



# ***Brillantasia patula* Aqueous Leaf Extract Averts Hyperglycemia, Lipid Peroxidation, and Alterations in Hematological Parameters in Alloxan-Induced Diabetic Rats**

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**Abstract:** The protective effects of aqueous leaf extract of *Brillantasia patula* against hyperglycemia, lipid peroxidation, and alterations in hematological parameters in diabetic Wistar rats were investigated. The study consisted of six treatment groups, with five animals each, designated as Group-1 (healthy), Group-2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kgbw of extract, respectively). Rats were administered their respective doses orally, and daily, for 14 days. Thereafter, the effects on serum glucose levels, liver and kidney functions, lipid peroxidation, free radical scavenger and hematological parameters were analyzed. Blood glucose levels reduced markedly in diabetic rats given the plant extract relative to diabetic control. Both serum creatinine and urea decreased significantly in treated diabetic rats at extract doses of 1000 mg/kgbw and above. Reductions in serum cholesterol ( $p < 0.05$ ) and triglyceride levels ( $p < 0.05$ ) were also observed. Elevated total serum protein and globulin in diabetic control was decreased in all treated groups. Haematological indices of groups given the extract were noticeably enhanced. Similarly, kidney, heart and liver glutathione (GSH) levels increased significantly in groups treated compared to diabetic control; lipid peroxidation in kidney and heart also decreased significantly in all the treated groups. Liver catalase activity improved. Serum alanine and aspartate aminotransferases activities widely lowered in Groups 3 and 4. The study indicates that *Brillantasia patula* aqueous leaf extract exhibits potential hypoglycemic effect, prevents lipid peroxidation, boosts haematological parameters, and could protect liver and renal damage associated with diabetes especially at doses of 500 - 1000 mg/kgbw.

**Keywords:** Diabetes Mellitus, *Brillantasia patula*, Hypoglycemic Effect, Lipid Peroxidation, Antioxidants, Haematological Indices

## **1. Introduction**

Diabetes mellitus is a group of heterogeneous, autoimmune, hormonal, metabolic, hyperlipidaemia and obesity disease [1]. It is typified by inappropriate high blood glucose level caused by complete or relative deficiency of insulin or resistance to the action of insulin caused by receptor cells. It can be categorized into two: Type 1 (insulin

deficiency) and Type 2 (insulin receptor cells not active) [2]. It is also characterized by elevated total or low density lipoprotein (LDL) cholesterol in the blood, polyuria, albuminuria, renal enlargement and a rise in serum creatinine [3].

Different plants extracts have been used in the management of many different illnesses [4, 5] and many of these plant species have been demonstrated to have hypoglycemic effect [6]. Many indigenous plants, shrubs, herbs, twigs and leafy vegetables are taken as food, spices or

used in medicinal purposes in Nigeria [7]. Evaluation of the efficacy of plants in areas where there is no availability of safe modern drugs has also been advocated [8].

The use of plants in the management of diseases lies on their chemical compositions which give unique physiological roles in the human body [9]. The active components of most plants are tannin, flavonoid, alkaloids, phenol compounds, saponin, glycoside, anthraquinones etc [10]. Phytochemicals isolated from plant sources are used for the prevention and treatment of cancer, heart disease, diabetes mellitus and high blood pressure [11]. *Brillantasia patula* is a medicinal plant used for animals in Africa. *B. patula* belongs to the family Acanthaceae; it is a shrubby plant of about 3m height and can be found in Nigeria, Togo, West Cameroun and across Uganda and Angola. Yaws and rheumatism have also been treated with the leaves of this herb. The decoction is taken to ease childbirth, menstrual pain and stomach ache. It is reported to have anti-plasmodial and analgesic potentials [12].

In this study, we investigated the protective effects of aqueous leaf extract of *Brillantasia patula* against hyperglycemia, lipid peroxidation, and alterations in haematological parameters in alloxan-induced diabetic Wistar rats.

