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Original Article

Response of Crude Leaf Extract of *Ageratum Conyzoides* on Hormonal and Biochemical Assay in Streptozotocin Induced Diabetic Male Wistar Rats

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Abstract

Effects of *Ageratum conyzoides* (*AC*) on hormonal and biochemical assay in male diabetic rats were examined. Twenty four adult male wistar rats divided into four groups of six rats (n=6) each, Nondaibetic control received 2 ml/kg bw distilled water, Diabetic control given distilled water as placebo, Diabetic rats treated subcutaneously with 5 units/kg bw of insulin, Diabetic rats treated orally with 400 mg/kg bw of AC for 28 days. Blood were collected every 3 days from rat's tail for glucose estimation using one touch glucometer. The rats were sacrificed by using chloroform and blood collected for sera preparation by cardiac puncture. AC significantly ($p<0.05$) decreased fasting blood glucose, Total cholesterol, Low density lipoprotein cholesterol levels and triglycerides levels in diabetic rats compared with diabetic control (DC) rats . AC also improved serum enzymes, hormone profile of rats. AC extract is therefore capable of improving hyperglycemia and hyperlipidemia in diabetic rats.

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Introduction

Diabetes mellitus is a metabolic disease characterized by hyperglycaemia and glycosuria due to absolute or relative lack of insulin (1). It is an age long, serious metabolic disorder with complications that result in significant morbidity and mortality (2).

According to Chukwuma (3), chronic hyperglycemia during diabetes has been shown to cause glycation of body protein, which in turn leads to secondary complications that affect the eyes, kidneys, nerves and arteries. It has gradually found its root in Africa, especially in Nigeria where westernized ways are imbibed (4). Diabetes mellitus is a chronic, debilitating and often deadly disease (5). It is a condition that arises when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin produced (6). Diabetes is a metabolic disorder of multiple aetiologies, characterized by chronic hyperglycaemia with disturbances of carbohydrates, fat and protein metabolism owing to overproduction and underutilization of glucose (7). The important metabolism affected by diabetes is the lipid metabolism which has the potential to develop atherosclerosis and cardiovascular complications (8). Atherosclerosis is a condition in which an artery wall thickens due to accumulation of fat, is the leading cause of death worldwide (9). Recently there has been a decrease in the prevalence of atherosclerosis-related deaths possibly due to effective management of the risk factors that predispose to this disorder (10). The major identified risk factors are elevated LDL-cholesterol, reduced HDL-cholesterol, hypertension and non-insulin dependent diabetes mellitus (11). Lowering of serum cholesterol, particularly LDL fractions is therefore considered as one of the strategies that can delay the on-set of hyperlipidemic disorders in humans (12). The prevalence of type 2 diabetes is rising at an alarming rate throughout the world, due to increases in life expectancy, obesity and sedentary lifestyles and it is destined to become one of the world's most important and costly disease of particular cause for concern is the dramatic rise of type 2 diabetes in children and adolescents (13) In type 2 diabetes mellitus lipid abnormalities are almost the rule and typical finding are elevation of total and VLDL cholesterol, triglyceride concentration, lowering of HDL cholesterol and a predominance of small, dense LDL particles (14). Herbal extracts are often used in folk medicine to improve lipid profile and prevent heart diseases (15). Plants provide an alternative strategy in search for new drugs (16). The reducing effects of blood glucose by a large number of plants have been confirmed in animal models and clinical studies (17).

Ageratum conyzoides is a common annual herbaceous weed with long history of traditional medicinal use in many countries especially in the tropical regions, extracts and metabolites from this plant is widely utilized in traditional medicine as a purgative, analgesic and as a heart tonic (18, 19). Herbal preparations from the leaves of *Ageratum conyzoides* has been used in the treatment of high blood pressure, fever, diabetes, pneumonia and numerous infectious diseases (20). It is reputed to possess varied medicinal properties (21) including the treatment of wounds and burns (22). In Cameroon and Congo, it is used traditionally to treat fever, rheumatism, headache, and colic (23). Some other communities use the plant as an antibiotic, antidysenteric and antilithic agent (24). Present study focused on the effects of crude leaf extract of *Ageratum conyzoides* on hormonal and biochemical assay in streptozotocin induced diabetic male wistar rats.

