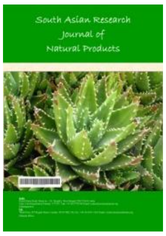

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Effect of Aqueous Extracts of Flower, Leaf, Stem and Root of *Ageratum conyzoides L* on Glucose, Lipid Profile and Liver Markers on Streptozocin Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Type 2 diabetes is the most recorded form of diabetes. It accounts for about 80% to 90% of all recorded cases of diabetes mellitus. The use of plant medicine is a very common practice from ancient time and it is considered the safer and less expensive therapeutic strategy for managing of various diseases including diabetes mellitus. The aim of this study is to investigate the antidiabetic effect of *Ageratum conyzoides* as claimed by herbal practitioners and to provide scientific evidence or evidences to back up the claims. Standard procedures were deployed in the aqueous extraction of the different parts (leaf, flower, stem, root and all parts) of the plant. Subsequently, diabetes was induced into albino wistar rats using streptozotocin at 55mg/kg. 40 rats weighing 180g to 240g were divided into eight groups A to H, groups B to H were induced with diabetes. Groups A and B were labelled normal and diabetic controls respectively. C was treated with standard drug (Glibenclamide) at 1000mg/kg, groups D, E, F, G and H were treated with flower, leaf, stem, root and all parts extracts respectively at 2000mg/kg. Treatment in all groups was done for 28 days after which the rats were anesthetize, sacrificed and assayed for lipid profile, enzyme and kidney functions. Significant differences were observed in the weights of the various groups at ($p<0.05$). After treatment, glucose level of the root, all parts, stem, flower and leaf extracts were statistically significant at ($p<0.05$). Elevated levels of cholesterol, triglycerides and LDL were significantly reduced ($p<0.05$) in roots, flower, all parts, stem and leaf while low HDL levels were increase in

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leaf, flower, root, stem and all parts. Creatinine and urea levels were reduced significantly (p<0.05). Total protein and serum albumin levels increased significantly (<0.05) in the root, leaf, stem, flower and all parts. Total and direct bilirubin levels were reduced significantly after treatment (p<0.05). Also, serum AST, ALT and ALP were reduced significantly in treatment groups. The results recorded indicates that *A. conyzoides* possess antihyperglycemic and antilipidemic activities at 2000 mg/kg.

Keywords: Ageratum conyzoides; streptozotocin; diabetes mellitus; glucose.

1. INTRODUCTION

Diabetes Mellitus (DM), is a disease of endocrine disorder in man and is considered one of the major health concerns globally today [1]. It is a disease of disordered metabolism of carbohydrate, protein and fat, caused by the complete or relative insufficiency of insulin secretion and/or insulin action [2]. It is characterized by a chronic hyperglycemic condition resulting from insufficient action of insulin. The main pathophysiological features of type 2 diabetes, which represents a great majority of diabetic cases, are impaired insulin secretion and increased insulin resistance. The impairment of pancreatic β-cell function notably shows progression over time.

It is a chronic disorder caused by decreased insulin production in the pancreas, or by the ineffectiveness of the insulin action on target tissues; this result in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, particularly the blood vessels and nerves [3]. The classical symptoms of diabetes include polyuria, glycosuria, weight loss, polydipsia, and polyphagia [4]. Derangements of carbohydrate metabolism in diabetes lead to chronic hyperglycemia in diabetes, which is associated with long-term damage, dysfunction and failure of various organs, especially the heart, eyes, blood vessels, kidneys, and nerves [5].

Plants have been of tremendous help to animals from time immemorial. Plants have been used by animals especially human beings as sole source of energy in the form of food and also medicine and beautification; the most important of these been the green plants [6].

In Nigeria and some parts of the world, history of traditional medicine show case thousands of plant species which have been used for many years in the practice of healing traditionally. In most part of Nigeria today, extracts from plants are still being used in their crude forms for the treatment or management of diseases. In most cases the therapeutic effects and other benefits derived are yet to be scientifically validated. Hence, there is a need for necessary scientific evaluation because of the rapid disappearances of forest habitats, and with time those in possession of this indigenous knowledge might die without transferring this knowledge and information to the next generation [7].