## 2. Materials and Methods

### 2.1. Experimental Animals

Female wistar rats that weighed 88 -206 g and thirty in number were used in this study. They were bred in the animal house of African Research Laboratory, Isiokolo, Delta State. They were kept in constructed cages with wire gauze under control condition of 12 light/12 dark cycle. The animals were fed *ad libitum* on water and growers mash obtained from Top feeds, Sapele, Delta State. All the experimental animals were taken care of in line with the principles of the National Institutes of Health (NIH Publications No. 8023, revised 1978).

### 2.2. Chemicals

Alloxan monohydrate used for this study was obtained from Alpha Chimika, Mumbai, China. All other reagents used were of standard quality also.

### 2.3. Induction of Diabetes in Experimental Rats

Rats were fed normal feed and water for one week after which they were fasted for 12 hr before intraperitoneal injection of a dose of 120 mg/kg body weight of alloxan monohydrate [1]. Blood collected from tail reins was used to confirm diabetes induction using a glucometer (EasyGluco®, US Diagnostics). The level of random blood glucose considered to be normal in albino rats ranges from 70-140 mg/dl. Rats with glucose level above 200 mg/dl were considered as diabetic.

### 2.4. Experimental Procedure

Leaves of *Brillantasia patula* were obtained at Ovu-Inland,

Ethiopia East Local Government Area, Delta State. They were carefully identified and authenticated at the Botany Department of the University of Benin, Benin city. The study consisted of six treatment groups, with five animals each, designated as Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). Rats were given their apportioned doses orally, and daily, for a period of 14 days. After which the effects on serum glucose levels, liver and kidney functions, lipid peroxidation, free radical scavenger and hematological parameters were analyzed.

### 2.5. Preparation of Serum

Rats were sacrificed by cervical decapitation and blood was collected from the rats using syringe and EDTA container. This was allowed to clot and serum was stored at -20°C in the refrigerator until they are requested for use.

### 2.6. Preparation of Tissue Homogenate

0.5 g of kidney, liver and heart was separately homogenized in 4.5 ml of normal saline and centrifuged for 10 min at 4000 g. The supernatants got were then stored at 4°C until needed for use.

### 2.7. Biochemical Assays

Total cholesterol, triglyceride, reduced glutathione and lipid peroxidation (malondialdehyde level) were assayed according to the method explained by Allain et al. [13], Fossati and Prencipe [14], Nakamura et al [15], and Deniz et al [16], respectively. The serum was used for the assay of alanine aminotransferase (ALT), aspartate aminotransferase (AST) as well as determination of total protein, creatinine, urea, haemoglobin (Hb) concentration, packed cell volume (PCV) and catalase activity were determined by the methods outlined by Reitman and Frankel [17], Lyne [18], Bartels et al. [18], Palton et al [19], Cheesbrough [20] and Aebi [21], respectively.

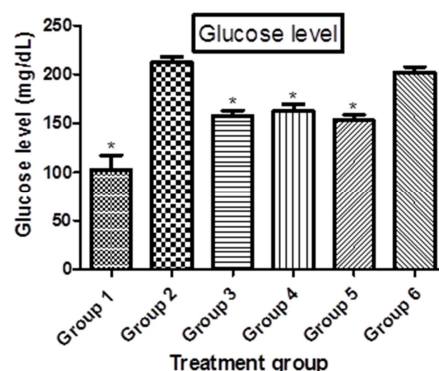
### 2.8. Statistical Analysis

Statistical analysis was done using one-way analysis of variance (ANOVA) and comparison of mean values was done by Dunnet's post hoc test, using GraphPad Prism 5.0 software. Values of  $p < 0.05$  were taken significant. Results were expressed as mean  $\pm$  SD.

