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Subacute Toxicity and Hepatoprotective Effects of *Sarcocephalus latifolius* in Alloxan 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

Various studies suggest that mortality due to liver disease in diabetic patients is very high; however, the recognition of DM as the primary cause of chronic liver disease is neglected in medical practice, we therefore evaluated the activities of *Sarcocephalus latifolius* leaf powder on the liver function of alloxan – induced diabetic rats. Forty-five healthy female albino rats were randomly assigned into 9 different groups; diabetes was induced intraperitonealy with 160 mg/kg of alloxan. Normal and diabetic rats were administered orally with 300, 600, 750 mg/kg/ b.w of *S. latifolius*. After 28 days, the animals were sacrificed for biochemical and histological studies.
The body weight of the normal and diabetic rats increased significantly with *S. latifolius* treatment, the increase observed in the blood glucose was brought down upon treatment with *S. latifolius* leaf powder. The activity of ALT increased significantly with 750 mg/kg of *S. latifolius* leaf powder, while

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low dose of the plant decreased it significantly in diabetic rats. GGT activity only decreased in the diabetic rats treated with 300 mg/kg of *S. latifolius* whereas albumin increased significantly ($p<0.05$) in all the groups administered *S. latifolius* powder relative to the untreated diabetic group. Bilirubin concentration only increased significantly ($p<0.05$) in the group administered 750 mg/kg of *S. latifolius* leaf powder. Histological changes including infiltration of the sinusoids and focal area by inflammatory cells and mild portal congestion were observed in all the groups except the normal and diabetic rats treated with 300 mg/kg of *S. latifolius* leaf powder. The result of the study showed that *S. latifolius* could only be encouraged for diabetes management only at low dose and might be hepatotoxic at high dose.

Keywords: Subacute toxicity; hepatoprotective; Sarcocephalus latifolius; alloxan; diabetics.

1. INTRODUCTION

Diabetes mellitus (DM) has been considered globally as one of the major health problem today. The prevalence of diabetes has been shown to be progressively on increase and prevalence of diabetes among adult is 8.5%, reaching 422 million adults in 2014, 9.3% (463 million people) in 2019 and possibly 578 million adults by 2030 [1,2]. Between 2019 and 2030, there will be 10.2% increase of diabetes prevalence in adults in high income and low income developing countries with higher prevalence in the high income countries [2]. WHO projects that diabetes will be the 7th leading causes of death in 2030 [3]. This suggests that studies must be carried out to provide adequate therapies and strategies to manage and curb the prevalence of the ongoing scourge.

Till date, the treatment regimen available for diabetes mellitus involves lifestyle modifications with diet and exercise and pharmacologic therapies as necessary to meet individualized glycemic goals. However, the available drug therapy does not provide an efficient control of blood glucose to avoid complications and no satisfactory effective therapy is yet available to cure DM [4]. The setbacks faced in presents anti-diabetic therapies call for innovative treatment therapies that are cheap, readily available, less toxic and effective compared to synthetic drugs. One dominant remedy for treating diabetes mellitus and other ailments in Nigeria is the use of medicinal plants by traditional medical practitioners. The use of herbal remedies and several indigenous plants in the preparation of herbs to cure any form of diseases, and sickness is on the rise [5]. One major medicinal plant used by traditional healers to remediate ailments in Nigeria is *Sarcocephalus latifolius. S. latifolius* (African peach) is one of the numerous plant species reported to have medicinal value. The plant is usually known as 'Africa cinchona' or 'Africa quinine' because of its reported anti-malarial activity [6]. Extract from various parts of *S. latifolius* was reported to have a wide range of medicinal properties and it is commonly used in the treatment of malaria, hypertension, diarrhea and dysentery and dental problems [7,8,9]. Studies have shown that extracts of various parts of *S. latifolius* have shown the presence of bioactive compounds such as; tannins, flavonoids, alkaloids, saponins and anthraquinones [10]. In this study, we aimed to evaluate the activities of *S. latifolius* leaf powder on the liver function of alloxan – induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Materials

Materials and instruments used throughout the study include: Plastic cages, drinkers, sanitizer, cotton wool, animal feeds, methylated spirits, paper tape, universal bottles, 5ml and 2ml syringe, stainless plates, surgical glove, sensitive weighing scale, accu check, distilled water, heparinized capillary tube, phosphate buffer solution, petri dish, scalpel, centrifuge, measuring cylinder.

2.2 Experimental Animals

Healthy female Wistar rats with average weight of 230 g, which have not been subjected to previous experimental activities, were used. Their weights were determined prior to feeding. The rats were acclimatized for 2 weeks. The experimental animals were housed in standard plastic cages and provided access to food and water ad-libitum.

2.3 Collection and Preparation of Plant

The plant *S. latifolius* was gotten and identified by a Taxonomist at the Department of Pure and Applied Biology, Ladoke Akintola University of Technology (LAUTECH) Ogbomoso, Oyo State.

The fresh leaves of *S. latifolius* were air dried for three weeks. It was pounded and later blended to powdered form. The leaves were sieved to get a complete powdery form. The plant powder was preserved in a desiccator until it was ready to use.

2.4 Animal Grouping

A total number of 45 female Wistar rats were randomly selected and divided into nine (9) different treatments groups, each groups comprises of 5 healthy animals.

Group A: the control group,
Group B: untreated diabetes mellitus group,
Group C: served as diabetes mellitus treated with 300mg/kg of *S. latifolius* powder,
Group D: served as non- diabetic rats treated with 300mg/kg of *S. latifolius* powder,
Group E: served as diabetes mellitus treated with 600mg/kg of the *S. latifolius* powder,
Group F: served as non- diabetic rats treated with 600 mg/kg of the *S. latifolius* powder,
Group G: served as diabetes mellitus treated with 750 mg/kg of *S. latifolius* powder,
Group H: served as non- diabetic rats treated with 750mg/kg of the *S. latifolius* powder,
Group I: served as diabetes mellitus treated with Metformin.

