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Evaluation of antihyperglycemic activity of aqueous stem bark extract of *Boswellia dalzielii* in alloxan-induced diabetic Wistar rats

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Abstract

Background Diabetes mellitus is one of the leading causes of morbidity and mortality globally. Although synthetic hypoglycemic agents are commonly used to manage this disorder, such medications, besides being unable to cure the disease, are expensive and associated with side effects. Conversely, medicinal plants have emerged as effective, safe and affordable alternative treatments. *Boswellia dalzielii* plant has been reported to possess ethnomedicinal properties for the treatment of various health conditions; however, scientific studies exploring this plant as antihyperglycemic agent are still limited. Thus, this study evaluated the antihyperglycemic activity of aqueous stem bark extract (ASBE) of *B. dalzielii* in alloxan-induced diabetic Wistar albino rats.

Methods Phytochemical screening of the ASBE of *B. dalzielii* was conducted. Twenty male Wistar albino rats weighing 100–150 g divided into 4 groups (A–D) of five rats were used for the study. Group A served as the normal control and received neither ASBE of *B. dalzielii* nor glibenclamide. The treatment for the other three groups was as follows: Group B, 10 mg/kg of glibenclamide (diabetic control); Group C, 500 mg/kg ASBE of *B. dalzielii*; and Group D, 1000 mg/kg ASBE of *B. dalzielii*. Treatments were administered orally every 24 h for a period of 2 weeks. Blood glucose level and body weight were evaluated at weeks 0, 1 and 2. Histomorphological features of the rats' pancreas in all the groups were compared.

Results The phytochemical analysis revealed the presence of alkaloids, saponins, tannins, cardiac glycosides, flavonoids, carbohydrates, steroids and triterpenes. The two different doses of the plant extract significantly reduced blood glucose level at weeks 1 and 2 (all $p < 0.05$), with the 1000 mg/kg dose demonstrating a greater reduction compared with glibenclamide at week 2 ($p = 0.014$). However, only the 500 mg/kg dose led to restoration, albeit slight, of the pancreatic islet cells.

Conclusion This study suggests that *B. dalzielii* plant exhibits a potent antihyperglycemic activity evidenced by reduced blood glucose levels and slight restoration of pancreatic islet cells. This plant could be, therefore, considered in the treatment of diabetes mellitus.

Keywords Alloxan, Blood glucose levels, *Boswellia dalzielii*, Diabetes mellitus, Hypoglycemia

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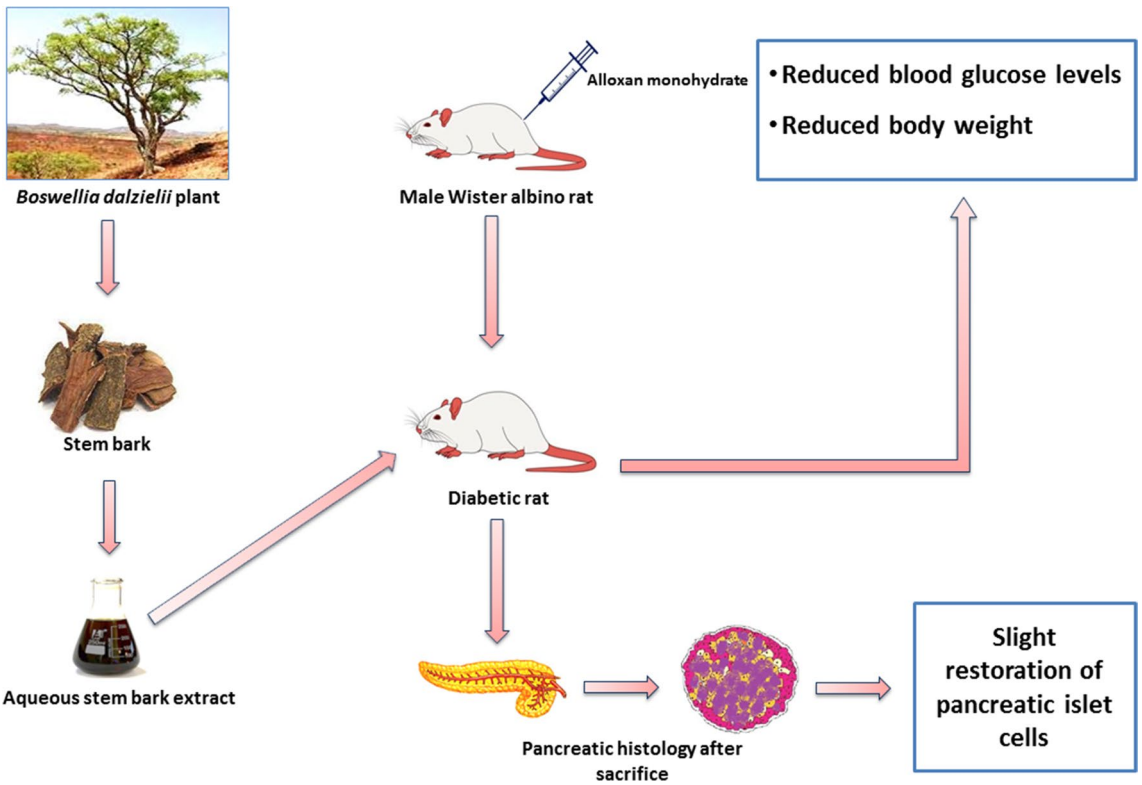
Graphical Abstract



