Stigma Maydis (Cornsilk) As Hypoglycemic Agent: A More Potent Antidiabetic Herbal Therapy Than Metformin

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***Abstract*—The antidiabetic properties of stigma maydis (corn silk) was studied in comparison with metformin in 30 male and female albino rats for 10 days. The animals were given low, medium and high oral dosages of the extract for 0, 7, 8, 9 and 10 days compared with metformin. The extract LD_{50} was 1620.19mg/kg. There was significant difference (P<0.05) in the group of animals treated with low dose which had high glucose level than control treated with metformin for the period of 10 days. But the group administered with medium dose of the extract had low blood glucose level than metformin on day 10 and was significantly different p<0.05. Also on day 10 the group with high dose of the extract had very drastic reduction in blood glucose level (P<0.05)at hypoglycemic level which some animals died. A combination of the extract and metformin showed a more hypoglycemic situation with increase mortality. It is concluded that extract of stigma maydis (corn silk) has high antidiabetic properties and more potent than metformin in the treatment of diabetes.**

Keywords—Corn silk, metformin, hypoglycemia, diabetes.

INTRODUCTION

The health need of the people and the curiosity of healing has made the exploration of alternative medicine very necessary. Reasons are that the present orthodox drugs are not very potent, and are not often within the reach of the poor and not often available and also may be with side effects. Plants are the sources of herbal remedies and can be used to treat a lot of ailments particularly the chronic ones and other infectious diseases, (Duraipandiynn, 2006). The synthesized drugs are not as good as direct extract of the herbs and so are often associated with resistance as in many infectious diseases, eg malaria ,(Bjorkman1990).Phytochemicals from plants are very safe with less or no side effects. Plants derivatives as anticancer, anti-microbial, antioxidant, antidiarrhoeal, wound healing and analgesic are very potential properties necessary for solving health problems which orthodox drugs may not have,(Sharma,2011). Interestingly, the bioactive compounds that make up the active ingredient of herbal, therapies are now successfully isolated with very sensitive equipment e.g. the high performance liquid chromatography (HPLC) (Jimmy 2017), Bird, 1989). Also non-chromatographic techniques e.g. immunoassay with the use of monoclonal antibodies (MABS) phytochemical assay, Fourier-transform. Infrared spectroscopy (FTIR) are also used for the analysis of active compounds in the plant extracts (Maebe, 2013).

The most common cause of hyperglycemia is diabetes. And diabetes occurs when the fasting blood glucose level is higher than the post meal blood glucose and the individual with high blood glucose level is said to be hyperglycemic.(American diabetic Association 2006), Umpierreze (2002). But sometimes healthy normal subjects may present a fasting blood glucose value higher than the post meal blood glucose value. But there is a common perception that the post prandial glucose level should be higher than fasting glucose level, (Warade, 2014). A drop in blood glucose below the normal range of 7-10g/dl leads to hypoglycemia (Villinies 2017). Symptoms include impaired mental functioning, irritability, twitching, weakness in arm and leg muscles, sweating, loss of consciousness lethargy, shaking (Sewice, 2017) (Malout, 1985) and such low sugar level may result in death (Lelhinger, 2017). Hypoglycemia may also result from medications due to diabetes (Shamaony, 1994). Also very high blood glucose can be life-threatening if such triggers condition as diabetic ketoacidosis in types 1 and 2 and hyperosmolar coma in type 2, (Elmehdawi, 2010) and with time the diabetes may damage the heart, blood vessels, eyes (retinopathy) kidneys, nerves and the high risk of heart disease and stroke (Dharmasera 2010). The damage can result in reduced blood flow (Wendland, 2012). Diabetes can lead to foot ulcers and amputation (Moxy, 2011). Retinopathy is an important cause of blindness in diabetes due to damage to small blood vessels in the retina (Frank, 2004). And diabetes is reported to be the leading cause of kidney disease (Aucic 2017). Gestational diabetes in pregnant women can lead to congenital malformations e.g. still birth and perinatal death, obstetric complications, maternal morbidity and mortality (Johnson, 2015). Pre-eclampsia and eclampsia in the mothers and shoulder dystocia in the offspring are reported (Wendland et al 2012). Diabetes has serious effect on the economy. The International Diabetes Federation (IDF) estimates that the total global health