In view of the above reasons, this research is focus on probing scientifically, the claims by local herbal practitioners the use of *Ageratum conyzoides* for the management of type 2 diabetes.

2. MATERIALS AND METHODS

2.1 Plant Materials

Ageratum conyzoides L. was obtained from Jos metropolis. The plant was identified and verified with a voucher number (FHJ 246) at the Herbarium Department of Federal College of Forestry Jos, Plateau State.

2.2 Experimental Animals

Adult male wistar strain albino rats weighing from 180-240g were used to carry out the study. A minimum of twenty (40) adult albino rats were divided into 8 groups with 5 rats each.

2.3 Experimental Design

The animal groupings is as follows;

GROUP A- Normal control**,** GROUP B- Diabetic control, GROUP C – Diabetic + Glibenclamide (1000mg/kg b.wt), GROUP D- Diabetic + leaf extract (2000mg/kg b.wt)**,** GROUP E- Diabetic + flower extract (2000mg/kg b.wt)**,** GROUP F- Diabetic + stem extract (2000mg/kg b.wt)**,** GROUP G- Diabetic + root extract (2000mg/kg b.wt) and GROUP H- Diabetic + All parts extract (2000mg/kg b.wt)

2.4 Feeding and Randomization

After randomization into various groups and before the start of the experiment, the rats were acclimatized to the animal house condition [8,9,3]. The rats were maintained on a standard rat feed consisting (70% Carbohydrate, 14.50% protein, 7.0% Fat, 7.20% fibre and 1.20% mineral) for 28 days.

2.5 Experimental Induction of Diabetes

Diabetes was induced by intraperitoneal injection of streptozotocin at (55mg/kg) in seven (7) groups namely Group B, C, D, E, F, G and H. The animals were left for 48 hours after which diabetes was confirmed from the fasting blood glucose using one touch glucometer. Usman et al. [10] reported that blood glucose level reach 126mg/dl and accompanied with hyperglucosuric test 48 hours after streptozotocin induction. Prior to each study the animals will be made to fast for 14 hours but will have free access to water [11].

2.6 Preparation of Plant Extracts

The leaf, flower, stem, root and all parts of *Ageratum conyzoides* was collected and air dried at room temperature under shade. The dried plant was pounded to powdery form using pestle and mortar. They were then sieved into a fine powder using mesh size of 180 micron. The powder was stored in an airtight container until required for use. The preparation of the plant extract was carried out using distilled water. One hundred (100) grams of the fine powder was soaked in one (1) Litre of distilled water for 24 hours (to ensure maximum extractions of phytochemicals). The mixture was filtering using whatman filter paper No 1 to remove all extractable matter. The filtrate was dried in the oven at a temperature of 50-60^{o}C for two weeks. The solid extract was kept in the refrigerator in an air tight container to be reconstituted in distilled water before use for treatment of diabetic rats.

2.7 Administration of the Extract

A. conyzoides L. Flower, leaf, stem, root and all parts (whole plant) extract was administered through oral route at a dose of 2000 mg/kg body weight daily for 28 days. The lethal dose of different parts of the plant administered via oral route was found to be above 5000 mg/kg since no mortality was recorded at 5000mg/kg. This informed the choice of 2000 mg/kg dose of plant administered to rats.

2.8 Blood Collection

Blood was collected after decapitation of rats. It was collected in both EDTA and plain sample bottle using the method of blood collection described by Parasuraman et al. 2010 and was centrifuged in sterile centrifuge tubes. EDTA collected blood was taking for haematological analysis while the blood collected in plain sterile sample bottle was allowed to clot for 40 minutes and spun at 3,500 rpm for 10 minutes. Serum was separated and analyzed for different parameters [12].