Background

Diabetes mellitus (DM), a common chronic metabolic disorder characterized by abnormal glucose homeostasis resulting in hyperglycemia (high blood glucose levels [BGLs]), is one of the leading causes of morbidity and mortality globally. According to current estimates, about 573 million adults (aged 20–79 years) are living with DM and this figure is projected to rise to 783 million by 2045 if no effective prevention methods are implemented [1]. In 2021, DM accounted for 6.7 million deaths representing 1 death every 5 seconds [2]. Moreover, the global healthcare expenditures on people with DM were estimated to be 966 billion USD and are projected to reach 1054 billion USD by 2045 [1]. Accordingly, the escalating prevalence, deaths, and healthcare expenditure due to DM inflict a colossal social, financial and health system burden globally [3].

The impact of living with DM is concerning, particularly in low- and middle-income countries as the prevalence is growing rapidly and the majority of DM-related deaths occur in these regions owing to the higher number of undiagnosed cases in addition to factors such as lack of education, low levels of income, difficulty in accessing healthcare and medications, and insufficient health expenditure [4, 5]. This is especially true to Sub-Saharan African countries like Nigeria with an estimated DM prevalence of 11.2 million people (5.8%) [6], and a mortality rate of 30.2 per 100,000 population [7] suggesting that effective preventive and treatment strategies are highly needed.

Although DM is commonly treated with the use of synthetic hypoglycemic agents such as insulin secretagogues (sulfonylureas, meglitinides), insulin sensitizers (biguanides, metformin, thiazolidinediones) and α-glucosidase inhibitors (miglitol, acarbose), these medications are unable to cure the disease since they cannot restore normal glucose homeostasis [8]. Additionally, they are often associated with side effects [9], besides being inaccessible and unaffordable for most people, especially in low-resource or rural settings [10]. Conversely, medicinal plants have been employed by humans since ancient times to prevent or cure diseases including DM [11]. Indeed, traditional medicinal practitioners from various parts of the world claim to cure DM or at least lessen its major symptoms and progression owing to the potent antidiabetic properties of medicinal plants

[12]. Consequently, herbal diabetic medicines have emerged as effective, safe and affordable alternative treatments for DM.

Of the various medicinal plants discovered to possess potent ethnomedicinal properties is the *Boswellia dalzielii*–commonly known as "Frankincense tree" belonging to the family *Burseraceae.* The plant is a tall tree growing up to 13 m high and produce aromatic white flowers [13]. It is widely spread in many African countries such as Burkina Faso, Togo, Cameroon, Benin, Ghana, Ivory Coast, Nigeria and Central African Republic [13, 14], and has been traditionally used as a medicament for several diseases and ailments. In northern Nigeria, this plant is locally called *Hannu* or *Ararrabi* in the Hausa language (meaning to prevent bad luck) [15].

Although *B. dalzielii* plant, particularly the stem back extract, has been widely reported as antibacterial, antifungal, antiinflammatory, antiarthritic and antispasmodic agents [13, 16–20], scientific studies exploring this plant as antihyperglycemic agent are still limited [21]. Thus, the purpose of this study was to evaluate the antihyperglycemic activity of aqueous stem bark extract (ASBE) of *B. dalzielii* in alloxan-induced diabetic Wistar rats for potential use in the treatment of DM.

Methods

Material and reagents

Alloxan monohydrate was purchased from Sigma St. Louis (Missouri, USA). Ketamine (Ketamine®) was purchased from Panpharma Gmbh (Rotexmedica, Germany). Diazepam (Valium®) was purchased from Hoffman-La Roche Ltd. (Ontario, Canada). BGLs were measured using digital glucometer (Accu-check advantage, Roche Diagnostic, Germany). Body weight of the rats was measured using a digital electronic lab weighing scale (KERRO, BL-2000, China).

Collection of plant materials

Fresh stem bark of *B. dalzielii* was collected from Kufena village, Zaria, Kaduna State, Nigeria, and botanical authentication of the plant parts took place at the herbarium unit of Department of Biological Sciences, Ahmadu Bello University (ABU), Zaria, Kaduna State, Nigeria. The voucher sample (0900121) and photographs were deposited at the institute for future reference.