Materials and Methods

Chemical / Reagents

Assay kits used for the hormonal and biochemical assays of Lipid profile- Triglycerides (TG), Total cholesterol(TC), High density lipoprotein (HDL), Aspartate aminotransferase (AST), Alanineaminotransferase (ALT), Testosterone, Follicle stimulating hormone (FSH) and Leutinizening hormone (LH) were obtained from Randox Laboratories Ltd, Admore Diamond Road, Crumlin, Co., Antrim, United Kingdom, Qt94QY: glucose and Alpha amylase were from Agape Diagnostics LTD. Streptozotocin (STZ – Sigma, St Louis MO, USA).

Plant Material

Plant materials were collected from the Research Farm, Faculty of Agricultural Sciences, Ladoke Akintola University of Technology (LAUTECH) Ogbomoso, Oyo State, Nigeria in April, 2016. Samples of *Ageratum conyzoides* were identified and authenticated by Prof. A.J. Ogunkunle of the

Department of Pure and Applied Biology and Sample of the plant voucher deposited for reference purpose.

Extraction of Plant Material

The leaves were thoroughly washed in sterile water and were air dried to a constant weight in the laboratory. The air-dried leaves were weighed using Gallenkamp (FA2406B, England) electronic weighing balance and were milled with automatic electrical Blender (model FS-323, China) to powdered form. Four hundred and fifty-four grams of the milled plant sample was later soaked in 800 ml of Phosphate buffered saline (PBS) for 48 hours (25) at room temperature, and was later filtered through cheese cloth and then through Whatman #1 filter paper (26), the filtrate was concentrated using a rotary evaporator (Rotavapor® R-210) at 42–47°C.

Phytochemical Screening

Phytochemical analysis of the aqueous leaf extract of *Ageratum conyzoides* was done qualitatively and quantitatively by modification of method of Soni and Sosa (27). High performance liquid chromatography was adopted to quantify the vitamins by modifications of the report by Grindberg and Williams (28). Minerals content such as sodium, calcium, Potassium, iron, zinc and phosphorus were determined using modification of method described by Akubugwo *et al*., (29)

Acute Oral Toxicity Study of *Ageratum conyzoides* Extract

The acute oral toxicity study for *Ageratum conyzoides* extract was conducted using the Organization for Economic Cooperation and Development (OECD). Guidance Document on Humane End points that should reduce the overall suffering of animals used in this type of toxicity test. The test used was the limit dose test of the up and down procedure. Briefly, 5 animals were weighed and individually identified. The first animal was given the test dose – *Ageratum conyzoides* extract 1000 mg per kg body weight. The second and third animals were concurrently dosed and the fourth and fifth animals sequentially dosed. The results were evaluated as follows (S = Survival, X =death). The animals were observed individually at least once during the first 30 minutes after dosing, periodically during the first 24 hours (with special attention given during the first 4 hours), and daily thereafter for a total period of 14 days. All observations were systematically recorded with individual records maintained for each animal.

Animals

Male wistar rats were procured from the Experimental Animal Unit of the Department of Animal production and Health of Federal University of Technology, Akure, Ondo State, Nigeria were authenticated and used throughout the study. They were housed in plastic cages and maintained under standard natural photoperiodic condition of twelve hours of darkness and twelve hours of lightness (D:L; 12:12h dark/light cycle) at room temperature (25-32^{0}C) and humidity of 60-65%. The rats were fed with standard rat chow at a recommended dose of 100 g/kg as advised by the International Centre of Diarrheal Disease Research, Bangladesh (ICDDR, B) daily. Drinking water was supplied *ad libitum*. They were acclimatized for two weeks before commencement of the administration. The weighs of the rats were documented at procurement, during the period of acclimatization, at commencement of administrations and once a week throughout the period of the experiment, using an electronic analytical and precision balance (FC2124A, England).

Ethics committee

All the authors hereby declare that all the experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards provided in the “Guide for the Care and Use of Laboratory Animals” prepared by the National Academy of Sciences and Published by the National Institute of Health (30).

