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Evaluation of the hypoglycemic and hypolipidemic effects of aqueous *Eleusine coracana* seed extract

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ABSTRACT

Patients with diabetes mellitus almost always have secondary hyperlipidemia which requires tight control of the blood glucose level with drugs. *Eleusine coracana* (EC) is widely used in northwestern Nigeria for the treatment of diabetes by traditional healers who consider it to be effective and safe. This study evaluated the hypoglycemic and hypolipidemic effects of *Eleusine coracana* seed extract in alloxan-induced hyperglycemic Wistar rats. All the doses of EC prevented a sustained increase in the blood glucose level after glucose loading. The antihyperglycemic effect was dose dependent and reached a maximum level at 120 and 180 minutes, and there was a significant reduction in blood glucose level in all the treated groups as compared to the normal control and metformin diabetic control groups. There were steady reductions in the levels of serum triglycerides (TG's) and high density lipoprotein (HDL) in a dose dependent pattern in the treated group as compared to the metformin diabetic control group. EC extract also reduced serum triglycerides (TG's) and high density lipoprotein (HDL) in all the doses tested. This study has shown that aqueous *Eleusin coracana* seed extract remarkably reduced serum blood glucose level in both normal and alloxan-induced diabetic rats at the studies doses. Furthermore, the extract showed a significant hypolipidemic effect with decreases in serum total cholesterol and low density lipoprotein levels. These findings showed that EC seed extract has therapeutic potential in combating the multi factorial disorders which are a part of the major complications of diabetes, and further studies should be conducted to determine the mechanism of the action of its hypoglycemic and hypolipidemic effects.

Keywords: *Eleusine coracana*, hypoglycemic and hypolipidemic effects

INTRODUCTION

Diabetes mellitus has become a serious public health problem worldwide, and its prevalence is rising faster than earlier estimated. Whereas, the prevalence of diabetes mellitus was estimated to rise from 4.0% in 1995 to 5.4% in 2025 (while the number of adults with the disease was estimated to rise from 135 million to 300 million over the same period of time), its prevalence was found to have risen to 8.5% in 2014 (WHO, 2018; King et al., 1998). The disturbing aspect is the fact that the prevalence of the disease is rising more rapidly in middle- and low-income countries where a 170% numerical increase in the number of people affected (from 84 million in 1994 to 225 million in 2025) is expected to occur as compared to a 42% increase in developed countries (from 51 million in 1994 to 72 million in 2025) (King et al., 1998). In addition, whereas majority of people with diabetes in the developing countries are ≥ 65 years, the majority of people with diabetes in the developing countries are in the age range 45-64 years (King *et al.*, 1998). Diabetes is a chronic disease that requires long term attention and treatment to limit the development of its devastating complications and to manage them when they occur (Peter, 2002). Diabetes is a major cause of blindness, kidney failure, heart attack, stroke and lower limb amputation; and it was estimated to be the seventh leading cause of death in 2016, with an estimated 1.6 million deaths directly caused by the disease, and with almost half of deaths occurring before the age of 70 years (WHO, 2018).

According to the International Diabetes Federation (IDF) the impact of diabetes mellitus on health care spending will be enormous, with an estimated direct health care expenditure on diabetes worldwide of between 213-396 billion dollars for the year 2025; and in some countries, particularly in sub-Saharan Africa, it may

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reach as much as 50- 90% of their total health care budget (IDF, 2003 and Wild *et al.*, 2004). In patients with diabetes mellitus, the level of triglyceride and cholesterols in plasma are frequently elevated (i.e., hyperlipidemia). The abnormal high concentration of serum lipids in diabetic patients is believed to be mainly due to an increase in the mobilization of free fatty acids from the peripheral fat depots (Bopanna *et al.*, 1997). These secondary hyperlipidemias are always associated with absence or marked insufficiency of insulin. In addition, the low density lipoprotein (LDL), and high density lipoprotein (HDL) levels are also elevated in diabetes mellitus (Mary and John, 2007). Patients with diabetes mellitus almost always have secondary hyperlipidemia which requires tight control of the blood glucose level with drugs (Umesh and Micheal, 2007).

