitory activity of bioactive compounds from Maize (*Zea mays* L.). *Chem Biol Drug Des*. 2014; 83: 119–125

[15] Kyselova Z, Stefek M, Bauer V. Pharmacological prevention of diabetic cataract. *J Diabetes Complications*. 2004; 18(2): 129–140.

[16] Guo H, Guo J, Jiang X, Li Z, Ling W. Cyanidin-3-O-b-glucoside, a typical anthocyanin, exhibits antilipolytic effects in 3T3-L1 adipocytes during hyperglycemia: Involvement of FoxO1-mediated transcription of adipose triglyceride lipase. *Food Chem Toxicol*. 2012; 9:3040-7.

[17] Milind P, Isha D. *Zea mays*: A modern craze. *Int. Res. J. Pharm.* 2013; 4(6): 39-43.

[18] Tiwari P, Kumar B, Kaur M, Kaur G, Kaur H. Phytochemical screening and Extraction; A Review. *Internationale Pharmaceutica Sciencia*. 2011; 1(1): 99-106.

[19] Ram J, Moteriya P, Chanda S. Phytochemical screening and reported biological activities of some medicinal plants of Gujarat region, *J Pharmacog Phytochem.* 2015; 4(2): 192-198

[20] http://www.diabetes.co.uk/diabetes_care/fasting-blood-sugar-levels

[21] Bhogireddy N, A. Naga vamsi krishna A, Ramesh B, Pradeep kumar M, Reddy OVS, Gaddaguti V, Raj kumar K, Pola PK, Venkataraman B. Anti-inflammatory and anti-diabetic activities with their other ethnomedicinal properties of the plants. *J. Med. Plants Stud.* 2013; 1(5): 87 - 96.

[22] Vadlamani S, bala durga Devi KBD, Poosarala A, Bapatla VK. Identification of plant sources from North Andhra Pradesh exhibiting immunomodulatory activity using BALB/c models. *Int J Pharm Bio Sci.* 2016; 7(1): (B) 295 - 300.

[23] Alam EA. Evaluation of antioxidant and antibacterial activities of Egyptian Maydis stigma (*Zea mays* hairs) rich in some bioactive constituents. *J Am Sci.* 2011; 7(4): 726 -8.

[24] Rauter AP, Martins A, Borges C, Mota-Filipe H, Pinto R, Sepodes B, Justino J, Antihyperglycaemic and protective effects of flavonoids on streptozotocin-induced diabetic rats. *Phytother Res*. 2010; 24: S133 - S138