Experimental animals

Wistar strain male albino rats weighing between 100 and 150 g from the Animal House, Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmaceutical Sciences, ABU, Zaria, Kaduna State, Nigeria were obtained and housed under standard environmental conditions. The animals were allowed free access to food (grower and starter mash) and water for a period of two weeks to get acclimatize before the commencement of the experiment. All animal procedures and experimental protocol were strictly followed in accordance with the National Research Council, Guide for the Care and Use of Laboratory Animals [22]. The study was approved by the Research and Ethical Committee on the use of laboratory animals of Nigerian Defence Academy, Kaduna, Kaduna State, Nigeria.

Preparation of plant extract

The fresh stem bark was cleaned, air-dried and pounded into a coarse powder using a mortar and pestle. The powder obtained was extracted with water using a soxhlet apparatus, and the solvent was removed in a vacuum and evaporated using a rotary evaporator at 60 °C to obtain extraction yield of 121.13 g of the plant extract. The extracted yield was then stored in a refrigerator at 4 °C till usage. To prepare the different dosages of the plant extract (500 and 1000 mg/kg) for the study experiment, 5 g/5000 mg and 10 g/1000 mg of the plant extract were each dissolve in 10 ml of distilled water. Dosage administered to each animal was calculated using the formula: volume = dose/stock × animal weight (kg).

Phytochemical screening

Phytochemical screening of the ASBE of *B. dalzielii* was conducted at the Pharmacognosy Department, Faculty of Pharmaceutical Sciences, ABU, Zaria, Kaduna State, Nigeria following standardized protocols as reported in the literature [23–25]. The extract was screened for alkaloids using Mayer's test and Wagner's test, saponins using Frothing test, tannins using Ferichloride test, anthracene derivatives using Bontrager's test, cardiac glycosides using Keller–Killiani test and NaOH test, flavonoids using Shinoda test and NaOH test, carbohydrates using Mollish test, and steroids and triterpenes using Liebermann–Burchard test.

Acute toxicity test

The median lethal doses (LD50) of the ASBE of *B. dalzielii* were determined in 12 rats in accordance with the method described by Lorke [26], which involves two phases. In the first phase, the rats were divided into three groups with each group consisting of 3 animals. They were then treated with the extract at doses of 10, 100, and 1000 mg/kg body weight orally and observed for 24 h for signs of toxicity. In the second phase, 3 rats were divided into three groups with each group consisting of 1 animal. They were also treated with the same extract but at doses of 1600, 2900, and 5000 mg/kg body weight orally. The

median lethal dose (LD50) was obtained using the second phase.

Induction of diabetes mellitus

Twenty male Wistar strain albino normoglycemic rats (weighing 100–150 g) were used for the study. They were fasted overnight for the duration of 12 h but allowed water ad libitum. DM was induced in fasted rats by a single intraperitoneal injection of Alloxan Monohydrates at the dose of 150 mg/kg body weight [27]. The animals were allowed free access to 5% glucose solution to overcome the drug-induced hypoglycemia [28]. BGLs of these rats was estimated 72 h after Alloxan administration, and diabetes was confirmed by blood samples collected from the tip of the tail using Accu-check Advantage digital glucometer. Animals with BGLs equivalent to or more 200 mg/dl were declared diabetic [29] and were used in the entire experimental group.

Experimental design

The study animal rats were divided into four groups (A–D) of five rats ($n=5$) as follows:

> Group A: represents normal control group and received 10 ml/kg of sterile distilled water orally.
> Group B: represents diabetic control group and received a 10 mg/kg of glibenclamide orally.
> Group C: represents experimental group and received oral dose of 500 mg/kg ASBE of *B. dalzielii.*
> Group D: represents experimental group and received oral dose of 1000 mg/kg ASBE of *B. dalzielii.*

All animals fasted overnight for 12 h prior to baseline determination of BGLs and treatments (oral feeds). All treatments were administered on daily basis for 2 weeks. Both BGLs (measured by collecting blood samples from the tip of their tail artery using the digital glucometer expressed in mg/dl) and body weight (by measuring with the KERRO, BL-2000 digital electronic lab weighing scale expressed in grams [g]) were measured at week 0 (first day of treatment), week 1 (7th day of treatment) and week 2 (14th day of treatment).

Histopathological investigation of pancreas

At the end of the study, 1 animal selected randomly from each of the study groups was sacrificed using Ketamine and Diazepam injections intramuscularly at a dose of 75 mg/kg and 5 mg/kg, respectively. An incision was made in the abdomen and the pancreas was removed, washed with cold saline and preserved in 10% buffered formalin. Section of the pancreas was stained in hematoxylin and eosin and then observed with a light microscope at $\times 250$ magnification. The histology was conducted at the Gross Anatomy Research Laboratory, Department of Human Anatomy, Faculty of Basic Medical Sciences, ABU, Zaria, Kaduna State, Nigeria.