3. RESULTS AND DISCUSSION

Weight variation was observed across all groups generally as shown in Table 1 above. The weight of normal control group was seen to increase significantly ($p<0.05$), whereas other groups induced with diabetes and treated with aqueous extracts of flower, leaf, stem and root of *A. conyzoides L* were seen to decrease significantly ($p<0.05$). This observation agrees with the findings by Atawodi et al. [13] that there was decline in the weights of streptozotocin-induced diabetic rats but treatment with plant extracts could be highly ameliorative effect.

Table 1. Weight difference before and after administration

Group	Treatment	Initial weight (g)	Final weight (g)	Weight difference (g)
A	DC	182.13±3.246	175.50±3.854	-6.63±0.740
B	NC	223.93±23.115	210.87±24.480	13.06±2.705
C	D + Glibenclamide	226.83±6.170	226.17±6.424	-0.66±2.504
D	D + Flower	195.97±2.214	191.97±3.467	-4.00±5.563
E	D + Leaf	239.50±3.942	211.30±6.835	-28.20±10.578
F	D + Stem	221.17±6.204	206.63±8.888	-14.53±5.305
G	D + Root	208.90±3.267	203.73±2.143	-5.16±1.930
H	D + All Parts	230.27±2.050	219.10±1.522	-11.16±3.385
p-values	-	0.0009	0.0635	0.0057

Values are expressed as mean ± SEM, n = 5

Table 2. Glucose level before and after 28 days of administration

Group	Treatment	Initial glucose (mg/dl)	Final glucose (mg/dl)
A	DC	273.00±9.192	302.00±9.192
B	NC	81.25±0.000^{A}	83.33±1.027^{A}
C	D + Glibenclamide	293.33±37.068^{B}	90.00±4.416^{AD}
D	D + Flower	239.00±32.835^{A}	99.33±1.650^{AD}
E	D + Leaf	276.00±11.923^{B}	101.33±2.656^{AD}
F	D + Stem	308.33±20.001^{B}	96.00±12.748^{AD}
G	D + Root	269.33±50.533^{A}	60.66±2.392^{AC}
H	D + All Parts	309.67±48.837^{B}	83.00±1.780^{AC}
P-Values	-	<0.0001	<0.0001

Values are expressed as mean ± SEM, n = 5
If p value is less than 0.05, there is significant difference in mean values
^{a}*Values are significantly low when compared with diabetic control (p < 0.05)*
^{b}*Values are significantly high when compared with diabetic control (p < 0.05)*
^{c}*Values are significantly low when compared with normal control (p < 0.05)*
^{d}*Values are significantly high when compared with normal control (p < 0.05)*

Table 3. Effect of aqueous extract of *Agerantum conyzoides* on serum lipid profile concentration of streptozotocin induce diabetic rats

Group	Treatment	Chol (MG/DL)	TG (MG/DL)	HDL (MG/DL)	LDL (MG/DL)
A	DC	101.46±0.486	148.73±1.794	40.57±0.841	62.06±0.166
B	NC	67.36±11.071^{a}	106.70±5.340^{a}	58.65±0.224^{b}	36.21±8.106^{a}
C	D +Glibenclamide	76.96±15.923^{ad}	68.56±3.532^{ac}	53.12±2.731^{ac}	52.02±14.029^{ad}
D	D + Flower	38.25±0.712^{ac}	60.60±3.722^{ac}	57.99±2.598^{bc}	16.85±0.479^{ac}
E	D + Leaf	54.59±0.533^{ac}	57.05±0.392^{ac}	71.42±0.560^{bd}	29.29±0.336^{ac}
F	D + Stem	51.42±0.861^{ac}	82.11±1.668^{ac}	61.11±1.120^{bd}	22.18±1.410^{ac}
G	D + Root	37.09±2.990^{ac}	69.55±2.364^{ac}	56.56±1.944^{bc}	21.32±1.674^{ac}
H	D + All Parts	42.62±3.310^{ac}	89.73±16.010^{ac}	60.89±0.090^{bd}	16.78±0.631^{ac}
p-values	-	<0.0001	<0.0001	<0.0001	<0.0001