## 3. Results

### 3.1. Effect of *B. patula* Aqueous Extract on Blood Glucose Levels

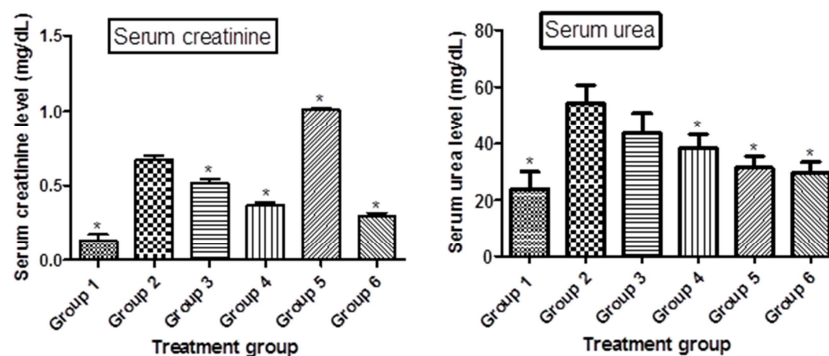
Blood sugar levels significantly increased ( $p < 0.05$ ) in the diabetic rats without treatment (Group2) and significantly decreased ( $p < 0.05$ ) upon administration of the different concentrations of the plant's aqueous extract when matched with the diabetic control (group 2) (Figure 1).



**Figure 1.** Random blood glucose level (mg/dl) in diabetic rats treated with *Brillantasia patula* aqueous extract. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

### 3.2. Effect of *B. patula* Aqueous Extract on Kidney Function

A significant reduction in serum creatinine levels was observed in group 3, 4 and 6 (lowest) while a significant increase ( $p < 0.05$ ) in group 5 (highest) was observed when compared with group 2 (Figure 2). The urea levels significantly decreased ( $p < 0.05$ ) in all groups treated with the aqueous extract when compared with the diabetic rats (Group 2) (Figure 2).

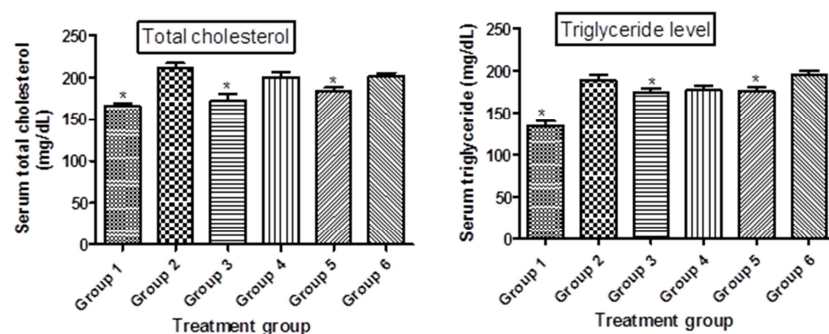


**Figure 2.** Effect of *Brillantasia patula* aqueous leaf extract on serum creatinine (mg/dl) and serum urea concentrations (mg/dl) of alloxan-induced diabetic rats. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