Statistical analysis

Descriptive statistics of mean and standard error of measurement (mean $\pm$ SEM) were used to summarize the data. To analyze the effect of treatment on body weight and BGLs, a within- and between-subjects design analysis of variance (ANOVA) with group (normal control, diabetic control, 500 mg/kg ASBE of *B. dalzielii*, 1000 mg/kg ASBE of *B. dalzielii*) as between-subjects factor and time (week 0, week 1, week 2) as within-subjects factor was applied using the General Linear Model. Post-hoc test with Least Significant Difference (LSD) was used for multiple pairwise comparisons in case of any significant ANOVA. All statistical analyses were performed using SPSS version 23.0 (IBM Co., Armonk, NY, USA) with the level of significance set at $p<0.05$.

Results

Phytochemical screening

The results of the phytochemical screening revealed the presence of all the expected constituents (alkaloids, carbohydrates, cardiac glycosides, flavonoids, saponins, steroids, tannins and triterpenes) in the ASBE of *B. dalzielii* except anthraquinones (Table 1).

Acute toxicity test

The results of the acute toxicity test in the first and the second phase revealed no mortality. Therefore, the LD50 was determined to be above 5000 mg/kg.

Table 1 Phytochemical screening of aqueous stem bark extract of *B. dalzielii*

Phytochemicals	Presence of phytochemicals
Alkaloids	+
Anthraquinones	–
Carbohydrates	+
Cardiac glycosides	+
Flavonoids	+
Saponins	+
Steroids	+
Tannins	+
Triterpenes	+

+ve represents the presence of phytochemicals, –ve represents the absence of phytochemicals

Effect of aqueous stem bark extract of *B. dalzielii* on body weight

As shown in Table 2, within-subjects ANOVA revealed that there was a statistically significant change in body weight for the normal control ($p = 0.008$) and diabetic control ($p = 0.021$) groups across the weeks. Post-hoc analysis with LSD showed a significant increase in body weight from week 0 to week 1 ($p < 0.05$) and from week 0 to week 2 ($p < 0.05$) but from week 1 to week 2 ($p > 0.05$) for the normal control and diabetic control groups. However, no statistically significant change in body weight was observed for the two experimental groups across the weeks ($p > 0.05$) even though there was a trend indicating a reduction in body weight (Table 2).

Between-subjects ANOVA revealed that there was no statistically significant difference ($p > 0.05$) in body weight between the groups at all time points (Table 2). Figure 1 shows the trend of body weight scores among the groups across the weeks.

Effect of aqueous stem bark extract of *B. dalzielii* on blood glucose level

As shown in Table 3, there was a statistically significant change in BGLs in the two experimental groups (500 mg/kg ASBE of *B. dalzielii*, $p = 0.016$; and 1000 mg/kg ASBE of *B. dalzielii*, $p = 0.001$) across the weeks as revealed by within-subjects ANOVA. Post-hoc analysis with LSD showed a significant reduction in BGLs between week 0 and 1 ($p < 0.05$) and between

Table 2 Effect of aqueous stem bark extract of *B. dalzielii* on body weight

Group ($n = 5$)	Treatment given	Dose	Body weight (g)			*F* value[rm]	*p* value[rm]
			Week 0	Week 1	Week 2		
A	Normal control (distilled water)	10 ml/kg	125.0 ± 313^{a}	134.8 ± 3.86^{b}	137.4 ± 3.60^{b}	36.68	0.008*
B	Diabetic control (Glibenclamide)	10 mg/kg	122.6 ± 2.13^{a}	125.8 ± 2.05^{b}	130.8 ± 3.61^{b}	18.13	0.021*
C	ASBE	500 mg/kg	126.0 ± 7.07	122.4 ± 7.33	121.8 ± 8.15	2.491	0.230
D	ASBE	1000 mg/kg	125.0 ± 3.52	123.0 ± 3.97	120.0 ± 2.55	3.552	0.162
	F value[bs]		0.109	1.501	2.661		
	p value[bs]		0.954	0.252	0.083		

Values are presented in mean ± SEM; ASBE, aqueous stem bark extract of *B. dalzielii*; values in the same row having different letters of alphabets are statistically significant