Values are expressed as mean ± SEM, n = 5
If p value is less than 0.05, there is significant difference in mean values
^{a}*Values are significantly low when compared with diabetic control (p < 0.05)*
^{b}*Values are significantly high when compared with diabetic control (p < 0.05)*
^{c}*Values are significantly low when compared with normal control (p < 0.05)*
^{d}*Values are significantly high when compared with normal control (p < 0.05)*

Table 4. Effect of aqueous extract of *Agerantum conyzoides* on serum urea and creatinine concentration of streptozotocin induce diabetic rats

Group	Treatment	Creatinine (µmol/l)	Urea (µmol/l)
A	DC	66.29±0.423	8.57±0.362
B	NC	56.84±0.592^{a}	5.64±0.193^{a}
C	D + Glibenclamide	49.19±1.489^{ac}	5.37±0.387^{ac}
D	D + Flower	53.27±0.175^{ac}	6.78±0.806^{ad}
E	D + Leaf	49.56±0.192^{ac}	7.47±0.081^{ad}
F	D + Stem	41.06±0.792^{ac}	5.80±0.156^{ad}
G	D + Root	53.07±1.901^{ac}	5.03±0.172^{ac}
H	D + All Parts	55.43±2.388^{ac}	5.13±0.717^{ac}
p-values	-	<0.0001	<0.0001

Values are expressed as mean ± SEM, n = 5
If p value is less than 0.05, there is significant difference in mean values
^{a}*Values are significantly low when compared with diabetic control (p < 0.05)*
^{b}*Values are significantly high when compared with diabetic control (p < 0.05)*
^{c}*Values are significantly low when compared with normal control (p < 0.05)*
^{d}*Values are significantly high when compared with normal control (p < 0.05)*

Table 5. Effect of aqueous extract of *Agerantum conyzoides* on serum total protein, albumin, total bilirubin and direct bilirubin concentration of streptozotocin induce diabetic rats

Group	Treatment	TP(g/L)	ALB (g/L)	TB (mg/dl)	DB (mg/dl)
A	DC	58.55±0.222	32.61±0.856	8.01±4.352	0.52±0.082
B	NC	71.20±0.623[b]	36.56±0.980[b]	1.42±0.129[a]	1.20±0.029[b]
C	D + Glibenclamide	61.85±1.499[bd]	38.36±0.473[bd]	1.36±0.250[ac]	1.09±0.043[bc]
D	D + Flower	60.20±1.898[bc]	35.88±0.170[bc]	0.98±0.071[ac]	0.64±0.056[bc]
E	D + Leaf	60.09±0.670[bc]	33.56±0.203[bd]	2.97±0.021[ad]	1.33±0.120[bd]
F	D + Stem	63.54±3.374[bd]	34.91±0.750[bc]	1.93±0.356[ad]	1.06±0.095[bc]
G	D + Root	64.08±1.539[bd]	37.85±0.991[bc]	1.37±0.257[ac]	0.93±0.061[bc]
H	D + All Parts	67.22±0.312[bd]	37.54±0.406[bd]	1.26±0.077[ac]	0.74±0.063[bc]
p-values	-	<0.0001	<0.0001	0.0623	<0.0001

Values are expressed as mean ± SEM, n = 5
If p value is less than 0.05, there is significant difference in mean values
[a]Values are significantly low when compared with diabetic control (p < 0.05)
[b]Values are significantly high when compared with diabetic control (p < 0.05)
[c]Values are significantly low when compared with normal control (p < 0.05)
[d]Values are significantly high when compared with normal control (p < 0.05)

Table 6. Effect of aqueous extract of *Agerantum conyzoides* on serum enzyme concentration of streptozotocin induce diabetic rats

Group	Treatment	ALP (µ/L)	ALT (µ /L)	AST (µ/L)
A	DC	111.27±2.252	32.00±1.080	71.80±2.059
B	NC	46.56±1.217[a]	20.66±0.623[a]	40.69±1.093[a]
C	D + Glibenclamide	70.65±1.309[ad]	21.00±0.408[ad]	46.03±1.281[ad]
D	D + Flower	65.40±5.283[ad]	25.33±1.929[ad]	64.75±0.316[ad]
E	D + Leaf	96.85±4.546[ad]	29.00±0.408[ad]	66.01±0.041[ad]
F	D + Stem	96.87±9.696[ad]	30.33±0.623[ad]	66.15±0.316[ad]
G	D + Root	63.40±5.564[ad]	21.66±1.312[ad]	46.52±1.474[ad]
H	D + All Parts	95.39±7.705[ad]	22.33±0.849[ad]	55.36±4.814[ad]
p-values	-	<0.0001	<0.0001	<0.0001