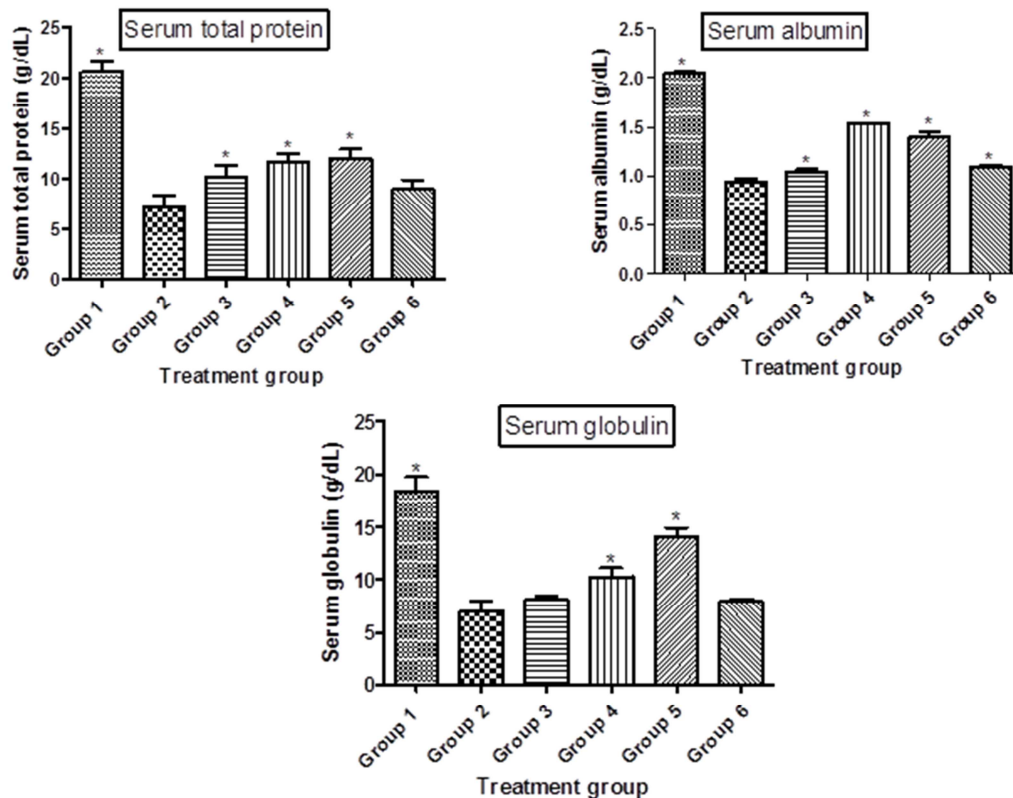
### 3.3. Effect of *B. patula* Aqueous Extract on Lipid Profile and Soluble Protein

There was a reduction in triglyceride levels in groups 3, 4 and 5 when compared with the diabetic control (group 2); triglyceride level, however, increased ( $p < 0.05$ ) in group 6 rats (Figure 3). Whereas there was significant decrease ( $p < 0.05$ ) in cholesterol levels groups 3 and 5 animals,

decrease in serum cholesterol levels observed in groups 4 and 6 animals was not significant when compared to the diabetic control ( $p > 0.05$ ). The aqueous extract markedly reduced ( $p < 0.05$ ) serum total protein in all the treated groups when compared with the diabetic control. Similar trend was revealed by the result of serum concentrations of albumin and globulin (Figure 4).



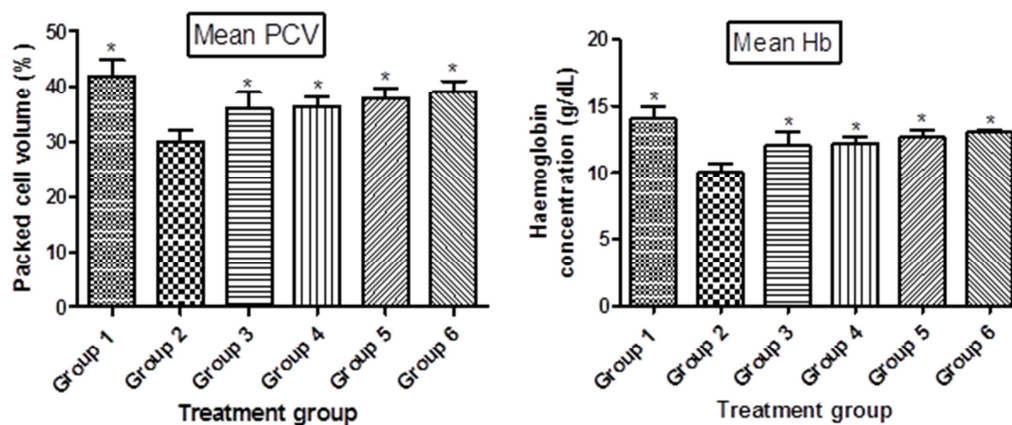
**Figure 3.** Effect of *Brillantasia patula* aqueous leaf extract on serum triglyceride and total cholesterol level (mg/dL) of alloxan-induced diabetic rats. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.