Induction of Experimental Diabetes

Diabetes was induced by a single intraperitoneal injection of a freshly prepared streptozotocin (STZ) solution (60 mg/kg body weight) in acidified saline solution. Control animals received only the acidified

saline solution at pH 4.5. Diabetic rats were those with persistent fasting blood glucose more than 250 mg/dl, 72h after injection of streptozotocin (31). Animals which received only acidified saline solution served as the negative control.

Experiment Design and Animal Grouping

Twenty-four healthy male adult (12-14 weeks old) wistar rats weight 200- 220 g were used for this study. The rats were randomly divided into four groups (A, B, C and D) of six (n=6) rats each. Group A which served as control were given distilled water 2 ml/kg body weight each daily for 28 days. Group B Diabetic control; diabetic rats given distilled water as placebo, Group C Diabetic rats treated subcutaneously with 5 units/kg.body weight of insulin, and Group D Diabetic rats treated orally with 400 mg/kg body weight of *Ageratum conyzoides* for 28 days. The extract was administered once daily for six days within a week through oral gavage. the rats were then kept for the next 24 hours on 5% glucose solution bottles in their cages to prevent hypoglycemia. Blood was collected once every 3 days through the rat's tail vein for glucose estimation using One Touch Glucometer; the experimental period was 28 days. At the end of the experimental period which was twenty-eight days, food was withdrawn from the rats and they were fasted overnight but had free access to water. They were then euthanized under chloroform vapor and sacrificed. Immediately, blood samples were collected for sera preparation by cardiac puncture into sterile plain tubes. Serum samples were separated from the clot by centrifugation at 3,000 rpm for 10 minutes using bench topcentrifuge (MSE Minor, England) and stored frozen until needed for analysis. All analysis was completed within 24 hours of sample collection.

Hormonal Analysis

Hormonal profile of the following endocrine markers (Testosterone, Follicule stimulating hormone and Leutenizing hormone) was carried out using method of immunoassay (ELISA) method (Randox Laboratories Ltd, Admore Diamond Road, Crumlin, Co., Antrim, United Kingdom, Qt94QY). according to the manufacturer's instructions.

Biochemical Assays

The concentration of the respective parameters; Triglycerides (TG), Total cholesterol (TC) and high density lipoprotein (HDL) was read directly using chemistry analyser (spectrophotometer), whereas the concentration of VLDL was extrapolated by dividing the respective concentration of TG by 5 while LDL-cholesterol estimated using the method by Friedewald (32) that LDL-C = TC -(HDL-C) – VLDL, AST and ALT was determined using Reitman and Frankel (33). Glucose concentrations in blood were determined by One Touch Glucometer. Quantitative determination of glucose and Alpha amylase in serum using Agape Diagnostics LTD, (CNPG3 Methodology) based on (34).

Data Presentation and Statistical Analysis

Data were expressed as Mean±SEM. Statistical differences between the groups were evaluated by one-way ANOVA, followed by Dunnets comparison test to compare between treated and control groups. Differences yielding $p<0.05$ were considered statistically significant. Statistical analyses of data were performed using GraphPad Prism 5 for Windows (GraphPad Software, San Diego, California, USA).

Results

Acute oral Toxicity Studies

There were no deaths of rats dosed 1000 mg/kg body weight of the plants extract both within the short and long outcome of the limit dose test of Up and Down method (Table III). The LD50 was calculated to be greater than 1000 mg/kg body weight /orally.

Phytochemical screening

Qualitative analysis of *Ageratum conyzoides* aqueous crude leaves extract shows the presence of alkaloids, phlobatannins, flavonoids, tannins, terpenoids, cardiac glycoside, saponins, steroids, sodium, potassium, calcium and phosphorous (Table I). After the quantitative analysis, total saponins, total phenol and total flavonoids had higher values compared to

TABLE I : Qualitative Phytochemical Analysis of Aqueous crude Extract of Ageratum conyzoides.

S/N	*Phytochemicals*	*Status*
1	Cardiac glycosides	+
2	Tannins	+
3	Saponins	+
4	Steroids	+
5	Alkaloids	+
6	Flavonoids	+
7	Phenolic acid	+
8	Terpenoids	+
9	Phlobatannins	+
10	Quinones	–
11	Coumerins	–
12	Anthracene	–
13	Sodium	+
14	Potassium	+
15	Calcium	+
16	Phosphorous	+
17	Zinc	–
18	Iron	–

+ Present, – not present

TABLE II : Quantitative phytochemical analysis of aqueous crude extract of Ageratum conyzoides.