Also, achieving good glycemic control and preventing or delaying the onset of complications requires regular physical exercise, and maintaining a normal body weight in addition to drug treatment and regulated/restricted diets which are often difficult for patients to adhere to (WHO, 2018). Worse of all, the treatment is for a lifetime, the drugs are scarce and relatively expensive, and patients with diabetes are known to be especially at high risk for experiencing drug therapy problems (DTPs) as they are subject to receive multiple drug therapies for their diabetes co-morbidities (Huri and Ling, 2013; Cipolle *et al.*, 2013). The common DTPs among patients with chronic medical conditions include unnecessary drug therapy, need for additional drug therapy, ineffective drug therapy, dosage too low, dosage too high, adverse drug reaction, and non-adherence (Cipolle *et al.*, 2012).

In many developing countries including Nigeria, use of medicinal plants for treatment of diverse diseases is popular as they are cheap, readily available and are believed to be effective and safe. Hypoglycemic and/or hypolipidemic properties have been demonstrated in several plant species including *Vernonia amygdalina* (Erato *et al.*, 2005; Okolie *et al.*, 2008), *Aloe vera* (Okyar *et al.*, 2001), *Allium sativum* (Garlic) (Eidi *et al.*, 2006), *Eugenia jambolina* (Pepato *et al.*, 2005), *Terminata chebula* (Sabu and Kuftan, 2002), and *Eleucine coracana* (Okoyomoh *et al.*, 2013). *Eleucine coracana* is extensively cultivated and consumed in the tropics and sub-tropics. It is very common in Africa (especially Senegal, Niger and Nigeria), and Asia, where it is called different names including finger millet, African millet, Ragi (India), Tamba (Hausa-Nigeria), Dendi (Leeni-Niger), Kpana (Birom-Nigeria), Changari (Fulani-Nigeria), Sarga (Kaniri-Nigeria), Oka tamba (Ibo-Nigeria), and Oka gbegi (Yoruba-Nigeria) (Burkill, 1985). In Sokoto State, Nigeria (the study area), similar to the situation across the country, the majority of the populace reside in the rural areas where access to healthcare services is poor, as the health facilities are majorly located in the urban areas; and even where the services are available they are too poor to buy the expensive anti-diabetic drugs. They inevitably rely on traditional preparations and mostly present late at the health facilities when complications have set in. *Eleusine coracana* is widely used in northwestern Nigeria for the treatment of diabetes by traditional healers who consider it to be effective and safe. To the best of our knowledge, this folkloric claim has not been validated scientifically in Sokoto, Nigeria. This study was conducted to evaluate the hypoglycemic and hypolipidemic effects of aqueous *Eleusine coracana* seed extract.

MATERIALS AND METHODS

Collection, identification and preparation of plant seeds' extract

Eleusine coracana (finger millet) seeds were purchased at the Kara market, Sokoto, Nigeria. The seed was identified by taxonomists at the Botany Department, Faculty of Science, Usmanu Danfodiyo University, Sokoto, Nigeria, and the specimen voucher was deposited at the Botany Department's herbarium (the plant and seeds are shown in Figures 1 and 2 respectively). The plant seeds were air dried to constant weight at room temperature in the Pharmacology & Therapeutics Department's laboratory, Usmanu Danfodiyo University, Sokoto, Nigeria. The dried material was then pulverized into dry powder using crushing machine. About 500 grams of the powder was obtained during the extraction using 2 liters of distilled water in Soxhlet apparatus, and the percentage yield was calculated from the extracted residue (w/w). The extracted residue was kept in the refrigerator at 4 degree Celsius. The extract was reconstituted in distilled water at an appropriate concentration for each use whenever desired.

Animal, drug, chemical and equipment

A total of 150 Wistar rats of both sexes weighing 100-350g were used in this study. They were obtained from the National Institute for Trypanosomiasis Research's animal house, Vom, near Jos. They were housed in separate cages, and kept in a room maintained at 12 hours light/dark cycle and temperature of 28-34 degree Celsius. The animals were allowed free access to water and food (growers mash) from Vital Feed Nigeria Limited, Jos, Nigeria, before the beginning of the

experiment. The animals were kept in this condition for two weeks before the commencement of the experiment (acclimatization). Only food was withheld from the rats the night preceding the experiment (to make them fast). A dispensable form of Metformin (Guamet 500), with Batch number 370094, manufactured by Medreich Limited, Avalahalli, Bangalore, India; Alloxan from Avighkar Laboratory Technology and Chemicals, India, with Lot No-230500D; and Glucose meter (Accu-chek active) from Roche Group Limited, Germany were used for the study.