**Figure 4.** Effect of aqueous leaf extract of *Brillantaisia patula* on serum total protein, serum globulin and serum albumin levels in diabetic experimental rats. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

### 3.4. Effect of *B. patula* Aqueous Extract on PCV and Hb

The result of packed cell volume (PCV) shown in Figure 5 revealed that there was a significant increase in PCV in all the groups given the extract in comparison with group 2, the diabetic control ( $p < 0.05$ ). There was also an increase in haemoglobin concentration in diabetic rats treated with the plant extract when compared with group 2, the diabetic control ( $p > 0.05$ ).



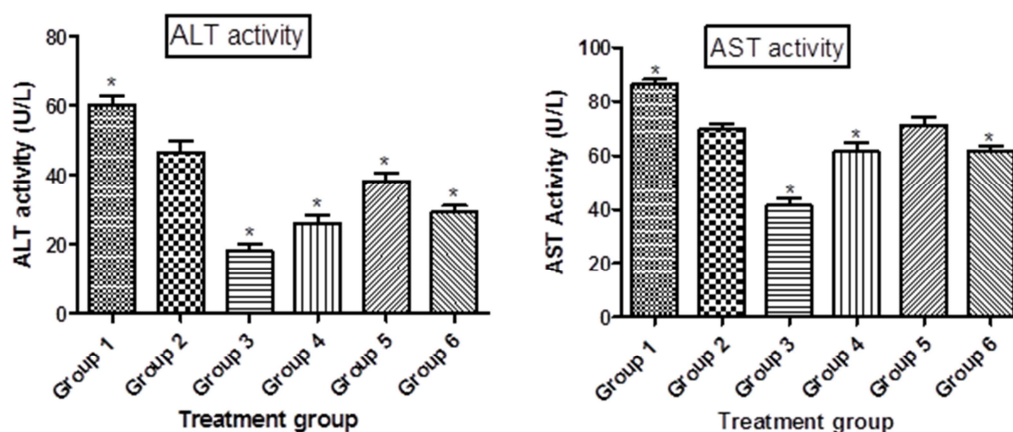
**Figure 5.** Packed cell volume (%) and haemoglobin concentrations (g/dL) in diabetic experimental rats treated with aqueous leaf extract of *Brillantaisia patula*. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

### 3.5. Effect of *B. patula* Aqueous Extract on Liver Function

The result of serum alanine aminotransferase (ALT) revealed that all treated groups showed significant reduction in the activity of ALT when juxtaposed with the positive

diabetic control ( $p < 0.05$ ) (Figure 6). Aspartate aminotransferase (AST) activity was also significantly reduced in groups 3, 4 and 6 while there was no significant difference in the activity of AST in group 5 when compared with the diabetic control ( $p > 0.05$ ).