Values are expressed as mean ± SEM, n = 5
If p value is less than 0.05, there is significant difference in mean values
[a]Values are significantly low when compared with diabetic control (p < 0.05)
[b]Values are significantly high when compared with diabetic control (p < 0.05)
[c]Values are significantly low when compared with normal control (p < 0.05)
[d]Values are significantly high when compared with normal control (p < 0.05)

The fasting blood glucose was determined as described by Clark and Lyons [14] using glucometer. Glucose levels of animals before and after induction of streptozotocin are presented in Table 2. Administration of STZ to the rats produced a significant increase (P<0.05) in glucose concentration of rats in all treated groups, except for normal control group which did not change significantly (P>0.05).

The principle of the test is based on the fact that the test strip has a small spot impregnated with glucose oxidase and other components. The glucose in the blood sample reacts with the glucose oxidase to form gluconic acid, which then reacts with ferricyanide to form ferrocyanide. The electrode oxidizes the ferrocyanide, and this generates a current directly proportional to the glucose concentration. The total charge passing through the electrode is proportional to the amount of glucose in the blood that has reacted with the enzyme [13].

The glucose level for diabetic control remained high 28 days after it was confirmed that the glucose level increased beyond normal. Furthermore, across all the treated groups, significant reduction in glucose levels was observed.

Lipid profile serum for each group was determined. Table 3 shows the results of the lipid profile for each group. Results for each group indicates that the mean values of cholesterol, triglyceride, low density lipoprotein and high density lipoprotein are statistically significant (p < 0.05). Cholesterol level is significantly high in diabetic control group when compared with treated groups. So also triglyceride and low density lipoprotein respectively. High density lipoprotein which is a good lipoprotein is significantly low in diabetic control group compared to treated groups.

The results recorded in Table 4 is reflective of the fact that dyslipidemia a condition usually present in diabetes in the form of increased triglycerides and decreased HDL cholesterol level, is usually associated with an accelerated and increased risk of coronary artery disease (CAD), cerebrovascular disease, and peripheral vascular disease and may also lead to sudden cardiac death [15].

Lipids play an important role in the emergence of diabetes mellitus. Dyslipidemia as a metabolic abnormality is always associated with this disease condition. Abnormal lipid metabolism have been reported in patients with diabetes mellitus accompanied by the risk of other diseases like cardiovascular arteriosclerosis [16].

According to a study by Ozder [17] significantly higher mean serum levels of total cholesterol, triglycerides and LDL cholesterol were observed in patients with diabetes. These elevated parameters are well known risk factors for cardiovascular diseases among patients.

In diabetic condition, there are many factors which may affect blood lipid levels, because of the interrelationship between carbohydrates and lipid metabolism. Therefore, any abnormality in carbohydrate metabolism will lead to disorder in lipid metabolism and vice versa.

Several studies have established that insulin is implicated in liver apolipoprotein production and also in the regulation of enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, both of which are found to cause dyslipidemia in diabetes mellitus [17].

Defects in normal insulin secretion and high glucose level in the blood could lead to changes in plasma lipoproteins in patients with diabetes. In the case of type 2 diabetes, the obesity/insulin-resistant metabolic disarray that is at the root of this form of diabetes could lead to lipid abnormalities exclusive of hyperglycemia. Lipoprotein abnormalities commonly present in type 2 diabetes, also termed noninsulin-dependent diabetes mellitus, include hypertriglyceridemia and low plasma HDL cholesterol. Also, low density lipoprotein (LDL) are converted to smaller, perhaps more atherogenic, lipoproteins also called small dense LDL [18].