NB: Diabetes was induced by i.p administration of 150 mg/kg of alloxan to animals in cages B, C, E, G and I.

2.5 Experimental Design

At the end of the two weeks acclimatization, the animals were fasted overnight and groups B, C, E, G, and I were administered 150mg/kg of alloxan intra peritoneally. The fasting blood sugar (FBS) was determined 48 hours after induction, and animals with FBS ≥ 200mg/dl were considered diabetic. Upon diabetic induction**,** the animals were treated with *S. latifolius* leaf powder for a period of 28 days. Nadia et al*.* [10] had earlier reported the LD_{50} of the aqueous extract to be greater than 5000 mg/kg/b.w., therefore doses lower than the LD_{50} were selected in this study. Regular monitoring of weight was ensured throughout the experiment and the weights were recorded in grams. In addition, the FBS was determined prior animal sacrifice.

2.6 Blood Collections

At the end of the 28 days treatment, the animals were fasted overnight and sacrificed by cervical dislocation. The blood samples were collected through retro-orbital process into sterile plane bottles and allowed to clot. Samples were centrifuged at 4000 rpm for 5 minutes to obtain the serum. The liver was excised and preserved in formalin buffer for histological examination.

2.7 Biochemical Analysis

Aspartate transaminase (AST), alkaline phosphatase (ALP), and alanine aminotransferase (ALT) were assayed by means of reagent kits of the Randox Laboratories Ltd, UK. All the analyses were colorimetric and carefully performed according to the specifications of the manufacturer. Serum ALP assay procedure was described by Wright et al*.* (1970), whereas ALT and AST assays were described by Reitman and Frankel [11]. Absorbance was read for ALP, ALT and AST at 405 nm, 550 nm and 546 nm respectively. Bilirubin was assayed by it reaction with diazotized sulphanilic acid [12].

Determination of GGT was carried out following the method described by Szasz (1968). The principle was based on the conversion of substrate; L- gamma - glutamyl- 3- carboxy – 4 nitroanilide, in the presence of glycylglycine to 5-amino-2-nitrobenzoate by gamma- GGT in the sample which was then measured at 405 nm.

2.8 Histology Examination of the Liver

The histological procedure was carried out by the method described by Biswas *et al*. (2010) with some modifications. The Liver from both the treated and control groups was processed with automatic tissue processor (STP 120) by tissue processing method as described by Galen and Gambino (1975). Histology preparation was done in 4 µm tissue sections with a Microtome (Leica, RM 2145). These sections were then de-paraffinated in xylene, dehydrated through a graded ethanol series, and stained with haematoxylin and cleared in xylene I and xylene II and these organs were preserved for microscopic examination. The slides prepared by this process were observed under microscope (Model Nikon Labophot. 223425 Japan) and photographed through Nikon labophot Advanced Research Microscope, Model 223425 Japan, with Sony Digital 12.1 MEGA PIXELS.

2.9 Data Analysis

Data obtained are expressed as Mean ± Standard error of mean. The data was subjected

to one-way analysis of variance (ANOVA) and differences between means were determined using the Graph Pad Prism 5 (Graph Pad Software Inc., San Diego, CA). The level of significance was set at $p<0.05$.

3. RESULTS

3.1 Effect of *S. latifolius* Leaf Powder on Body Weight in Alloxan- induced Diabetic Female Wistar Rats

Fig. 1 shows the effect of *S. latifolius* leaf powder on body weight in alloxan- induced diabetic female wistar rats. Before the induction of diabetes, the body weights of the rat were of no significant differences. However, after the induction of diabetes, there was a significant ($p<0.05$) decrease in the body weight of the all the diabetic groups except the control group. The administration of *S. latifolius* leaf powder at doses, of 300mg/kg b.w, 600mg/kg b.w and 750mg/kg b.w to the diabetic rats significantly ($p<0.05$) increased the body weight. Significant ($p<0.05$) decrease in weight was however observed in the metformin group despite metformin intervention upon diabetes induction.

3.2 Effect of *S. latifolius* Leaf Powder on Blood Glucose Level in Diabetic Induced Female Wistar Rats

Fig. 2 illustrate the effect of *S. latifolius* leaf powder on the blood glucose level in diabetic female wistar rats. There was no significant difference ($p<0.05$) in the blood glucose level of rat before the induction of diabetes. However, after the induction, glucose level increased significantly ($p<0.05$) in DM, DM+EX (300 mg/kg), DM+EX (600 mg/kg), DM +EX (750 mg/kg), and Metformin (500 mg/kg) groups. The administration of *S. latifolius* leaf powder at doses 300mg/kg, 600 mg/kg, 750 mg/kg body weight cau sed significant decrease ($P<0.05$) in the blood glucose levels of the powder treated groups. These effects surpassed the metformin group.

3.3 Effect of *S. latifolius* Leaf Powder on Alanine Aminotransferase (ALT) Activity in Diabetic Female wistar Rats

Fig. 3 illustrate the effect of *S. latifolius* leaf powder on alanine aminotransferase (ALT) activity in diabetic female Wistar rats. There was a significant ($p<0.05$) increase ($P<0.05$) in the alanine aminotransferase activity of the DM group when compared to the control group. However, the administration of *S. latifolius* leaf powder at 300 and 750 mg/kg b.w caused significant ($p<0.05$) decrease ($P<0.05$) in the alanine aminotransferase activity of diabetic rats. The ALT activity when normal rats were administered 750 mg/kg b.w *S. latifolius* leaf powder increased significantly ($p<0.05$) when compared with the normal control group whereas the activity varied insignificantly ($p>0.05$) when the leaf powder was administered to normal rats at 300 mg/kg and 600 mg/kg.