Induction of diabetes mellitus in rats

Diabetes was induced in the rats by a single intra-peritoneal injection of freshly prepared alloxan monohydrate (150mg/kg) dissolved in normal saline, after overnight fasting for 12 hours (Al Shamony *et al.*, 1994; Federiuk, 2004). Blood samples were collected after 72 hours to determine the glucose level. Those with a blood glucose level >140mg/dl were considered to be diabetic and selected for the study.

Determination of the effect of *Eleusine coracana* on oral glucose loading

The experimental procedures were performed to mimic type 2 diabetes mellitus of human. Hyperglycemia was induced by 10g/kg oral glucose loading (Cunha, *et al.*, 2008). Blood samples were obtained by tail tipping (making an incision on the tail for blood to sip out) and the glucose level was determined using Accu-chek active glucose meter. Twenty rats (fasted overnight) were divided into 5 groups of four rats each. Group 1 received 5ml/kg distilled water only; Group 2 received 100mg/kg of extract; Group 3 received 200mg/kg of extract; Group 4 received 400mg/kg of extract; while Group 5 received 100mg/kg of metformin. The rats in the respective groups were given the treatments 30 minutes prior to the glucose loading and blood samples were taken for glucose level measurement immediately before the glucose loading (0 minute), and then subsequently at 30, 60, 90, 120, and 180 minutes.

Determination of the effect of 28 days dosing of *Eleusine coracana* on glucose and lipid status of alloxan induced diabetic rats

The rats were divided into six groups of six each. Group 1 served as normal control and received 5ml/kg distilled water through feeding tube by gavages, while groups 2-6 were the diabetic groups (following induction with Alloxan). The serum glucose level was assessed by measuring the blood glucose level by tail tipping (Frode and Medeiros, 2008). Group 2 rats received 100mg/kg of extract dissolved in distilled water; Group 3 rats received 200mg/kg of extract dissolved in distilled water; Group 4 rats received 400mg/kg of extract dissolved in distilled water; Group 5 rats served as positive diabetic control and received metformin 100mg/kg dissolved in distilled water; while Group 6 rats served as negative diabetic control which received 5ml/kg of distilled water only. All the animals received the specified doses daily for 28 days. At day 29, all the animals were sacrificed by ether inhalation after the blood sample has been taken for blood glucose and lipids analysis by cardiac puncture.

Data analysis

Data analysis was carried out using Graph-pad statistical software package. Statistical comparisons between the controls and treatments were performed by analysis of variance (ANOVA), followed by Tukey-Kramer. Data were presented as mean ± standard error of mean (SEM). All levels of statistical significance were set at $p < 0.05$.

Figure 1: *Eleusine coracana* (Finger millet) plant

Figure 2: *Eleusine coracana* (Finger millet) seeds

RESULTS

Effect of Eleusine coracana (EC) on mean blood glucose level following oral glucose loading

A single oral dosing of EC on hyperglycemic induced rats by oral glucose loading showed a peak value of serum glucose level for all the groups at 30 minutes. This hyperglycemia was maintained until 60 minutes and later returned to its initial value at 90-120 minutes. All the doses of EC prevented an increase in blood glucose level after glucose loading, and also showed significant reduction ($P<0.05$) in glucose level. The antihyperglycemic effect was dose dependent and reached a maximum level at 120 and 180 minutes (Table 1).

Effect of *Eleusine coracana* (EC) extract on the body weight, serum lipid profile, and blood glucose levels of Wistar rats after 28 days treatment

Administration of aqueous extract of EC on the animals after 28 days showed no significant difference ($p > 0.05$) in the body weight of the treated and control groups (Table 2). There were significant differences ($P<0.05$) in the serum levels of total cholesterol (TC) and low density lipoprotein (LDL) in the treated group as compared to normal control and metformin diabetic control groups. There were marked reductions in serum total cholesterol at a dose of 400mg/kg, and serum low density lipoprotein (LDL) at a dose of 100mg/kg. There were steady reductions in the levels of serum triglycerides (TG's) and high density lipoprotein (HDL) in a dose dependent pattern in the treated group as compared to the metformin diabetic control group. EC extract also reduced the serum triglycerides (TG's) and high density lipoprotein (HDL) levels in all the doses tested (Table 3). Oral administration of EC extract showed no significant difference in ($P>0.05$) serum glucose level between tested group and normal control, but there was significant reduction in blood glucose level in all the treated groups as compared to normal control and metformin diabetic control groups (Table 3).