Hyperglycemia may exacerbate hypertriglyceridemia. Therefore, normalizing glucose levels will improve dyslipidemia (Parhofer et al., 2002) [20], but may not be sufficient enough to achieve the strict lipid goals required to prevent the emergence of atherosclerosis [19].

Most professional associations recommend LDL-C to be below 100 mg/dl (2.6 mmol/l). In addition, lipid goals include triglycerides <150 mg/dl (1.7 mmol/l) and HDL-C >40 mg/dl (1.0 mmol/l). However, it should be noted that there is considerable heterogeneity with respect to atherosclerosis risk in patients with diabetes mellitus. Understanding the pathophysiology of diabetic dyslipidemia is key to understanding why diabetic patients have an increased risk for atherosclerotic disease [19].

The fact that a significant lowering effects of cholesterol, triglyceride and LDL was observed in diabetic infected and treated groups of albino rats explains the antidiabetic effect of *Ageratum conyzoides*. This claim was confirmed in a study by Atawodi et al*.,* [13] who observe and recorded that several phytochemical components of plant extracts, such as fibre [20], saponins [21] and flavonoids [22], are found to possess antihyperlipidaemic effects.

Table 4 shows the serum levels of creatinine and urea. Creatinine and urea in diabetic control are significantly increased ($p < 0.05$) when compared with treated groups. An increase in creatinine and urea levels was observed in diabetic control when compared with normal control and a significant reduction ($p < 0.05$) was also observed in treated groups when compared with diabetic control. Elevated levels of blood creatinine and urea concentrations are eminent indication of renal dysfunction which gave rise to a flow of these biochemical substances into the blood serum [23]. Therefore, pathologic conditions that impair renal function gave rise to an increase in creatinine and urea levels in the blood of the organism. It is imperative to note that an eminent increase in blood levels of creatinine and urea is the result and indication of prolonged diabetes mellitus complications which may result into diabetic nephropathy [24].

Study by Bamanikar et al., [25] shows that a poorly controlled blood sugar levels could cause an increase in the serum urea levels, which will in turn increase the chances of the patient suffering from diabetic nephropathy. The above assertion also agrees with the findings of other studies which reported that hyperglycemia is one of the major causes of progressive renal damage [26,27]. Therefore, the blood sugar lowering effect of *A. conyzoides* may in turn reverse the leakage of these biomarkers into the blood.

Table 5 show the levels of serum protein, albumin and bilirubin. The serum bilirubin were seen to increase significantly ($p < 0.05$) in diabetic control group compare to groups treated with plant extracts and standard drugs. On the other hand, protein and albumin level reduced significantly ($p<0.05$) in diabetic control group compared to normal control group and treated groups. This results are corroborating the fact that, insulin has been found to have an effect on protein metabolism. It increases the rate of protein catabolism and decreases the rate of protein anabolism.

Therefore, insulin deficiency will activate the catabolism of protein and this will in turn decrease the serum concentration of protein [28].

Raju & Raju, [29] asserted that insulin has an overall effect on protein metabolism, it increases protein synthesis and decreases protein degradation. Therefore insulin deficiency will result to an increase in the catabolism of protein. The increase in the rate of proteolysis will lead to an elevation in the concentration of amino acids in plasma, which in turn will reduce the amount of protein in the blood. Marshall et al. in a study conducted in 2004 reported that changes in protein concentration in the plasma could be as a result of increase in their catabolism rate, decrease in their anabolism and changes in their volume of distribution [30].

Albumin anabolism and secretion is decreased due to insulin deficiency. Garkuwa et al., [31] in their findings observed that both albumin and globulin levels are increased significantly after a hyperglycemic rat was administered a low dose of *curcumin* plant extract and compared to a diabetic control rat group. The increase in the serum albumin and globulin may signify an increase in the transport capacity of the blood. This might lead to an increase in lipid soluble hormones transport such as thyroid hormones and cortisol which increase glucose dynamicity, absorption and metabolism [31,32]. This signifies that serum albumin in diabetic patient reduces but when treated, it increases signifsicantly.