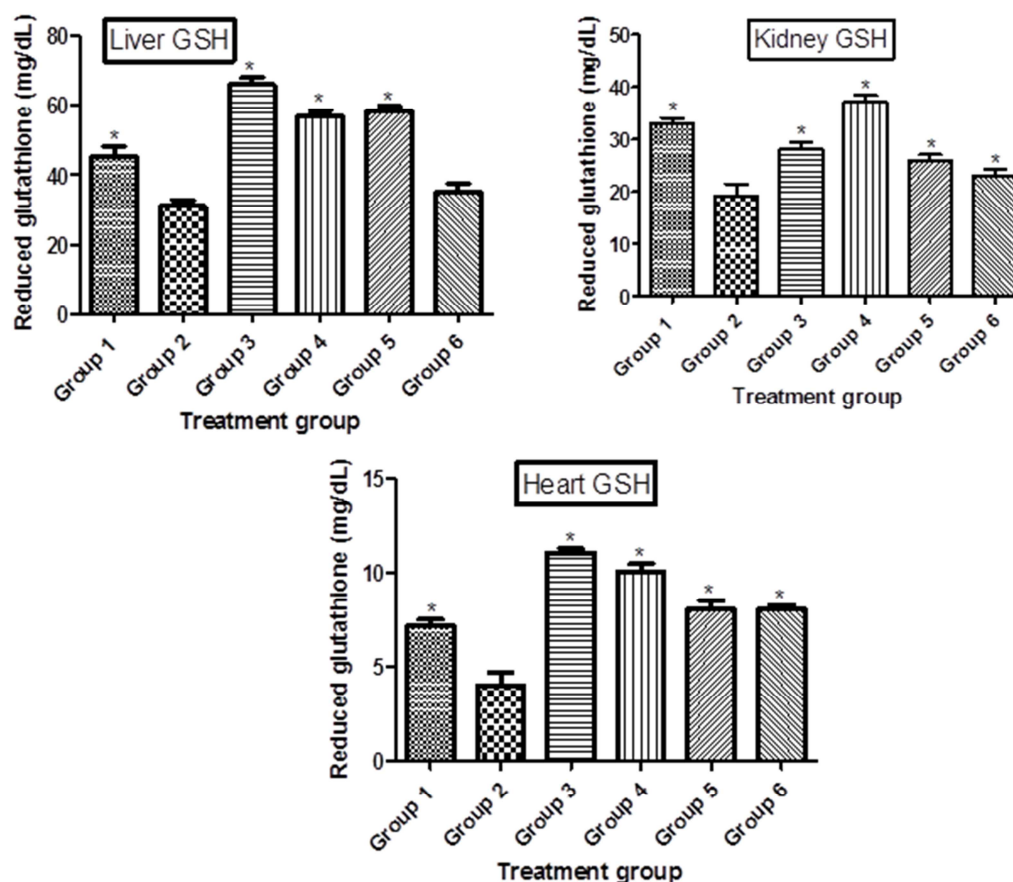


**Figure 6.** Effect of aqueous leaf extract of *Brillantasia patula* on serum alanine transaminase (ALT) and aspartate transaminase (AST) in diabetic experimental rats. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

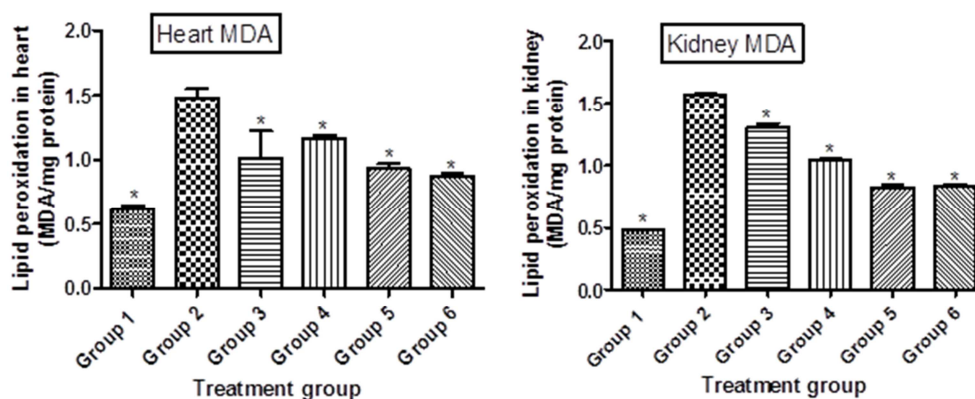
### 3.6. Effect of *B. patula* Aqueous Extract on Antioxidant Status of Rats