*$p < 0.05$

[rm] Analyzed with repeated measures ANOVA

[bs] Analyzed with between-subjects ANOVA

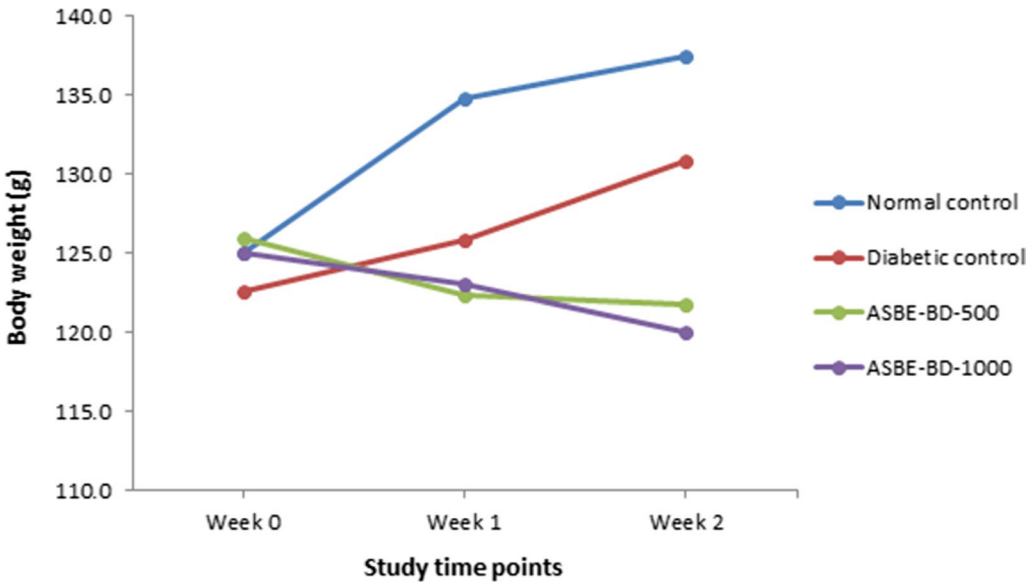


Fig. 1 A profile plot showing groups' mean scores in body weight at week 0, week 1 and week 2 of the study

Table 3 Effect of aqueous stem bark extract of *B. dalzielii* on blood glucose levels

Group ($n=5$)	Treatment given	Dose	Blood glucose levels (mg/dl)			F value^{rm}	p value^{rm}
			Week 0	Week 1	Week 2		
A	Normal control (distilled water)	10 ml/kg	$93.0 \pm 3.28^{\S}$	$92.4 \pm 3.11^{\S}$	$92.8 \pm 2.99^{\S}$	0.030	0.971
B	Diabetic control (Glibenclamide)	10 mg/kg	$202.2 \pm 8.33^{\dagger}$	$188.2 \pm 12.5^{\dagger}$	$186.2 \pm 11.9^{\dagger}$	5.246	0.105
C	ASBE	500 mg/kg	$208.6 \pm 6.88^{a\dagger}$	$179.4 \pm 5.0^{b\dagger}$	$174.4 \pm 5.41^{b\dagger}$	21.83	0.016*
D	ASBE	1000 mg/kg	$204.4 \pm 3.29^{a\dagger}$	$159.0 \pm 5.41^{b\P}$	$146.8 \pm 5.31^{b\P}$	119.25	0.001*
	F value^{bs}		88.23	33.63	35.08		
	p value^{bs}		0.000**	0.000**	0.000**		

Values are presented in mean ± SEM; ASBE, aqueous stem bark extract of *B. dalzielii*; values in the same row having different letters (a, b) of alphabets or values in the same column having different special characters (§, †, ¶) are statistically significant

*$p < 0.05$

[rm] Analyzed with repeated measures ANOVA

[bs] Analyzed with between-subjects ANOVA

week 0 and week 2 ($p < 0.05$) but between week 1 and week 2 ($p > 0.05$). For the normal and diabetic control groups, no statistically significant change in BGLs was observed across the weeks ($p > 0.05$).

Between-subjects ANOVA revealed statistically significant difference ($p > 0.05$) in BGLs between the groups across the weeks (Table 3). At week 0, post-hoc analysis with LSD showed that the diabetic control group and the two experimental groups were comparable ($p > 0.05$) and had higher BGLs compared to the normal control group ($p < 0.05$). At week 1, post-hoc analysis with LSD showed that the normal control group had lower BGLs compared with the diabetic control group and the two experimental groups ($p < 0.05$), but the experimental group treated with 1000 mg/kg ASBE of *B. dalzielii* had lower BGLs ($p = 0.014$) compared with the diabetic control group. At week 2, post-hoc analysis showed that the normal control group had lower BGL compared with the diabetic control group and the two experimental groups ($p < 0.05$), but the experimental group treated with 1000 mg/kg ASBE of *B. dalzielii* had lower BGL compared with the diabetic control group ($p = 0.001$) and the experimental group treated with 500 mg/kg ASBE of *B. dalzielii* ($p = 0.016$). Figure 2 shows the trend of BGLs among the groups across the weeks.