Table 6 shows the level of serum enzymes. This table shows the activities of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), and serum alkaline phosphatase (ALP) in diabetic rats and compare it with that of normal healthy rats used as normal control. The mean values for diabetic control, normal control and treatment groups are statistically significant ($p<0.05$). The activity of ALP in diabetic condition has not been largely reported but ALT and AST have been implicated in prolong diabetic condition. This assertion agree with the findings by Harris [33] in their findings, they reported that people with T2DM have a higher incidence of liver function abnormalities than individuals who do not have incidence of diabetes. Aminotransferase such as ALT and AST, activities are sensitive indicators of liver cell injury and are helpful in recognizing hepatocellular diseases. Chronic prolong elevation of liver enzymes is frequently found in Type-2 diabetic patients [33].

Serum aminotransferase such as ALT and AST indicate the concentration of hepatic intracellular enzyme that has leaked into the circulation. These are bio-markers for hepatocellular injury and are used as primary markers [34].

4. CONCLUSION

In conclusion, the results obtained clearly indicates that flower, Leaf, Stem, Root and whole plant Extracts of *Ageratum conyzoides L* possesses antidiabetic, antilipidemic effect and regulates liver markers.

ETHICAL APPROVAL

The animals were fed with standard feed throughout the period of the research. All experiments on animals were done in accordance with the guidelines of both the University of Jos ethical committee and the international guidelines for handling of laboratory animals. Ethical clearance were obtain and the number F17-00379 given to the research team.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Rohilla A, Ali S. Alloxan–induced diabetes, Mechanisms and effect. Int J Research Pharm Biomed Sci. 2012;3(2):819-23.
2. Ivorra MD, Paya M, Villar, A. A review of natural products and plants as potential anti- diabetic drugs. J.Ethnopharmacol. 2012;27:243-275.
3. Nagappa AN, Thakurdesai, PA, Raob NV, Singh J. Antidiabetic activity of Terminalia catappa Linn fruits. J. Ethnopharmacol. 2003;45-50.
4. Cooke DW, Plotnick L. Type 1 diabetes mellitus in pediatrics, Pediatr Rev. 2008;29(11):374–84.
5. Assim A, Khalid ABA. Assessment of care for type 2 diabetic patients at the primary care clinics of a referral hospital. Journal of Family and Community Medicine. 2006;13(1):13-18.
6. Luka, CD, Istifanus G, George M, Jesse NS. Effect of aqueous extract of *Dodonaea viscosa* Linn on some biochemical parameters in alloxan induced diabetic rats. Current Journal of Applied Science and Technology. 2018;27(3):1-7.
7. Idu M, Ndukwu BC. Studies of plants used in ethno medicine in Ethiope council area of Delta State.Nigeria. 2006;40.
8. Lorke D. A new approach to practical acute toxicity testing. Arch Toxicol. 1983;54:275–87.
9. Kumar GPS, Arulselvan P, Kumar DS, Subramanian SP. Antidiabetic activity of fruits of Terminalia chebula on streptozotocin induced diabetic rats. Journal of Health Science. 2006;52:283-291.
10. Miura T, Koike T, Ishida T. Antidiabetic activity of green tea (*Thea sinensis* L.) in genetically Type 2 diabetic mice. Journal of health science, 2005;51:708-710.
11. Usman UZ, Bakar ABA, Mohamed M. A review on experimental methods of diabetic research: Advantages and limitations. Annual Research & Review in Biology. 2015;7(2):100-108.
12. Ragavan S, Krishna Kumari. Antidiabetic effect of *T. arjuna* bark extract in Alloxan induced diabetic rats. Indian Journal of Clinical Biochemistry. 2006;21:123-128.
13. Parasuraman S, Raveendran R, Kesavan R. Blood sample collection in small laboratory animals. J. Pharmacol Pharmacother. 2010;1:87–93.
14. Atawodi SE, Oluwafemi AA, Humphrey CN. Antihyperglycaemic and hypolipidemic effect of methanol extracts of *Ageratum conyzoides* L (Asteraceae) in normal and diabetic rats. Tropical Journal of Pharmaceutical Research. 2017;16(5):989-996.
15. Clark L, Lyons C. Development of the first glucose enzyme electrode that rely on a thin layer of glucose oxidase on an oxygen electrode. Ann New York Acad Sci. 1962;109:29.
16. Vydehi V, Swetha M. Comparison of lipid levels in the diabetic and non-diabetic patients: a study in a tertiary care hospital. Int J Adv Med. 2017;4(6):1573-1577.
17. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. 2004;27(6):1496–1504.
18. Ozder A. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids in Health and Disease. 2014;13:183.
19. Ira JG. Diabetic Dyslipidemia: Causes and Consequences. The Journal of Clinical Endocrinology & Metabolism. 2001;86(3).
20. Parhofer KG, Laubach E, Geiss HC, Otto C. Effect of glucose control on lipid levels in patients with Type 2 diabetes. Dtsch. Med. Wochenschr. 2002;127(18):958–962.
21. Mary S, Mark H. Pathophysiology of diabetic dyslipidemia:implications for atherogenesis and treatment, Clinical Lipidology. 2011;6(4):401-411
22. Arvill A, Bodin L. Effect of Short-term Ingestion of Konjacglucomannanon Serum Cholesterol in Healthy Men. Am J ClinNutr. 1995;61:585-589.
23. Francis G, Kerem Z, Makkar HPS, Beckerm K. The biological action of saponins in animal systems: A Review. Br J Nutr. 2002;88:587–605.
24. Song EK, Hur H, Han MK. Epigallocatechingallate Prevents Autoimmune Diabetes Induced by Multiple Low Doses of Streptozotocin in Mice. Arch Pharmacol Res. 2003;26:559–563.
25. Atangwho IJ, Ebong PE, Eteng MU, Eyong EU, Obi AU. Effect of Vernonia amygdalina Del leaf on kidney function of diabetic rats. Int J Pharmacol; 2007;3:143‑8.
26. Idonije BO, Oloruntoba F, Oluba OM. Plasma glucose, creatinine and urea levels in type 2 diabetic patients attending a Nigerian teaching hospital. Res J Med Sci. 2011;5:1‑3.