Table 1: Mean blood glucose levels following oral glucose loading

Group	Serum glucose concentration (mg/dL)					
	0min	30min	60min	90min	120min	180min
Control	125.5 ± 7.9	177.2 ± 1.3	131.0 ± 13.3	110.7 ± 17.6	99.25 ± 12.7	90.8 ± 10.2
E/100mg/kg	101.5 ± 15.2	155.0 ± 8.1	129.2 ± 6.7	98.0 ± 8.4	115.5 ± 11.0	99.5 ± 9.2
E/200mg/kg	105.2 ± 12.3	194.7 ± 31.7	164.0 ± 22.1	113.2 ± 15.9	92.5 ± 10.5	94.5 ± 9.6
E/400mg/kg	184.7 ± 18.7	158.7 ± 3.5	145.5 ± 4.9	136.7 ± 2.3	147.6 ± 5.3	134.0 ± 9.6
M/100mg/kg	123.2 ± 12.7	175.7 ± 9.5	128.0 ± 7.5	115.7 ± 14.2	89.8 ± 13.1	88.2 ± 19.2
P value	0.0051	0.3980	0.2529	0.3671	0.0117	0.1023

E: Extract; M: Metformin; mg: milligram; kg: kilogram; dL: deciliter

Table 2: Effect of *Eleusine coracana* on the body weight of Wistar rats after 28 days Treatment

Group	Mi weight (g) ±SEM	Mf weight (g) ±SEM	Mc weight (g) ±SEM
N/Control	209.5 ± 22.0	209.4 ± 22.6	4.8 ± 1.9
E/100mg/kg	259.0 ± 29.2	268.1 ± 35.4	3.2 ± 1.8
E/200mg/kg	224.5 ± 22.5	227.1 ± 21.9	4.3 ± 1.7
E/400mg/kg	210.4 ± 13.7	212.6 ± 13.7	2.4 ± 0.9
M/100mg/kg	296.8 ± 21.2	297.9 ± 21.2	1.4 ± 0.4
DC/5ml/kg	208.1 ± 16.8	199.9 ± 23.6	2.5 ± 1.2
P value	0.3350	0.3890	0.5004

N: Normal; E: Extract; M: Metformin; DC: Diabetic control; Mi: Initial Mean weight; Mf: Final mean weight; Mc: Change in mean weight; g: gram; SEM: Standard error of mean

Table 3: Effect of *Eleusine coracana* on the serum lipid profile and blood glucose level of Wistar rats after 28 days treatment

Group	Serum lipid profile (mg/dL) ±SEM				Blood glucose level (mg/dL) ±SEM		
	TG's	TC	HDL	LDL	Mi blood sugar	Mf blood sugar	Mc blood sugar
N/Control	56.0 ± 7.8	69.0 ± 6.5	19.8 ± 1.4	37.2 ± 9.1	23.0 ± 7.4	111.2 ± 7.2	92.6 ± 4.4
E/100mg/kg	76.6 ± 11.2	60.8 ± 2.3	26.7 ± 5.6	19.0 ± 8.9	91.8 ± 39.6	253.8 ± 69.2	181.4 ± 57.0
E/200mg/kg	69.8 ± 6.8	71.0 ± 4.9	21.2 ± 1.7	35.8 ± 6.8	44.6 ± 45.9	223.3 ± 45.3	178.7 ± 52.5
E/400mg/kg	57.2 ± 6.3	53.6 ± 3.9	19.8 ± 1.8	*22.4 ± 5.3	80.7 ± 21.1	299.2 ± 59.9	218.5 ± 49.5
M/100mg/kg	81.8 ± 17.2	76.7 ± 5.8	25.2 ± 1.5	35.0 ± 5.4	44.3 ± 22.1	219.6 ± 72.4	175.3 ± 52.5
DC/5ml/kg	77.7 ± 3.1	106.0 ± 7.3	29.7 ± 6.0	61.5 ± 6.0	16.8 ± 16.3	307.1 ± 56.4	290.5 ± 74.6
P value	0.4215	*0.0010	0.4515	*0.0078	0.1623	0.1998	0.1639