S/N	*Phytochemicals*	*Quantity*
1	Vitamin A (mg/g)	3.04
2	Vitamin C (mg/g)	2.15
3	Vitamin D (mg/g)	3.34
4	Vitamin E (mg/g)	5.11
5	Total Tannins (%)	3.34
6	Total Saponins (%)	13.10
7	Total Flavonoids (%)	10.35
8	Total Phenols (%)	14.16
9	Total Alkaloids (%)	5.35

total taninins and the total alkaloids present. There were also high values of vitamins A, C, D and E (Table II).

Effect of crude leaf extract of *Ageratum conyzoides* and insulin on fasting blood glucose

Streptozotocin induced diabetes in rats significantly (P<0.05) increases the mean blood glucose level of diabetic control group to 429.70±12.45 mg/dl while its final mean concentration of 349.20±15.01 mg/dl was significantly higher than that of *Ageratum conyzoides* (154.3±11.25 mg/dl), INSULIN (81.32±3.70 mg/dl), and non-diabetic control (73.90±1.55 mg/dl) final concentrations. The mean value of serium glucose level in diabetic control group (14.13±0.54) was significant (p<0.05) higher than that of mean value non diabetic control group (6.65±0.45). Diabetic group treated with *Ageratum conyzoides* showed significant (p<0.05) decrease in mean serum glucose level (6.65±0.45) compared with diabetic control after 28days of oral administration of *Ageratum conyzoides extract* (Table IV).

TABLE III : This table shows results of acute toxicity test for Ageratum conyzoides (up and down procedure) in rats.

Test serial number	*Animal Identity*	*Dose of A.conyzoides mg/kg*	*Short term result (48 hrs)*	*Long term results (14 days)*
1	I	1000	S	S
2	LLT	1000	S	S
3	RLT	1000	S	S
4	TC	1000	S	S
5	LEP	1000	S	S
6	REP	1000	S	S

S = Survival; REP = Right ear pierced; LEP = Left ear pierced; TC = Tail cut; RLT = Right leg tagged; LLT = Left Leg tagged, I = Intact rat.

Effect of aqueous crude extracts of *Ageratum conyzoides* on serum lipids profile of diabetic and non-diabetic male rats

After 28 days of treatment there was significant (p<0.05) decrement in mean total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and VLDL concentrations in all diabetic groups treated with extracts and insulin when compared with the diabetic negative control however mean high density lipoprotein cholesterol (HDL-C) concentration was significantly (p<0.05) increased in treated diabetic group when compared with the diabetic control group (Table V).

Effect of treatment on serum enzymes in diabetic and non-diabetic male rats

There was significant (p<0.05) increased in Serum aminotransferase activities (AST and ALT) in diabetic control group relative to non-diabetic control group. Aqueous crude extract of *Ageratum conyzoides* and insulin significantly decreased AST and ALT in diabetic treated groups in comparison with diabetic negative control group. Alpha-amylase in diabetic control group (267.20±10.35U/L) increased significantly compared to non-diabetic control group (178.10±11.00U/L).Oral administration the extract

TABLE IV : Fasting blood glucose level of streptozotocin-induced diabetic and non diabetic male rats treated with 400 mg/kg aqueous crude leaf extracts of Ageratum conyzoides and 5 units/kg body weight of insulin.

Treatment groups	*Fasting blood glucose levels*		
	Initial (mg/dl)	*Final (mg/dl)*	*Serum glucose (mmol/L)*
A (N.control)	74.66±1.82	73.90±1.55	6.65±0.45
B(Diabetic control)	429.70±12.45*	349.20±15.01*	14.13±0.54*
C(Insulin)	555.40±12.60*	81.32±3.70	4.72±0.42*
D(Ageratum conyzoides extract)	509.70±4.06*	154.3±11.25*	9.26±0.41*

Values are expressed as Mean±SEM for n=6; *p<0.05, significantly dissimilar from control group. One-Way ANOVA.A- Non diabetic control, B- Diabetic control, C- Diabetic rat + 5 units/kg body weight of insulin, D- Diabetic rat + 400 mg/kg body weight of Ageratum conyzoides.