3.4 Effect of *S. latifolius* Leaf Powder on Aspartate Transaminase (AST) in Diabetic Rats

Fig. 4 illustrate the effect of *S. latifolius* leaf powder on aspartate transaminase (AST) activity in diabetic rats. The DM only group showed significant ($p<0.05$) increase in the activity of aspartate aminotransaminase when compared with the control group. However, after the administration of the plant powder at all doses and metformin, there was significant ($p<0.05$) decrease in the aspartate aminotransaminase activity. Similarly, no significant ($p>0.05$) increase was observed in the AST activity of the rats administered 300, 600 and 750 mg/kg body weight of *S. latifolius* leaf powder when compared with the control group.

3.5 Effect of *S. latifolius* Leaf Power on Gamma Glutamyltransferase (GGT) Activity in Diabetic Female Wistar Rats

Fig. 5 illustrate the effect of *S. latifolius* leaf power on gamma glutamyltransferase (GGT) activity in diabetic female wistar rats. There was a significant increase ($P<0.05$) in the activity of gamma glutamyltransferase of the DM group when compared to the control group. The administration of metformin and 300 mg/kg b.w, *S. latifolius* leaf power significantly decreased ($P<0.05$) the gamma glutamyltransferase activity of diabetic rats whereas, no significant ($p>0.05$) difference was observed in the other groups except the normal rats group administered 750 mg/kg b.w, when compared with the untreated diabetic group.

3.6 Effect of *S. latifolius* Leaf Powder on Albumin Level in Diabetic Female Rats

Fig. 6 illustrate effect of *S. latifolius* leaf powder on the level of albumin in diabetic female rats.

There was significant a decrease (P<0.05) in the albumin levels of the DM group when compared to the control and the treated groups. The administration of *S. latifolius* leaf powder at 300mg/kg b.w, 600mg/kg b.w, 750mg/kg b.w to both the diabetic and normal rats significantly increased (P<0.05) this albumin levels in the experimental rats.

3.7 Effect of *S. latifolius* Leaf Powder on Bilirubin Level in Diabetic Female Wistar Rats

Fig. 7 showed the effect of *S. latifolius* leaf powder on bilirubin levels in diabetic female wistar rats. There was a significant increase (P<0.05) in the bilirubin levels of the DM group when compared to the control group. However, the administration of *S. latifolius* leaf powder at doses, 300mg/kg b.w, and 600mg/kg b.w, significantly (P<0.05) decreased the bilirubin concentration when compared to the diabetic untreated group. The leaf powders at 750 mg/kg b.w significantly (p<0.05) increased the concentration of bilirubin in the diabetic and normal rats.

3.8 Effect of *S. latifolius* Leaf Powder on Histomorphology of the Liver in Alloxan-Induced Diabetic Female Rats

Fig. 8a-I is the representative liver photomicrograph of diabetic and normal rats treated with metformin and leaf powder of *Sarcocephalus latifolius*. Different morphological changes observed in the liver are indicated with arrows and reported in the legend.

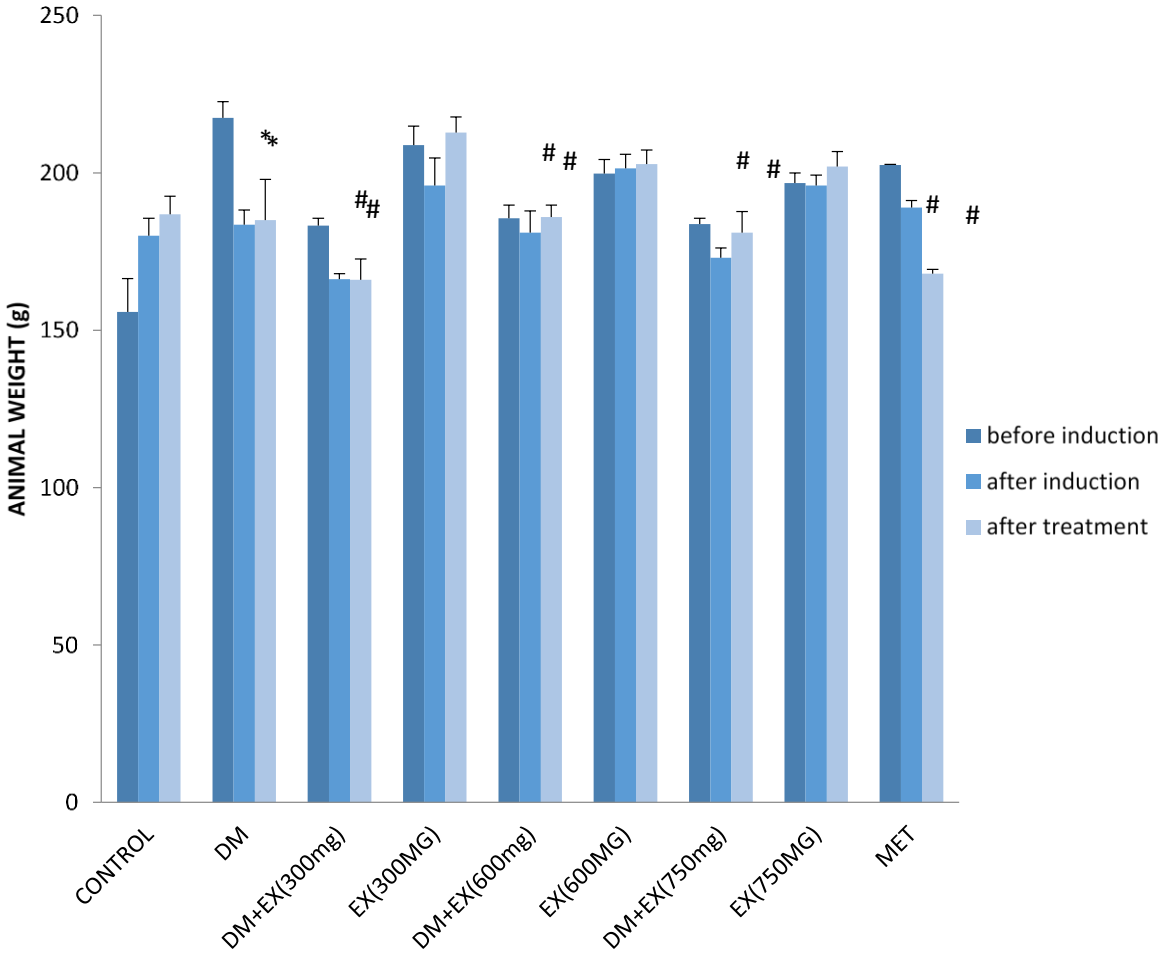

Fig. 1. Effect of *S. latifolius* leaf powder on body weight of diabetic female wistar rats. * represent insignificant different, # represent significant difference