N: Normal; E: Extract; M: Metformin; DC: Diabetic control; TG's: Triglycerides; TC: Total cholesterol; HDL: High density lipoproteins; LDL: Low density lipoproteins; Mi: Initial mean blood glucose level; Mf: Final mean blood glucose level; Mc: Change in mean blood glucose level; mg: milligram; kg: kilogram; dL: deciliter; SEM: Standard error of mean; *p < 0.05

DISCUSSION

This study evaluated the hypoglycemic and hypolipidemic effects of aqueous *Eleusine coracana* seed extract in alloxan-induced hyperglycemic Wistar rats. All the doses of EC prevented a sustained increase in the blood glucose level after glucose loading. The finding of significant reductions ($P < 0.05$) in blood glucose levels in all the treated groups as compared to normal control and metformin diabetic control groups in this study indicates that aqueous EC seed extract has hypoglycemic property. Similarly, the finding of significant differences ($P < 0.05$) in the serum levels of total cholesterol (TC) and low density lipoprotein (LDL) in the treated group as compared to normal control and metformin diabetic control groups in this study confirms the hypolipidemic property of EC seed extract. The hypoglycemic and hypolipidaemic properties exhibited by aqueous *Eleusine coracana* seed extract in this study is in concordance with the findings in other studies that also reported antihypoglycemic and hyperlipidemic effects of *Eleusin coracana* in alloxan- or stroptozocin-induced hyperglycemic Wistar rats (Yaro *et al.*, 2018; Shobana *et al.*, 2010; Ananthan *et al.*, 2004). The hypoglycemic effect of EC may be due to the presence of flavonoids, tannins, alkaloids, saponins, and cardiac glycosides in it, as the hypoglycemic activity of these chemical constituents have been reported in a previous study (Ahmed *et al.,* 2000). This study found no significant difference ($P>0.05$) in the body weight of the treated rats as compared to the control group after 28 days of oral administration of EC extract. This may be due to the absence of steroid among the chemical constituents of the extract (Johnson *et al.*, 1988).

The abnormal high concentration of serum lipid in diabetes is believed to be mainly due to an increase in the mobilization of fatty acids from peripheral depots, since insulin inhibits the hormone sensitive lipase. The marked hyperlipidemia that characterized diabetic state may therefore be regarded as a consequence of uninhibited actions of lipolytic hormones on the fat depots (Al Shamony *et al.*, 1994). It has also been demonstrated that insulin deficiency in diabetes mellitus causes a variety of derangement in metabolic and regulatory processes, which in turn leads to accumulation of lipids such as total cholesterol and triglycerides in diabetic patients (Goldberg, 1981). Alterations in serum lipid profiles are well known in diabetes, and these increase the risk of cardiovascular diseases in them (Mary and John, 2007). A reduction in

serum lipids, particularly total cholesterol (TC), low density lipoprotein (LDL), and triglycerides (TG's) level is considered to be beneficial in the long-term outcome of diabetes management. The hypolipidemic and hypoglycemic properties of aqueous EC seed extract observed in this study showed that it has therapeutic potential in combating the multi factorial disorders which are a part of the major complications of diabetes, and further studies should be conducted to determine the mechanism of the action of its hypoglycemic and hypolipidemic effects.

CONCLUSION

This study has shown that aqueous *Eleusin coracana* seed extract remarkably reduced serum blood glucose level in both normal and alloxan-induced diabetic rats at the studies doses. Furthermore, the extract showed a significant hypolipidemic effect with decreases in serum total cholesterol and low density lipoprotein levels. These findings showed that EC seed extract has therapeutic potential in combating the multi factorial disorders which are a part of the major complications of diabetes, and further studies should be conducted to determine the mechanism of the action of its hypoglycemic and hypolipidemic effects.

Source of support

Nil.

Conflict of interest

None declared.

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