TABLE V : Serum lipid profile in diabetic and non-diabetic male rats treated with 400 mg/kg aqueous crude leaf extracts of Ageratum conyzoides and 5 units/kg body weight of insulin.

Treatment groups	*Parameters*				
	TG (mg/dl)	*TC (mg/dl)*	*HDL-C (mg/dl)*	*LDL-C (mg/dl)*	*VLDL (mg/dl)*
A (N.control)	73.92±3.89	112.40±5.83	10.35±1.22	95.82±5.08	15.50±0.41
B (Diabetic control)	72.23±2.35	261.00±12.75*	63.94±2.50*	254.40±26.56	15.45±0.42
C (Insulin)	81.83±4.42	429.70±11.00*	70.51±3.01*	420.80±21.14*	17.29±0.52
D (Ageratum conyzoides extract)	63.93±3.04	113.90±5.10	54.81±3.82*	65.41±4.74*	14.07±0.56

Values are expressed as Mean±SEM for n=6; *p<0.05, significantly dissimilar from control. One-Way ANOVA. A- Non diabetic control, B- Diabetic control, C- Diabetic rat + 5 units/kg body weight of insulin, D- Diabetic rat + 400 mg/kg body weight of *Ageratum conyzoides*, TC: Total cholesterol; TG: Triglycerides; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol.

TABLE VI : Some serum enzymes in diabetic and non-diabetic male rats treated with 400 mg/kg aqueous crude leaf extracts of Ageratum conyzoides and 5 units/kg body weight of insulin.

Treatment groups	*Parameters*		
	AST (U/L)	*ALT (U/L)*	*Alpha-amylase (U/L)*
A (N.control)	20.47±1.39	25.35±2.71	178.10±11.00
B (Diabetic control)	75.72±3.42*	68.96±3.50*	267.20±10.35*
C (Insulin)	79.29±3.72*	56.24±4.83*	359.00±12.16*
D (Ageratum conyzoides extract)	42.95±2.20*	23.53±2.66*	294.20±12.80*

Values are expressed as Mean±SEM for n=6; *p<0.05, significantly dissimilar from control group One-Way ANOVA. A- Non diabetic control, B- Diabetic control, C- Diabetic rat + 5 units/kg body weight of insulin, D- Diabetic rat + 400 mg/kg body weight of Ageratum conyzoides, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT).

significantly decreased the level of the enzyme (294.20±12.80U/L) compared to insulin treated rats (359.00±12.16U/L), indicating protection of the pancreas. It is therefore observed that the enzyme level in the *Ageratum conyzoides* group (294.20±12.80U/L) was significantly increased (p<0.05) in comparison with non diabetic control (Table VI).

Effect of treatment on serum testosterone, Follicle stimulating hormone (FSH), Luteinizing hormone (LH) in diabetic and non-diabetic male rats

Fig. 1. Shows changes in serum testosterone, Follicle stimulating hormone (FSH), Luteinizing hormone (LH) in diabetic and non-diabetic male rats following 28-day treatment period. There was decrease in mean