Increase in reduced glutathione levels (Figure 7) in the heart was observed in all the groups given the extract when matched with the diabetic positive control (group 2). A similar trend in glutathione level was also seen in that of the kidney and liver (Figure 7). The results of heart and kidney

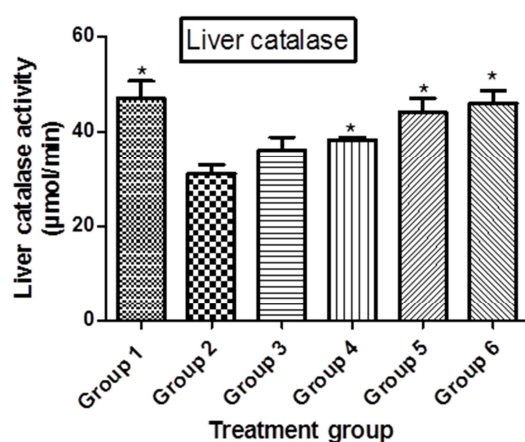
malondialdehyde (MDA) levels (Figure 8) revealed a marked reduction ( $p < 0.05$ ) in the levels of heart MDA in all the groups given the extract when matched with both negative control (group 1) and positive control (group 2). Significant increase was observed in liver catalase activity in animals in groups 4, 5 and 6 when compared with the diabetic control, but not in groups 3 (Figure 9).



**Figure 7.** Levels of reduced glutathione (mg/dL) in liver, kidney and heart tissues of diabetic experimental rats treated with aqueous leaf extract of *Brillantasia patula*. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.



**Figure 8.** Protective effect of aqueous leaf extract of *Brillantaisia patula* against lipid peroxidation in diabetic experimental rats. MDA, Malondialdehyde. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.



**Figure 9.** Catalase activity ( $\mu\text{mol/min}$ ) in liver of diabetic experimental rats treated with aqueous leaf extract of *Brillantaisia patula*. Group 1 (healthy control), Group 2 (diabetic control) and Groups 3-6 (diabetic rats treated with 500, 1000, 1500, and 2000 mg/kg bwt of aqueous extract of *B. patula*, respectively). \*Significantly differs from the diabetic control (Group 2) at  $P < 0.05$  using Dunnet's post hoc test.

## 4. Discussion

Diabetes is a non-communicable disease that affects large population of the world and is characterized primarily by elevated blood glucose (hyperglycemia) caused as a result of very little or deficiency of insulin, or when insulin receptors in the body do not respond appropriately to the presence of insulin [22, 23]. Alloxan has been reported severally to cause destruction of the B cells that are involved in the synthesis of insulin in the pancreas leading to an elevation of glucose level in the blood [24]. In this study, a marked rise ( $p < 0.05$ ) in glucose level was noticed in rats injected only with alloxan but with no treatment (group 2) compared to the healthy control (group 1). The significant reduction observed in blood glucose levels in treated animal groups could be due to the restoration of the B cells of the pancreas involve in the secretion of insulin due to the presence of some antinutritional factors in the plant extract. The bioactive compounds in the extract may also lead to increased transport of blood glucose to the peripheral tissues [22, 25].

The increase in triglyceride observed in some treated groups may probably be as a result of insufficient insulin availability to trigger the uptake or utilization of glucose. Unusually high concentration of serum lipids caused by increase in the transportation of free fatty acids from the peripheral fat depots due to inhibition of the sensitive lipase by insulin has been reported [26, 27]. This prominent high lipid in the blood may therefore be taken as a result of the uninhibited actions of hormones involved in lipids catabolism on the fat depots caused probably by administration of the extract of the herb. The decrease observed in other group may be an indication of progressive metabolic control of *Brillantaisia patula* aqueous leaf extract on mechanisms involved in reduction or elimination of cholesterol from the body. This hypolipidemic properties by many medicinal plant species and plant products has been reported [28, 29].