Histomorphological investigation of pancreas

The histology study of the pancreatic islet cells of the animals in all the groups are shown in Fig. 3.

In the normal control group (NC), the histology demonstrated a normal pancreas. The islet cells were full of centrally placed beta cells, appeared very compact, and surrounded by seroacinar cells. The nuclei capillaries were also normal (Fig. 3). In the diabetic control group (DC), the histology demonstrated a lack of restoration of the islet cells. A lymphatic infiltration which results in inflammation is demonstrated. These extensive necrotic changes are accompanied by fibrosis and atrophy. In the group treated with 500 mg/kg ASBE of *B. dalzielii* (500-BD), the histology demonstrated a slight restoration of the islet cells with evidence of destruction and atrophy (Fig. 3). In the group treated with 1000 mg/kg ASBE of *B. dalzielii* (1000-BD), the histology demonstrated a lack of islet cells with accompanying necrotic changes in the pancreas (Fig. 3).

Discussion

The rising prevalence of DM and the costs, as well as side effects associated with current synthetic medications, necessitate the discovery of affordable and safe alternative therapies to battle this troublesome disease. Indeed, the World Health Organization Expert Committee [30] has so far recommended medicinal plants for the management of DM as well as studies into exploring traditional medicines for this refractory disease. In the quest to search for natural remedies for DM, the present study was undertaken to evaluate the antihyperglycemic activity of ASBE of *B. dalzielii* in alloxan-induced diabetic Wistar rats for potential use in the treatment of DM. The findings of the present study revealed that the ASBE of *B. dalzielii* exhibits a potent hypoglycemic activity.

The phytochemical screening of the present study revealed the presence of alkaloids, saponins, tannins, cardiac glycosides, flavonoids, carbohydrates, steroids, and triterpenes. These phytochemicals exhibit either cytoprotective function on the pancreatic beta cells or insulino-protective function, resulting in hypoglycemic effects and fewer diabetes complications [31, 32]. More specifically, flavonoids are known to promote pancreatic beta cells proliferation leading to increased insulin secretion and sensitivity [33]. In another vein, flavonoids

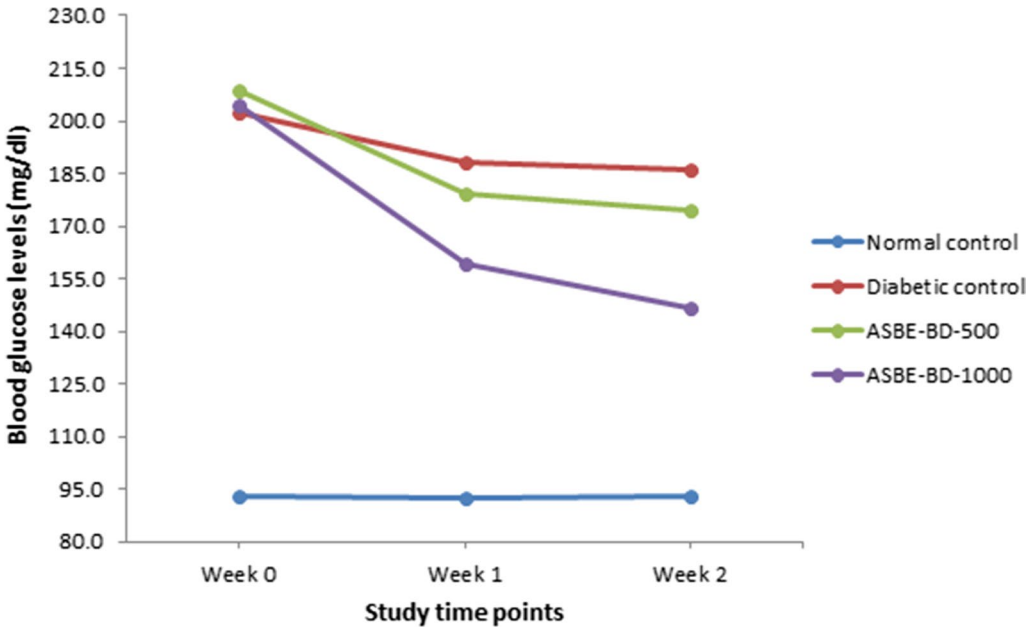


Fig. 2 A profile plot showing groups' mean scores in blood glucose levels at week 0, week 1 and week 2 of the study