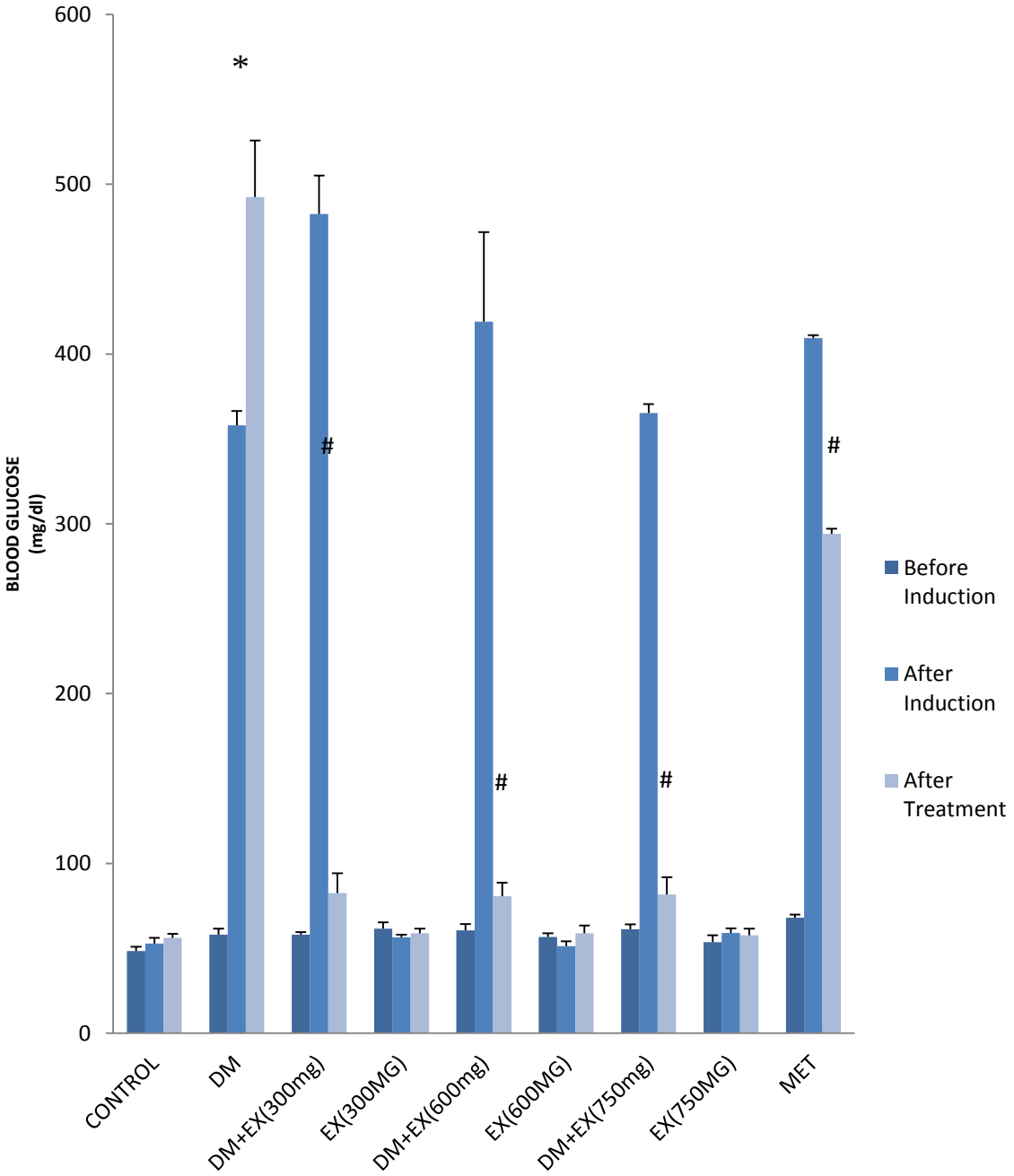

Fig. 2. Effect of *S. latifolius* leaf powder on blood glucose test in type 1 alloxan- induced diabetic female wistar rats. *- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group.

KEYS: DM: untreated diabetes mellitus group,DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder, EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder, MET: diabetes mellitus treated with Metformin

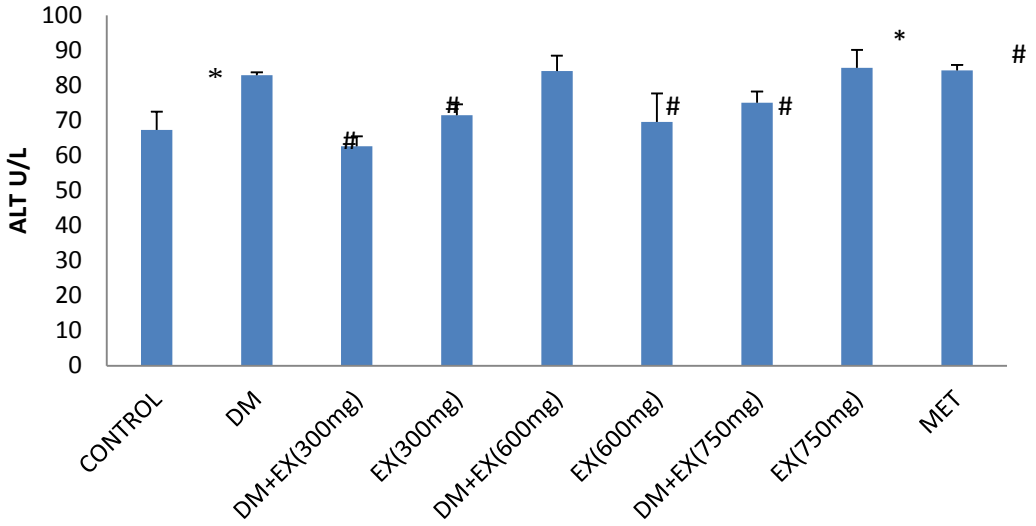

Fig. 3. Effect of *S. latifolius* leaf powder on alanine aminotransferase (ALT) in type 1 alloxan-induced diabetic female wistar rats

**- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group. KEYS: DM: untreated diabetes mellitus group, DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder, EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder, MET: diabetes mellitus treated with Metformin*

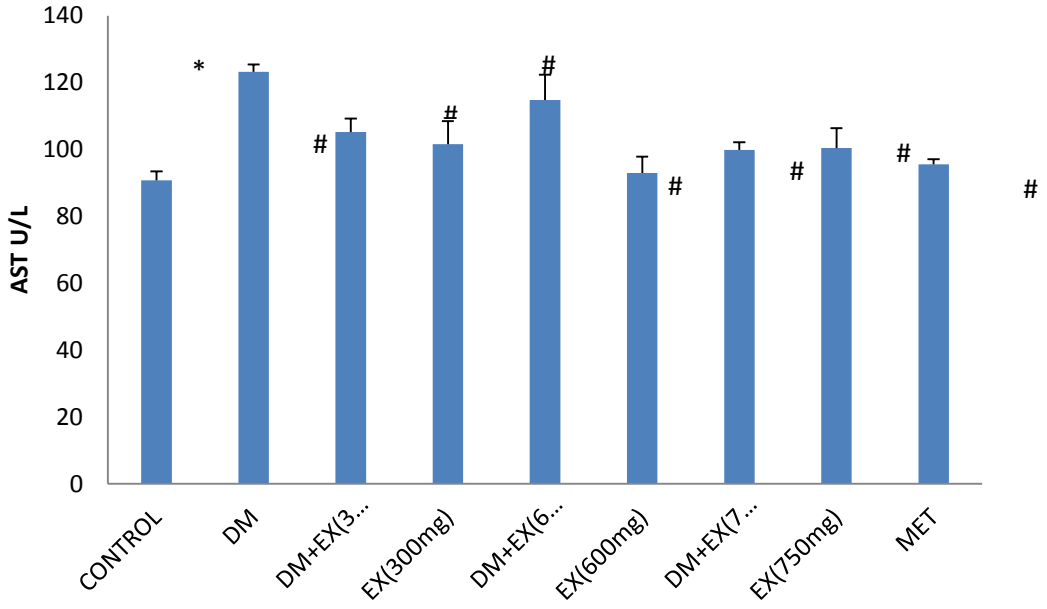

Fig. 4. Effect of *S. latifolius* leaf powder on aspartate transaminase (AST) in type 1 alloxan-induced diabetic rats

**- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group. KEYS: DM: untreated diabetes mellitus group, DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder, EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder, MET: diabetes mellitus treated with Metformin*

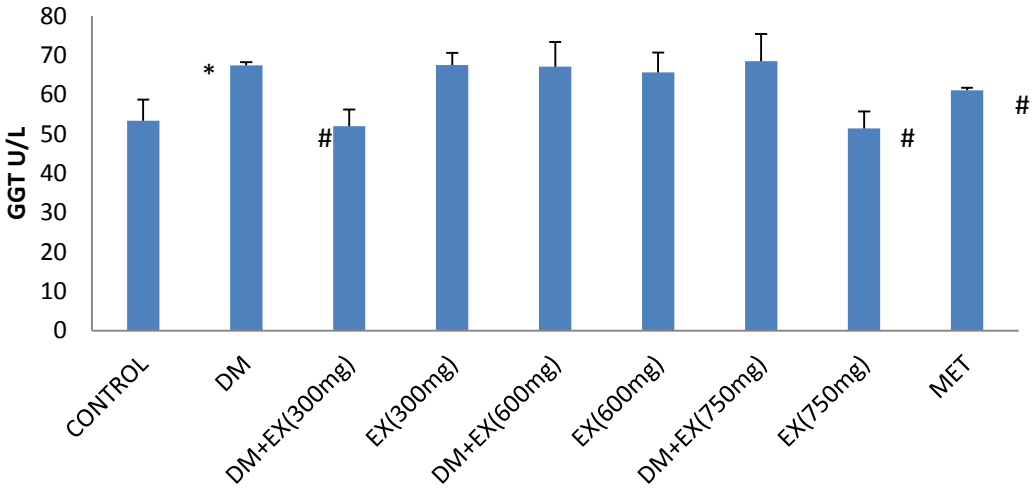

Fig. 5. Effect of *S. latifolius* leaf power on gamma glutamyltransferase (GGT) activity in diabetic female wistar rats

**- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group.*
KEYS: DM: untreated diabetes mellitus group, DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder, MET: diabetes mellitus treated with Metformin