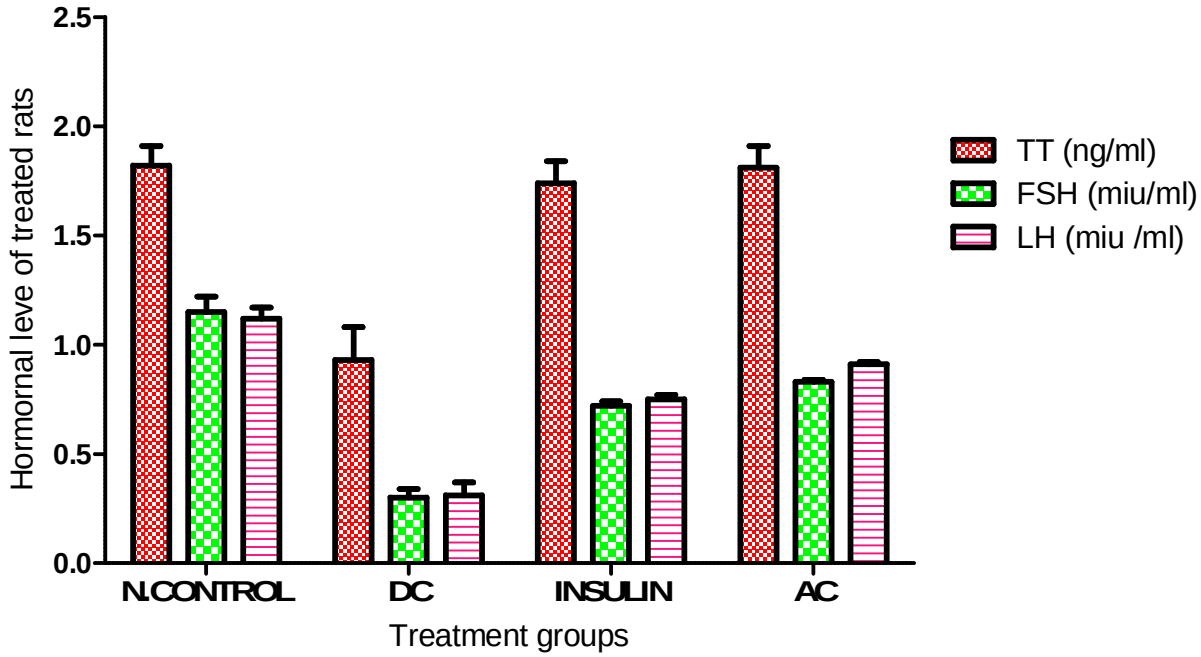

Fig. 1 : Serum testosterone (TT) , Follicle stimulating hormone (FSH), Luteinizing hormone (LH) in diabetic and non-diabetic male rats treated with 400 mg/kg body weight aqueous crude leaf extracts of Ageratum conyzoides and 5 units/kg body weight of insulin. Values are expressed as Mean±S.E.M, n=6 in each group, *represent significant dissimilarly from the control group at p<0.05. One-Way ANOVA, N.CONTROL: Non diabetic control, DC: Diabetic control, Miu: Milli international unit, ng: Nanogramme.

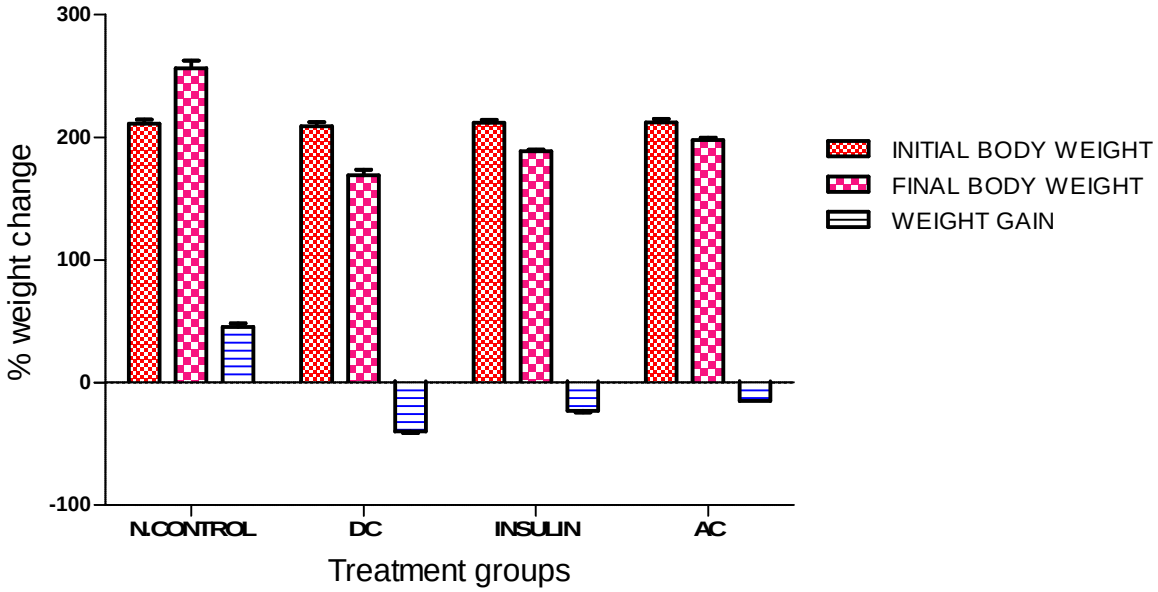

Fig. 2 : Change in body weight of control and diabetics rats treated with 5 units/kg body weight of insulin and 400 mg/kg body weight of Ageratum conyzoides for 28 days. N.CONTROL- Non diabetic control, DC- Diabetic control, AC- Ageratum conyzoides, Diabetic and the treated groups significant dissimilar from the control group. Values are expressed as Mean±SEM for n=6; *p<0.05, significantly dissimilar from control.