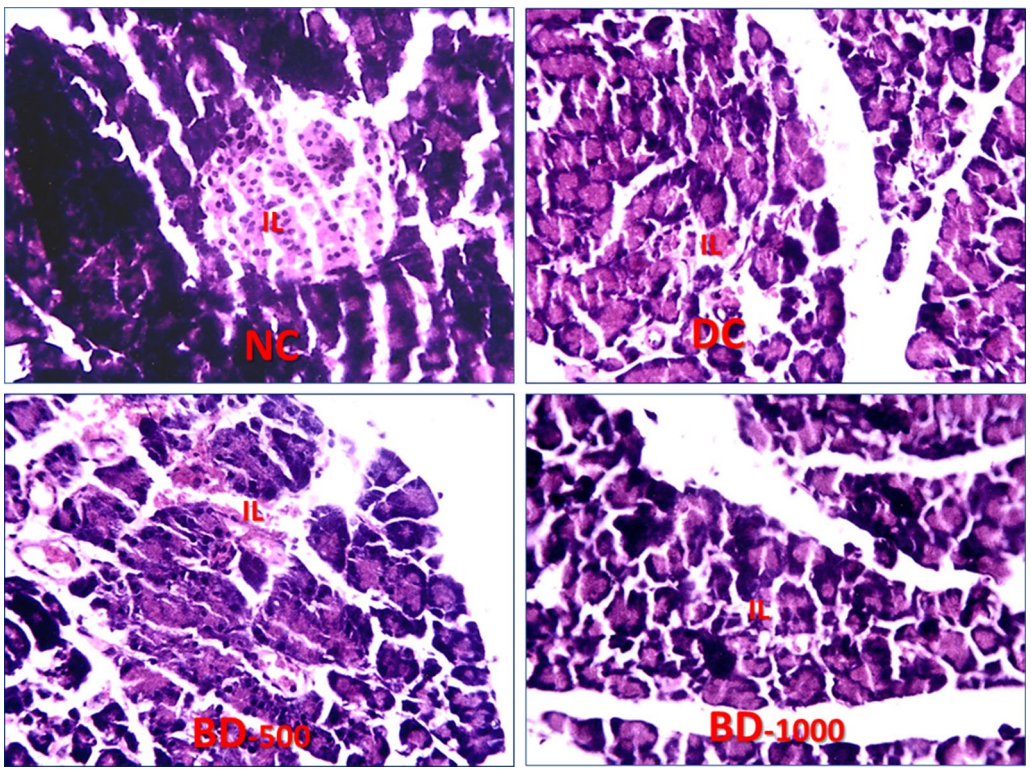


Fig. 3 Photomicrographs of sections of the pancreas from normal control (NC), diabetic control (DC), 500 mg/kg ASBE of *B. dalzielii* (BD-500) and 1000 mg/kg ASBE of *B. dalzielii* (BD-1000) groups. IL = Islets of Langerhans

and tannins may exhibit promising inhibitory potential against α-amylase and α-glucosidase thereby reducing postprandial hyperglycemia [34, 35]. Additionally, alkaloids play a key role against hyperglycemia by promoting glucose consumption and glycogen synthesis through various mechanisms by inhibiting or inducing multiple candidate proteins such as AMP-activated protein kinase, glucose transporters, glycogen synthase kinase-3, sterol regulatory element-binding proteins 1, glucokinase, glucose-6-phosphatase, and acetyl-CoA carboxylase [36]. The presence of these promising compounds in the ASBE of *B. dalzielii* may, thus, account for the antidiabetic effect observed among the diabetic Wistar rats in the present study. Similar to the findings of the present study, the study by Balogun et al. [21] found the presence of saponins, tannins and flavonoids in the ASBE of *B. dalzielii.* Additionally, the study by Mamza et al. [37] found the presence of similar phyto-compounds in addition to alkaloids, cardiac glycosides and carbohydrates. In contrast, the study by Nwinyi et al. [17] found the presence of only tannins in the ASBE of this plant. In a study [38] on the complete pharmacognostic evaluation of the leaves, stem bark and root of *B. dalzielii*, the presence of saponins, tannins, flavonoids, cardiac glycosides and terpenes were reported which all illustrate the therapeutic potentials of this plant.

Regarding body weight changes, our study demonstrated a significant increase in body weight in both the normal and diabetic control groups across time. The two experimental groups, however, had a decrease in body weight, albeit these changes were not statistically significant. While between-group analysis revealed no significant difference in the body weight between the groups at any study point, a decrease in body weight observed in the two experimental groups suggests a potential hypoglycemic activity induced by the different doses of ASBE of *B. dalzielii.* Reduced body weight is associated with low insulin resistance and optimal glycemic control [39]. The improvement in body weight among the experimental animals could be attributed to the activity of the phytochemicals such as flavonoids in the *B. dalzielii* plant [40]. In line with our study, a previous study also found a significant reduction in body weight among diabetic Wistar rats receiving an aqueous extract of various medicinal plants compared to normal and diabetic controls [41].