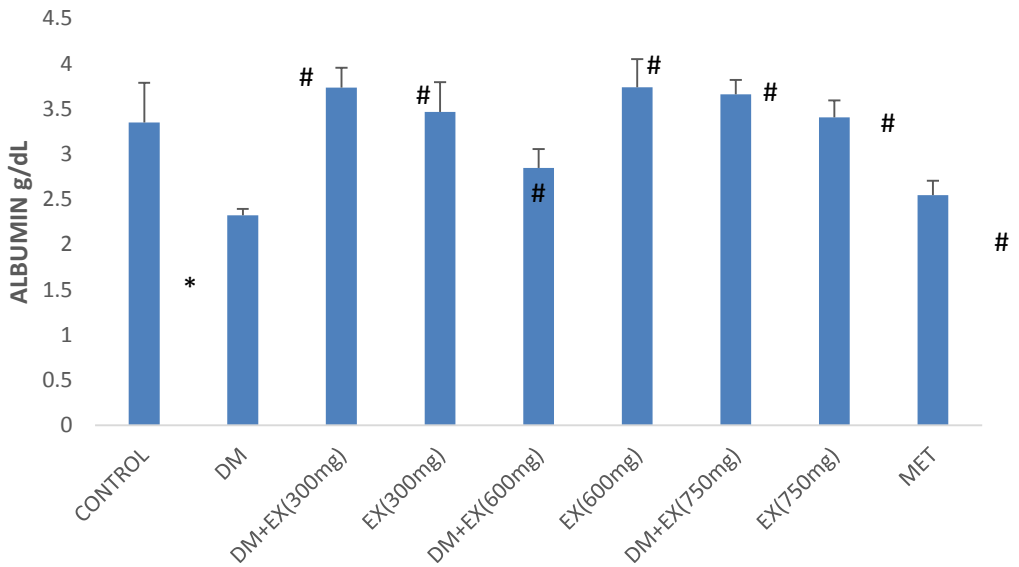

Fig. 6. Effect of *S. latifolius* leaf powder on albumin in diabetic female rats

**- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group.*
KEYS: DM: untreated diabetes mellitus group, DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder, EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder,
MET: diabetes mellitus treated with Metformin

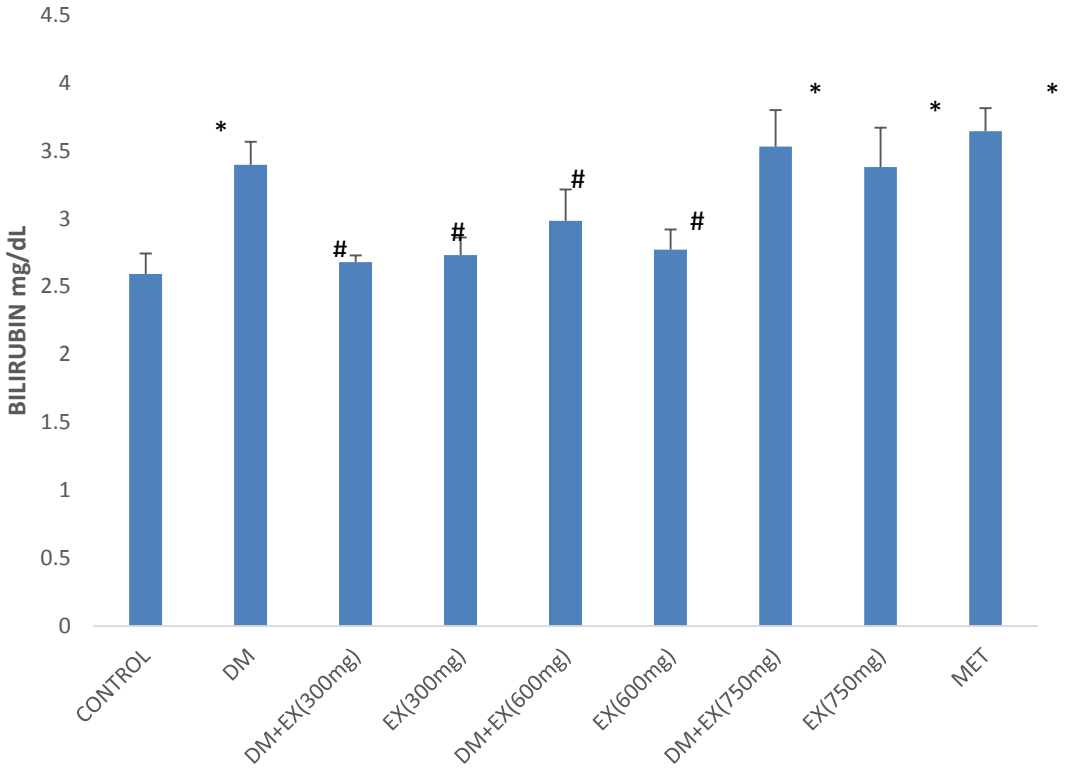

Fig. 7. Effect of *S. latifolius* leaf powder on bilirubin in type1 alloxan- induced diabetic on female wistar rats

**- significant at p<0.05 compared with control, #- significant at p<0.05 compared with DM group.*
KEYS: DM: untreated diabetes mellitus group, DM + EX(300 mg): diabetes mellitus treated with 300mg/kg of S. latifolius powder EX (300mg): normal rats treated with 300mg/kg of S. latifolius powder, DM + EX (600 mg): diabetes mellitus treated with 600mg/kg of S. latifolius powder, EX (600 mg normal rats treated with 600 mg/kg of the S. latifolius powder, DM + EX (750 mg): diabetes mellitus treated with 750mg/kg of S. latifolius powder, EX (750 mg): normal rats treated with 750mg/kg of the S. latifolius powder, MET: diabetes mellitus treated with Metformin

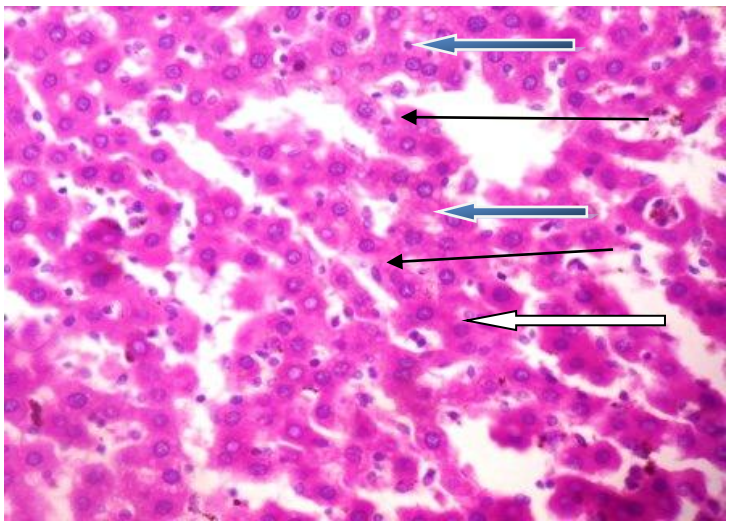

Fig. 8a. Control Group×400

Photomicrograph of a liver section stained with Haematoxylin and Eosin showing normal central venules without congestion (white arrow) , the morphology of the hepatocytes appear normal (blue arrow), the sinusoids appear normal and not infiltrated (slender arrow),no pathological lesion seen