The degradation of protein in the body ends up in urea production which is excreted from the body via kidney [30]. Creatinine is the final product of creatine kinase in the muscle cells. The amount of creatinine is a function of muscle mass and this is eliminated from the body through the kidney [30]. These two metabolites determine the healthy state of the kidney biochemically. Therefore an increase in these compounds is a reflection of kidney damage [30, 31]. The reduction in urea concentration observed in all the treated groups may probably be as a result of improvement of renal function by the administration of the aqueous extract of the leaf. A similar observation has been reported [32]. The decrease in creatinine concentration observed in some treated groups could be attributed to the effectiveness of the restoration of the impaired renal function by the presence of bioactive compounds extract [33, 34].

The effect of diabetes on protein metabolism has been previously reported [35]. The observed increase in serum total protein, albumin and globulin in diabetic animal groups treated with the aqueous extract of *Brillantaisia patula* (especially in groups 4 and 5 treated with 1000 and 1500 mg/kg bwt, respectively) could be attributed to some bioactive compounds present in the aqueous leaf extract activating the uptake of amino acids and protein synthesis as well as inhibiting protein degradation [35].

The use of hematological indices in establishing the harmful effects of xenobiotics has been reported [36]. Reduction of packed cell volume (anemia) associated with diabetes mellitus has been attributed to increase in non-enzymatic glycosylation of RBC membrane proteins. As they undergo the oxidation, free radical species are produced such as lipid peroxides that can result to destruction of red blood cells (RBC) [37]. The increased packed cell volume (PCV) and haemoglobin (Hb) noticed may be attributed to the phytochemical constituents of the extract improving the formation or release of erythropoietin in the stem cells of the bone marrow of the rats or lowering of lipid peroxidation by inhibition of the reaction by the plant extract [38].

Malondialdehyde (MDA) level, a biomarker of lipid peroxidation, is one of the major parameters used to ascertain the level of oxidant and antioxidant state of internal tissues in type 2 diabetics [39, 40]. The decreased concentration of malondialdehyde observed in the heart and kidney of the treated diabetic animal groups was an indication that lipid peroxidation was prevented. The decreased MDA levels in these tissues was also an indication of the inactivation of lipid peroxidation reactions and the decreased free radical generation caused by the components (phytochemicals) of extract of *Brillantasia patula*.

Reduced glutathione (GSH) is an endogenous antioxidant biomolecule that fights against free radicals released resulting from oxidative stress. This implies that, a rise in GSH level can lead to reduction in lipid peroxidation [41]. Decreased glutathione levels found in the diabetic group without treatment is a sign of lipid peroxidation. The increase noticed upon treatment could be as a result of the activation of the synthesis of the bioactive compound by the presence of some phytochemicals available in the extract or the bioactive component of the extract are able to mop up the generated free radicals from the system. Catalase activity (CAT) has been reported to decrease in diabetic rats induced with streptozotocin [42]. The significant increase in catalase activity of the liver in the treated groups was an indication of the ameliorating effect of the extract increasing the synthesis of the enzymes.

Alanine- and aspartate transaminases are biomarker enzymes for liver function. Increase in the activity of these enzymes in the serum is an indication of liver impairment and this leads to the rupture of liver membrane resulting to leakage of these biomarker enzymes into the blood. Elevation in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in rats induced with alloxan has been published [43, 44]. The decrease in the activities of these enzymes in the treated groups revealed that the plant aqueous extract has protective effect on the integrity of the liver. This is in line with the work of Rajangam *et al.* [45].

## 5. Conclusion

The findings of the present study indicate that *Brillantasia patula* aqueous leaf extract exhibits potential hypoglycemic effect, prevents lipid peroxidation, boosts haematological parameters, and could protect liver and renal damage

associated with type 2 diabetes, especially when administered at a dose range of 500 - 1000 mg/kgbw. Future studies to identify the bioactive constituents are, however, encouraged.

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