care spending on diabetes tripled over the period 2003-2013 i.e. increase in the number of diabetic patients and increase in per capita spending (Singh, 2009). But does this burden of health borne by all countries in the world particularly in Africa. If such is applied there would be drastic reduction in the mortality. About 422 million adult over 18 years of age are estimately living with diabetes (WHO 2014) increase in the number is attributed to population growth aging and life style, (NCD, 2016). Diabetes can be prevented via reduction in eating of sugary foods, (Jimmy 2018) healthy good living; such as exercise, eating healthy food, control of blood pressure, avoiding smoking and enlightenment. It is treated using antidiabetic drugs; insulin, glibenclamide, Metformin and herbal remedies, (Jimmy 2014) corn silk comes from Zea Mays, L., of the family Poacae also known as corn or maize, is a grain plant first domesticated by indigenous people of Mexico, (Eurek Alert, 2008) and introduced into Nigeria in the 16th century (Eurek Alert, 2008). It is cultivated mainly with economic relevance (Oladejo, 2012) for human consumption. It has long narrow leaves spaced alternatively on opposite side of the stem with ears enclosed in modified leaves called husks (Simmonds, 1979). The English name is corn or maize. It is called Akpakpa, Ibokpot in Ibibio and Oka in Igbo. The leaves, grains corn silk, stalk are used in ethno-medicine in the treatment of several ailments. The corn silk is used as antidiabetic and as diuretic agent traditionally. The silk decoction is consumed for the treatment of urinary and gallstones ailments, (Foster 1990). Corn generally is used in the treatment of amenorrhea, cystitis, diabetes; dropsy, dysentery, dysmenorrheal, gingivitis, gout, hepatitis, hypertension, inflammation, influenza, menorrhagia, metritis, nephritis, oliguria, kidney stones, prostatitis, rheumatism, tumors, urogenital, heart disorders ailments, warts, malaria, (prostate, disorders) etc. (Hashin, 2012). Phytochemical contents of corn silk are; saponins, alkaloids, flavanoids, tannins chlorogenic acid, phytosterols, (Ghorab, 2007). There also the contents of fatty acid, pantothenic and linoleic acid, steroids, glucose, sodium, potassium, iron, zinc and chloride as minerals with highest potassium concentration. Very significant in the roles of corn silk is in reducing hyperglycemia effect (Guo, 2009), nephrotoxicity (Sepehri; 2011) as antidepressant Ebrahimzadel 2009) as anti hyperlipidemic (Kaup, 2011) anti-fatigue agent (Hu et al 2010) anti-inflammatory (Wang 2011) hepato protective effect (Campo 2001) anti-hepatoma activity (Yang, 2014) and inhibitory x-amylase activity (Chen, 2013).

The antidiabetic properties of the corn silk prompted this study as it is not medically documented particularly its comparative efficacy assessment with orthodox metformin drug. This comparative study became necessary as some reports of the use of corn silk as anti-diabetic agents are done without standard laboratory assessment particularly the toxicity which is said to be negative. Also is the assessment of metformin potency and wider use as antidiabetic drug compared to other such drugs. The study is actually aimed at putting in the drugs shops alternative and effective herbal remedy for the treatment of diabetes.

MATERIALS AND METHODS

Plant Collection: The corn silks were harvested fresh from corn farms and identified in the Department of Botany and Ecological Studies of the University of Uyo, Akwa Ibom State, Nigeria.

Extraction of Corn Silk: Sac of fresh corn silk was chopped into pieces, air dried at room temperature to rid of moisture. It was macerated and dissolved in 50% ethanol. It was then filtered and the residue discarded, the filtrate was concentrated to dryness using evaporator. The yield of extract was 65.5g. It was put in a bottle and stored for use in the study in the refrigerator at -4^0C. The methods of Trease and Evans 1996 was used.

Acute Toxicity: Methods of Lorke, 1983 was used with 30 male and female albino mice weighed 18-20g. The mice were divided into 10 groups with 3 mice in each group and administered with extract as follows:

Group 1-1000mg/kg

Group 2 – 1250mg/kg

Group 3 – 1750mg/kg

Group 4-2000mg/kg

Group 5-2250mg/kg

Group 6 -2500mg/kg

Group 7-2750mg/kg

Group 8-3000mg/kg

Group 9-3250mg/kg and

Group 10-3500mg/kg.

The extract was administered intraperitoneally and signs of toxicity observed;

Preparation of Extract Stock Solution: 1g of the extract was dissolved in 10ml of distilled water and calculated as follows:

$$\frac{\text{Weight of animal}}{1000} \times \text{LD}_{50}$$

Stock solution = 100mg/kg

LD50 was calculated between 0 mortality and 100% concentration – $\text{LD50} = \sqrt{A \times B}$

$= \sqrt{1500 \times 1750}$

= 1620.19mg/kg

A = Maximum dosage that produce 0 mortality

B= Minimum dosage that produce 100 mortality

Low dose$= {}^{10}/_{100} \times 1620.19$

=162.02mg/kg

Middle dose=20% of LD_{50}

$= {}^{20}/_{100} \times 1620.19$

=324.04mg/kg

High dose =30% of LD_{50}

$=^{30}/_{100}$ x 1620.19

=486.06mg/kg

Preparation of Alloxan: 5g of alloxan was dissolved in 100ml of distilled water = $^{59}/_{100ml}$

1g=1000mg

5g=5000mg

=5000mg/100ml

=50mg/ml – stock

Inducement of Diabetes in Rats: Albino rats weighing 88-138g were used for the study. The methods of Javaid 2013 was used. Animals were induced for diabetes with a solution of alloxan monohydrate 50mg/ml given 1kg intravenously. After 72 hours blood was collected from the tail of the rats cut with scissors and glucose level determined using glucometer. Glucose level above 120mg/dl was considered to be diabetic (Jaraid, 2013).