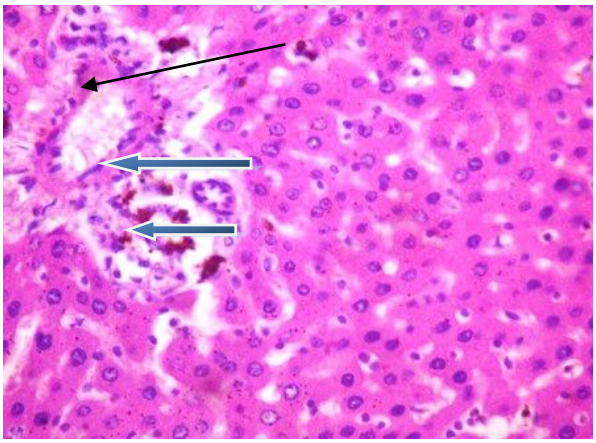

Fig. 8b. Untreated DM ×400

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules, normal portal tract,, the sinusoids show mild infiltrates and focal area of mild aggregate of nflammatory cells (slender arrow) and mild portal congestion (blue arrow)

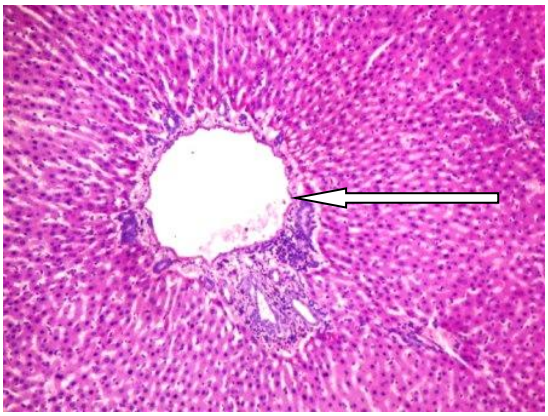

Fig. 8c. DM treated with extract 300mg/kg×400

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules without congestion (white arrow) and portal tract with very mild periportal infiltration of inflammtory cells , the morphology of the hepatocytes appear normal, the sinusoids appear normal and not infiltrated

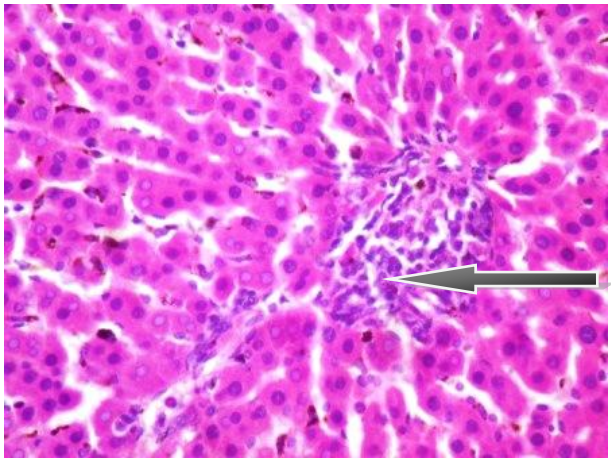

Fig. 8d. Extract only 300mg/kg

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules without congestion, the morphology of the hepatocytes appear normal, the sinusoids appear normal and not infiltrated, very mild aggregate of inflamatory cells seen (black arrow)

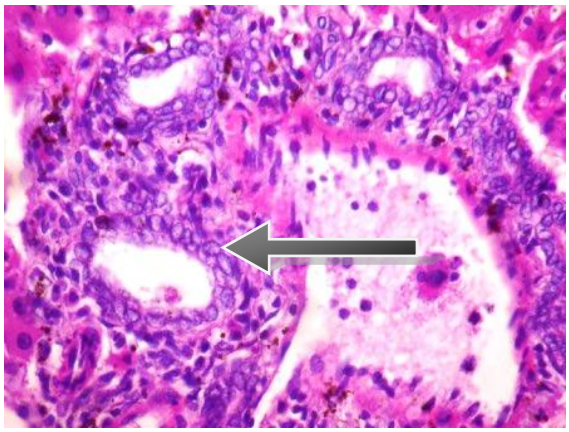

Fig. 8e. DM treated with extract 600mg/kg×400

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules without congestion, the portal tract show mild infiltration of inflammatory cells with bile duct cells hyperplasia (black arrow), the morphology of the hepatocytes appear normal, the sinusoids appear normal and not infiltrated

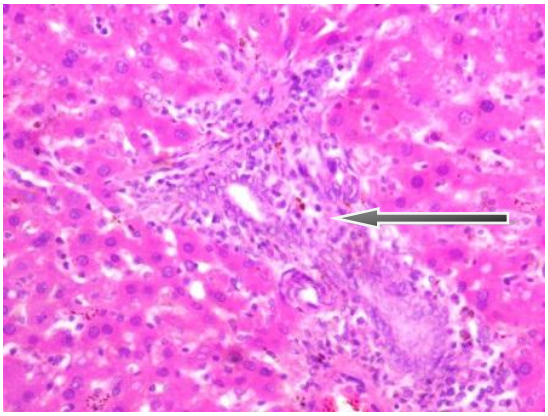

Fig. 8f. Extract only 600mg/kg×400

Photomicrograph of a liver section stained by Haematoxylin and Eosin showing mild to moderate portal triditis; there is moderate periportal infiltration of inflammatory cells (black arrow), the sinusoids is moderately dilateed and infiltrated by inflammatory cells