As regard to changes in BGLs, our results indicated that the experimental groups had a significant reduction in BGLs after week 1 and 2 of treatment, with the greatest reduction being more evident at week 2 of treatment. The normal and diabetic control groups, however, did not observe a significant reduction in the BGLs at any week of the study. While the different doses of ASBE of *B. dalzielii* demonstrated potent hypoglycemic activity across the weeks, between-group comparisons indicated that the 1000 mg/kg dose significantly reduced BGLs compared to the diabetic control group at week 2. This finding suggests that the stem bark extract of *the B. dalzielii* plant exhibit hypoglycemic activity better than a standard oral synthetic drug (glibenclamide) but in a dose-dependent manner. Supporting the results of the present study, the study conducted by Balogun et al. [21] found both 153 mg/kg and 297 mg/kg doses of ASBE of *B. dalzielii* to be effective at decreasing BGLs similar to that of 400 mg/kg of chlorpropamide (a standard hypoglycemic agent) among hyperglycemic rats. In addition, Yakubu et al. [15] found that a 400 mg/kg dose of various partitioned portions of crude methanol extract of *B. dalzielii* resulted in significant hypoglycemic activity compared with 2 mg/kg of glibenclamide in alloxan-induced hyperglycemic rats.

In the present study, alloxan monohydrate (a pyrimidine derivative, 2,4,5,6-tetraoxypyrimidine) [42] at a dose of 150 mg/kg was used to chemically induce type I diabetes in the study mice. The mechanism by which alloxan induces diabetes has been largely ascribed to rapid uptake by the beta cells and the formation of free radicals, to which beta cells have poor defense mechanisms to [43]. Thus, the hypoglycemic activity observed in the ASBE of *B. dalzielii* in our study could be accounted for by the antioxidant activity of the plant thereby blocking the formation of free radicals.

The results of histomorphological investigation of the pancreatic tissue in the current study revealed normal islet cells in the pancreas of the normal rats. Alloxan resulted in the destruction of the islet cells and we expect that the use of ASBE of *B. dalzielii* might cause significant restoration of these cells while reducing BGLs. However, slight restoration of the islet cells was observed in the rats receiving 500 mg/kg ASBE of *B. dalzielii* whereas neither the 1000 mg/kg dose of the plant extract nor the diabetic control group exhibited a discernible restoration of islet cells when compared with the normal control group. Although the lack of restoration of islet cells in the group receiving 1000 mg/kg ASBE of *B. dalzielii* is quite surprising given that the BGLs of this particular group significantly improved across time compared with the rest of the groups. Nevertheless, considering the duration of treatment in our study, which was relatively small, significant restoration is more likely to occur with longer follow-ups. In contrast to the present study, our previous work [44] showed that 1000 and 2000 mg/kg doses of ASBE of *Parinari macrophylla* resulted in restoration of the islet cells with the 2000 mg/kg dose being more evident after two weeks of treatment. The variations in results across these studies could be ascribed to the variations in the

efficacy of different plants besides the variations in the dosage administered. Thus, it is possible that regeneration of the islet cells could also be achieved with higher doses.

Conclusion

Based on the findings of the present study, it can be concluded that the ASBE of *B. dalzielii* exhibits a potent anti-diabetic activity in alloxan-induced diabetic Wistar rats owing to its hypoglycemic effect. Moreover, the plant extract led to a slight restoration of pancreatic islet cells. While this plant may potentially be considered in the treatment of DM, future rigorous scientific studies examining multiple doses and with longer follow-up are warranted to establish the most optimal treatment dose of this promising plant for the management of DM.

Abbreviations

ABU	Ahmadu Bello University
ANOVA	Analysis of variance
ASBE	Aqueous stem bark extract
BD	*Boswellia dalzielii*
BGLs	Blood glucose levels
DM	Diabetes mellitus
LD_{50}	Median lethal dose
LSD	Least significant difference
NaOH	Sodium hydroxide
NC	Normal control
SD	Standard deviation
SEM	Standard error of measurement
WHO	World Health Organization

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Author contributions

AAI, MSA and JA conceptualized and designed the study. AAI and AHU executed the experiments and analyzed the data. AAI and AAIJr were responsible for drafting the final manuscript. MSA and JA supervised the study. AAIJr, AUM and SH were responsible for statistical analysis and reviewing the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

The study was approved by the Research and Ethical Committee on the use of laboratory animals of Ahmadu Bello University, Zaria, Kaduna State, Nigeria (Ref: NDA/PGS/FS/M/1826/14). All animal procedures and experimental protocol were strictly followed in accordance with the National Research Council, Guide for the Care and Use of Laboratory Animals.

Consent for publication

Not applicable.

Competing interest

The authors declare that there are no conflicts of interest.

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