hormone profile of all the diabetic rats. There was significant difference between non diabetic and diabetic controlled and *Ageratum conyzoides* treated rats, and specifically between the diabetic rats fed only with extract and the rats that administered with insulin (p<0.05).

Effect of *Ageratum conyzoides* extracts on body weight of diabetic and non-diabetic male rats

There was observed decrease in mean body weight of all the diabetic rats however following the treatment with *Ageratum conyzoides* extracts and insulin revealed ameliorative potential of the extract. There was significant ($p<0.05$) improvement in the body weight of treated diabetic groups compared with the diabetic control. The final mean body weight of the diabetic rats treated with extract and insulin increased significantly relative to diabetic control rats (Fig. 2).

Discussion

This study was conducted in order to find out the antidiabetic activity of aqueous crude extract of *Ageratum conyzoides* in rats with STZ induced diabetes. In acute toxicity study, a scale proposed by Lorke (35) roughly classifies substances according to their LD50 as follows: Very toxic (LD50 < 1.0 mg/kg), toxic (LD50 up to 10.0 mg/kg), less toxic (LD50 up to 100.0 mg/kg) and only slightly toxic (up to 1000.0 mg/kg). Substances with LD50 values greater than 5,000 mg/kg are practically non-toxic. Based on this proposal, oral administration LD50 of 1000 mg/kg show that *Ageratum conyzoides* extract is less toxic. The high oral LD50 (> 3000 mg/kg) obtained suggested that the extracts are practically non-toxic through this route and are therefore safe in the rats and in traditional use orally for treatment of diseases. It has been reported photochemical components as responsible for some anti-diabetic activity of some plant extracts (19, 36). These natural components may act separately to cause the global hypoglycaemic effect (36). In this study, phytochemicals of antidiabetic found in *Ageratum conyzoides* include alkaloids, carbohydrates, cardiac glycosides, flavonoids, saponins, tannins, steroids, triterpenes, calcium, potassium, phosphorus, iron and vitamin. The findings from this study have shown that *Ageratum conyzoides* is rich in antioxidant constituents. This is in concordance with reports of Sunday *et al.,* (16). Streptozocin-induced hyperglycaemia has been described as a useful experimental model to study the activity of antidiabetic agents (37). It is generally accepted that Streptozocin treatment causes permanent destruction of â-cells, leaving less active cell resulting in a diabetic state which was indicated in diabetic control rats of this study (38). The results of present study revealed significant increase in blood and serum glucose levels in diabetic rats. Oral administration of *Ageratum conyzoides* extract thus reduces the blood glucose levels in diabetic rats. This revealed presence of hypoglycemic activities in the plant. The reduction observed in fasting blood glucose of treated diabetic rats is in conformity with earlier findings (16, 19, 39). It has been reported that the mode of reduction in blood glucose could be attributed to some active phytochemical constituents of *Ageratum conyzoides* (40). One of the active component of *Ageratum conyzoides* known as flavonoid has been reported to regenerate damaged beta-cells in diabetic mice (41, 42). *Ageratum conyzoides* may also act by preventing the death of β-cells or permit recovery of partially destroyed β-cells (43).

In this study *Ageratum conyzoides* crude aqueous extracts significantly decrease serum total cholesterol, triglycerides and LDL-cholesterol in diabetic rats. These extract might be useful in the prevention of atherosclerosis because of hypolipidemi property of the plant. According to lipid hypothesis, hypercholesterolemia which is higher concentrations of LDL and lower concentrations of functional HDL, as well as high triglyceride level are strongly associated with cardiovascular disease because these promote atheroma development in arteries (44). It has been documented that administration of antioxidants and minimal exposure to free radical may reduce LDL contribution to atherosclerosis (45). Abnormal low levels of cholesterol are relatively limited, but some studies suggest a link with depression, cancer and cerebral haemorrhage (46). Lipid abnormalities accompanying atherosclerosis is the major cause of cardiovascular disease in diabetes with high levels of TC and LDL as major coronary risk factors (47). Ability of *Ageratum conyzoides* leaf extract to lower the cholesterol level might be associated with presence of some phytochemical component of the plant extract, such as fibre (48), saponins (49) and flavonoids (50), possess antihyperlipidemic effects. Saponins prevent