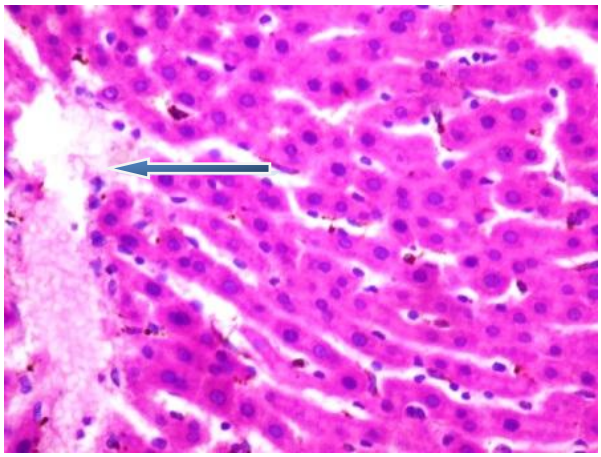

Fig. 8g. DM treated with extract 750mg/kg×400

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules without congestion, the morphology of the hepatocytes appear normal (blue arrow), the sinusoids appear normal and not infiltrated, no pathological lesion seen

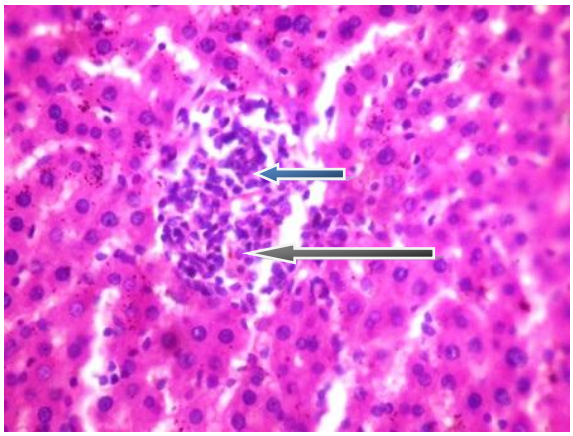

Fig. 8h. Extract only 750mg/kg×400

A Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal morphology of the hepatocytes(blue arrow), the sinusoids show mild infiltrates and focal area of mild aggregate of nflammatory cells (black arrow)

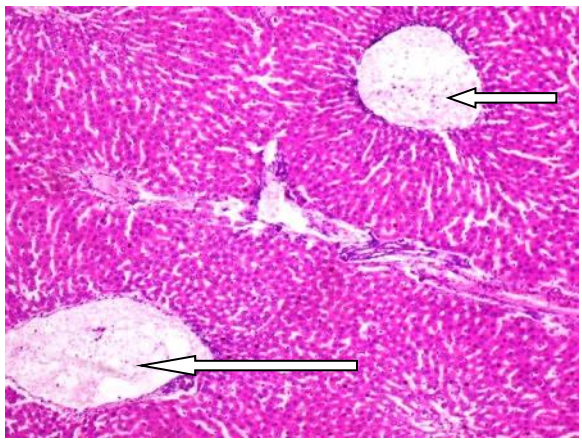

Fig. 8i. DM treated with metformin 150mg/kg

Photomicrograph of a liver section stained by Haematoxylin and Eosin showing normal central venules without congestion (white arrow), mild portal congestion the morphology of the hepatocytes appear normal, the sinusoids appear normal and not infiltrated

4. DISCUSSION

The liver is the master organ for carbohydrate metabolic homeostasis and releases glucose according to metabolic needs. Recently, liver damage has been documented as one of the major complication of diabetes mellitus. Indeed, various studies suggest that mortality due to liver disease in diabetic patients is very high; however, the recognition of DM as the primary cause of chronic liver disease is neglected in medical practice [13]. Though several pathways have been identified for liver damage, insulin resistance is the main cause because of oxidative stress and increased production of ROS [14]. Insulin resistance causes severe hyperglycemia, which has been associated with diabetic complication. In this present study, we aimed to evaluate the effects of *Sacrocephallus latifolius* leaf powder on liver function of alloxan-induced diabetic rats.

Alkaline phosphatase (ALP), aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and bilirubin are useful biomarkers of liver injury in humans and animals. Specifically, some of the biomarkers (e.g., albumin, globulin and total protein) are associated with functionality, while some with cellular integrity (e.g. transaminase); in addition, some are linked to the biliary tract (bilirubin, gammaglutamyl transferase (GGT), Lactate dehydrogenase (LDH) and alkaline phosphatase [15].

Alloxan as a potent chemical commonly used for the induction of diabetes produces hepatotoxicity

as an interlinked mechanism, which is visualized as elevated levels of ALP, ALT, and AST. Hepatic damage is characterized by elevation in serum liver enzymes viz ALT, ALP and AST. AST and ALT are the most common because they are readily released into the extracellular space by the hepatocytes (Ozer *et al.,* 2008). Thus, the high levels of AST, ALT and ALP observed in this study (Figs. 1-7) indicates hepatoxic effect of alloxan. However, restoration of these biomarkers to normal level by low dose of *Sacrocephalus latifolius* powder indicates possible amelioration of hepatic damage, which is attributable to the antidiabetic effects of the *Sacrocephalus latifolius* demonstrated in this study and previously reported by Orwa et al. [16]. In addition, our observations clearly indicate the possible hepatotoxicity of *Sacrocephalus latifolius* at high dose since the levels of the biomarkers assessed were elevated. In a previous study, the toxicity of the aqueous leaf extract was reported. According to the study, ALP, AST and ALT activities were significantly elevated while the morphology of the liver was gravely altered [17].

5. CONCLUSION

Although *Sacrocephalus latifolius was* effective in lowering the blood sugar in diabetic rats, its use for the management of diabetes might be accompanied with some deleterious effects on the liver integrity specifically when used at high dose. Summarily, the use of the plant could be encouraged for diabetes management since it was effective at lower dose without necessarily inflicting any damaging effect on the liver.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

NOTE

The study highlights the efficacy of "herbal remedies“ which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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