27. Bamanikar SA, Bamanikar AA, Arora A. Study of Serum urea and Creatinine in Diabetic and non-diabetic patients in in a tertiary teaching hospital. The Journal of Medical Research; 2016;2(1):12-15.
28. Anjaneyulu M, Chopra KQ. An antioxidant bioflavonoid, attenuates diabetic nephropathy in rats. Clinical & Experimental Pharmacology & Physiology. 2004;31:244-8.
29. Shrestha S, Gyawali P, Shrestha R, Poudel SM, Regmi P. Serum Urea and Creatinine in Diabetic and non-diabetic subjects. JNAMLS. 2008;9:11-2.
30. Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. Journal of Physiology and Pathophysiology. 2013;4(4):46-57.
31. Raju SM, Raju B. Illustrated medical biochemistry. 2nd Edition. Jaypee Brothers Medical Publishers ltd, New Delhi, India. 2010;645.
32. Marshall HE, Hess DT, Stamler JS. S-nitrosylation: Physiological regulation of NF-κB. Proc. Natl. Acad. Sci. USA. 2004; 101:8841–8842.
33. Garkuwa UA, Wahab AA, Yusuf T, Buhari I, Adamu BY, Adamu GN, Ibrahim A, Ladan AA. Effect of Curcumin on liver enzymes and liver proteins in alloxan-induced diabetic wistar rats. The Pharmaceutical and Chemical Journal. 2018;5(3):130-134.
34. Harris EH.Elevated liver function tests in Type 2 diabetes. Clin Diabetes. 2005; 23:3.
35. Westerbacka J, Cornér A, Tiikkainen M, Tamminen M, Vehkavaara S, Häkkinen AM. Women and men have similar amounts of liver and intra-abdominal fat, despite more subcutaneous fat in women: Implications for sex differences in markers of cardiovascular risk. Diabetologia 2004;47:1360-9.

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