Preparation of Metformin:

1tablet of metformin is 500mg, it was dissolved in 50ml of distilled water i.e. 500mg/50ml

=10mg/ml – stock and calculated as follows;

Adult weighs about 70kg = $^{70}/_{1000}$

Therefore stock concentration per animal

$=\frac{\text{Weight of animal}}{1000 \text{ Stock}} \times \frac{0.07}{}$

Administration of extract of corn silk and metformin

The rats induced with diabetes were divided into 6 groups for the metformin and extract administration with 5 rats in each group as follows:

Group 1-induced with alloxan without treatment

Group 2-induced with alloxan and treated with metformin;

500mg/kg (body weight

Group 3-Treated with corn silk in low dose 162.02mg/kg

(body weight)

Group 4-Treated with medium dose extract of corn silk,

324.04mg/kg (body weight) of corn silk extract, 486.06mg/kg body weight

Group 5-Treated with high dose extract of corn silk extract,

486.06mg/kg body weight

Group 6-Treated with a combination of corn silk extract and metformin.

The fasting blood glucose level was measured for 0 to 10 days using glucometer with glucose test strip.

Blood Collection and Glucose Levels

At the end of 8 hour fasting the tails of the rats were sterilized with alcohol using cotton wool dipped into it (5ml) the tail was cut with a pair of scissors. The blood was squeezed out and the first drop discarded and the second drop applied directly on the test strip and inserted into the glucometer reader and the glucose level measured in mg/dl.

Statistical Analysis:

Analysis of variance (one way ANOVA) was used to compare results among groups with Turkey Kramer's multiple comparison test using graph results presented as means and SEM. And the P-values less than 0.05 were considered significant.

Phytochemical Screening: The phytochemical screening was carried out in pharmacognosy laboratory of the University of Uyo, Akwa Ibom State, Nigeria.

Alkaloid Test: 0.1g of corn silk extract was added with 5ml aqueous HCL and boiled. Few drops of Dragendoff reagent was added to the filtrate. 1ml of filtrate was added to Mayer's and picric acid to 1ml of the extract. Reddish and cream precipitates respectively were formed indicating absent of alkaloids.

Tannins: 0.5g extract was added to 10ml of distilled water, filtered and filtrate added to ferric chloride. Blue black precipitate was observed confirming presence of tannins.

Glycosides: Fehling's solution was added to 0.5g of the extract and sulphuric acid added and boiled and a brick red colour formed confirming presence of glycosides.

Saponin: This is called frothing test: 0.5g of the extract added to 5ml distilled water boiled, frothing was observed confirming saponin.

Cardiac glycosides:

(a) **Salkowoki's Test:**

In this test 2ml chloroform and 2ml of sulphuric acid was added to 0.5g of the extract. A reddish brown colour was observed at the interphase of the two liquids confirming cardiac glycosides

(b) **Keller-killian Test:**

2ml of glacial acetic acid containing 1 drop of ferric chloride and 1ml of conc. Sulphuric acid added down the side of the tube were added to 0.5g of extract. A brown colour was observed at the interphase confirming cardiac glycosides.

(c)**Liberman's Test:** 2ml of acetic antiydride and 2ml of sulphuric acid was added to 0.5g of the extract.

A brown colour at the interphase was observed confirming cardiac glycosides.

Results:

The effects of corn silk extract and metformin on the blood glucose levels for the period of 0–10 days were as follows, table 1 144.20±1.16, 158.80±1.32, 164.20±1.24, 190.40±0.81 and 201.60±0.98 for days 0, 7, 8, 9 and 10 days respectively in group 1 induced with diabetes without treatment, and were significantly higher than other groups (P<0.05). For group 11, the values were 245.60±1.8, 121.60±0.98, 94.40±0.68, 88.00± 1.22, 86.00±1.64 for group 1 treated with metformin for day 0-10. For group 11, the values were 28.760±1.03, 266.20±1.56, 146.60±0.98 146.20±0.97, 145.00±1.67 for 0-10 days respectively, treated with corn extract low dosage. The values in group II and III were significantly lower than in group 1 (P<0.05). In group iv the values were; 334.00±1.26, 91.80±0.66, 88.20±0.80, 84.00± 0.7163.20±0.97, treated with medium dose of extract respectively for 0-10 days. The glucose level was significantly lower (P<0.05) than or groups 1-3. In group v, the values were 314.20±0.66, 81.00±0.84, 73.00±0.55, 68.00±0.95, 50.60±0.93 treated with high dose of silk extract for 0-10 days. The glucose levels were significantly, (P<0.05) lower than those in groups 1-4. In group VI, the values were 272.80±0.86, 86.60±1.47, 68.60±0.68, 62.00±1.00 and 49.20±1.36 treated with a combination of corn silk extract and metformin for 0-10 days. The glucose levels were significantly (P<0.05) reduced than in group 1-5 indicating hypoglycemia. The phytochemical studies showed the presence of tannins, glycosides and cardiac, glycosides which was highly positive and saponins. These findings are line with other reports (Ghorab, 2007). All these derivatives have medicinal application but of most important for this study is the phenolic glycosides which may be responsible for the high anti-diabetic activity of the corn silk extract, (Liu, 2016) as observed in this study.

Table 1: Effects of Comparative Corn Silk extract and Metformin on Blood Glucose Level

Groups	Day 0 Glucose (mg/dL)	Day 7 Glucose (mg/dL)	Day 8 Glucose (mg/dL)	Day 9 Glucose (mg/dL)	Day 10 Glucose (mg/dL)
I	144.20±16	158.80±1.32	164.20±1.24^{a,b}	190.40±81^{a,b,c}	201.60±0.98^{a,b,c,d}
II	245.60±1.83	121.60±0.98a	94.40±0.68^{a,b}	88.00± 1.22^{a,b,c}	86.00±1.64^{a,b,c,d}
III	287.60±1.03	266.20±1.56a	146.60±0.98^{a,b}	146.20±0.97^{a,b}	145.00±1.67^{a,b}
IV	334.00±1.26	91.80±0.66a	88.20±0.80^{a,b}	84.00±0.71^{a,b,c}	63.20±0.97^{a,b,c,d}
V	314.20±0.66	81.00±0.84a	73.00±0.55^{a,b}	68.00±0.95^{a,b,c}	50.60±0.93^{a,b,c,d}
VI	272.80±0.86	86.60±1.47a	68.60±0.68^{a,b}	62.00±1.00	49.20±1.36^{a,b,c,d}

Legend: a, b,c and d = significantly different from Days 0, 7, 8, 9 and 10 respectively at p < 0.05.

Group 1: Induced with diabetes without treatment

Group II: Induced with diabetes treated with metformin

Group III: Induced with diabetes treated with corn silk extract in low dose

Group IV: Induced with diabetes treated corn silk extract

medium dose

Group V: Induced with diabetes treated with high dose corn silk extracted

Group Vi: Induced with diabetes and treated with corn silk extract and metformin.

DISCUSSION

The effects of extract of corn silk on the blood glucose level for the period of 10 days have shown hypoglycemic potential of this extract. The various dosage effects of the extract have also shown its applicability in the circumstance of the disease diabetes. On the 7th day for instance, the low dose extract had minimal effect on the glucose level but its hypoglycemic effect was higher as the period of treatment progressed which has been shown on day 9 and the 10th. However, the blood glucose level were still not within the range but not too far from the normal range 100-125mg/dl (Villainies, 2017). At the dose on day 10, there was an onset of hypoglycemia. A condition of which the blood glucose is below the normal range. This confirms the fact that the extract is very potent shown in the high dose of the dosage on the tenth day of the administration of the extract. Hypoglycemia could also be presented due to medication with insulin, sulfonylureas, eating less meals, which is peculiar with diabetic patients (Service 2017), Yanai (2015), (Martin 2015). The demonstration of hypoglycemia has put this extract as a very potent anti-diabetic therapy. The high dose was given up to 10th day and there was the death of two rats on this date. If the therapy was extended to even 11 or 12 days then more clinical casualty would have emerged. Comparison of the corn silk extract with the normal orthodox drug; metformin in this study showed a very high potency of the extract than metformin. Metformin is one of the oldest anti-diabetic drug, it is associated with lower risk of it requiring other drugs after its administration. And the practice in some cases is start dosage with metformin in case of resistance insulin for example; (Reinberg 2014). A combination of metformin and corn silk extract showed drastic hypoglycemia which metformin only did not demonstrate. And the value of the fasting

blood glucose with extract alone was already on the hypoglycemic note at high dosage i.e lower than metformin. It implies that the over whelming hypoglycemic properties recorded in the combination therapy with metformin comes from corn silk extract.

CONCLUSION

It is concluded from the study that corn silk extract is a potent anti-diabetic herbal therapy, but should not be used without consultation.

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