excessive intestinal absorption of cholesterol and thus reduce the risk of cardiovascular diseases such as hypertension. Reducing serum lipids potential of *Ageratum conyzoides* extract could be explained be link to insulin releasing capacity of its phytochemical constituents. Present findings therefore consistent with the previous report by Sunday *et al.*, (16), Nyunaï *et al.,* (19), Giribabu *et al.*, (51). Our findings totally disagree with the postulation of Oyewole *et al.,* (52) that administration of *Ageratum conyzoides* at dosage of 200 and 500 mg/kg body weight after 14 days as no effect on lipid profile in rats.

Alanine aminotransferase, (ALT), aspartate aminotransferase (AST), are present in the hepatic and biliary cells and these enzymes are usually released from the hepatocytes and leak into circulation causing increase in their serum levels under hepatocellular injury or inflammation of the biliary tract cells resulting predominantly in an elevation of the alkaline phosphatase levels (53). *Ageratum conyzoides* consist of some phytochemicals constitutent such as flavonoids, tannins, saponins, phenolic acid, Steroid, Alkaloid and vitamins may play major roles in the hypolipidaemic effect of some plants. These chemicals help in recovery of vascularization of the pancreas and tend to act in capillaries (54, 55). Streptozotocin induced diabetic observed to be associated with increased serum enzyme activities (56). In our study increased in levels of the enzymes in diabetic control rats; ALT and AST was linked to injury to the hepatocydtes by streptozotocin which thus affects the liver function, since the enzymes are indisputably, markers of liver injury, they are localized in the cytoplasm under normal conditions and are released into the circulation under abnormal conditions therefore cause cellular damage (57). However oral consumption of *Ageratum conyzoides* for 28 days decreases the activities of these enzymes indicating the hepatoprotective effect of the plant extract. Pancreatic α-amylase is a key enzyme in the digestive system that catalyses the initial step in hydrolysis of starch to maltose and finally to absorbable glucose. Degradation of dietary starch leads to elevated postprandial hyperglycaemia. Retardation of starch hydrolysis by inhibition of pancreatic α-amylase is one of therapeutic approaches for the control of postprandial hyperglycaemia in pre-diabetes, diabetes and obesity (58). In this study *Ageratum conyzoides* inhibit pancreatic α-amylase which is in line as reported by Akkarachiyasit *et al.,* (59). *Ageratum conyzoides* may therefore be useful in regulating postprandial hyperglycaemia in type 2 diabetes patients by inhibit the pancreatic α-amylase.

More over there was derangement in serum testosterone, Follicle stimulating hormone (FSH), Luteinizing hormone (LH) in diabetic rats however after 28days of oral administration of the plant extract there was mark improvement in the hormone profile of the diabetic rats due to Phenolic compounds such as tannins, flavonoids and phenolic acids are considered to be the major contributors to the antioxidant capacity of *Ageratum conyzoides*. All phenols and particularly flavonoids are effective antioxidants because they donate electrons to radicals and break the radical chains.

Diabetes mellitus causes failure to use of glucose for energy which leads to increased utilization and decrease storage of protein responsible for reduction of body weight essentially by depletion of body proteins (60). Generally, there was loss of body weight in all the diabetic rats however after 28 days of treatment there was significant recovery of body weight in treated rats in comparison with diabetic and non-diabetic control rats. The ability of the *Ageratum conyzoides* extract to recover the body weight of the rat suggesting the extra pancreatic action of the extract and might be contributed by increased utilization of glucose by the tissues. In conclusion *Ageratum conyzoides* aqueous crude extract succeeded in controlling hyperglycemia in rats with streptozotocin induced diabetes. They also ameliorated all biochemical tests, pancreas functions and restored them to the normal state because of their antioxidant activity acquired by their possession of phenolic phytochemicals.

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