Original Article

Antihyperglycaemic potentials of *Newbouldia laevis* and *Adansonia digitata* leaf extracts on alloxan-induced diabetes in rats

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia and oxidative stress, with a rising global and national prevalence. Current conventional treatments in most cases have adverse effects. This study evaluated the antihyperglycaemic potentials of *Newbouldia laevis* (NL) and *Adansonia digitata* (AD) leaf extracts in alloxan-induced rats. Phytochemical screening and acute oral toxicity tests of NL and AD leaf extracts were conducted using standard procedures. *In vivo* antihyperglycaemic study of the crude extracts was conducted in rats. Induced rats were randomized into groups, and treated orally with NL and AD at 100, 200, and 400 mg/kgbw for 28 days. Fasting blood glucose (FBG) and bodyweights were monitored weekly. Both extracts contained significant levels of tannins, saponins, alkaloids, phenols, and flavonoids. Acute oral toxicity study revealed an LD_{50} above 2000 mg/kgbw for both extracts. NL showed a blood glucose-lowering activity of 57.47 ± 2.69 % which was significantly higher than that of AD (34.10 ± 2.85 %). NL administered at 400 mg/kgbw had a 57.47 ± 2.69 % FBG reduction which was not significantly different from Metformin (64.94 ± 2.43 %). Weight loss in induced rats was reversed following treatment with the extracts. These findings suggest that *N. laevis* extract possesses significant antihyperglycaemic effects, indicating its potential as a natural and cost-effective alternative for diabetes management.

Keywords: Newbouldia laevis; Adansonia digitata; Glycaemic control; Diabetes mellitus.

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INTRODUCTION

Diabetes mellitus (DM) comprises a collection of metabolic disorders typified by a persistently elevated level of blood glucose, that arises from insulin deficiency, insulin resistance, or a combination of both factors [1]. Chronic hyperglycaemia in *diabetes mellitus* causes cardiovascular disorders, retinopathy, neuropathy, and nephropathy [2]. The primary metabolic abnormalities associated with diabetes are inflammation, dyslipidemia, and hyperglycaemia.

These anomalies raise oxidative stress in cells and make different organs vulnerable to free radical damage as a result of their free radical generation [3]. Among diabetic patients, complications resulting in cardiovascular issues are the major cause of death and have been linked to a two- to four-fold increased mortality rate compared to those without diabetes [4].

With approximately 537 million cases worldwide, including 24 million in Africa, *diabetes mellitus* represents a significant global health crisis [5]. The condition's progressive nature frequently leads to devastating complications that substantially increase mortality risk [6]. Recent studies demonstrate that oxidative stress plays a pivotal role in accelerating complications of the disease [7]. Although numerous pharmacological interventions exist for diabetes management, developing effective treatment strategies remains challenging. Current antidiabetic medications often present limitations including inadequate glycaemic control and various adverse effects such as hypoglycaemia, cardiovascular complications, gastrointestinal disturbances, weight gain, lactic acidosis, renal impairment, and hepatotoxicity [8].

Medicinal plants have been used to treat many diseases, particularly when their therapeutic values have been backed by scientific evidence [9]. Several medicinal plants have been found to have anti-hyperglycemic properties that can be used to treat *diabetes mellitus* [10]. *Newbouldia leavis* is a tropical plant that is often called tree of life, fertility tree or boundary tree. It is called *Ogirisi* in Igbo, *Akoko* in Yoruba, and *Aduruku* in Hausa. There have been reports of therapeutic benefits from various parts of this plant [11]. *Adansonia digitata*, popularly known as baobab, is indigenous to Africa. The tree's seeds, fruit pulp, leaves, and stem bark have all historically been utilized to treat a variety of illnesses [12]. This study investigated the antihyperglycaemic potentials of *Newbouldia laevis* (NL) and *Adansonia digitata* (AD) leaf extracts in alloxan-induced rats.

MATERIALS AND METHODS

Ethics Approval and Informed Consent

Ethical approval for this study was obtained from the Directorate of Research and Development, Federal University of Technology Minna.

Collection and preparation of plant sample

Healthy and freshly harvested leaves of *Newbouldia laevis* and *Adansonia digitata* were collected in March from the Bosso and Tunga regions of Minna, Niger State, Nigeria. The plant specimens were authenticated at the Plant Biology department, Federal University of Technology, Minna, where voucher numbers FUT/PLB/EUPH/003 (*N. laevis*) and FUT/PLB/MAIV/008 (*A. digitata*) were assigned and deposited in the departmental herbarium. The collected leaves were air-dried for a period of 10 days. Leaves were grinded into powder using a Silver Crest blender (model SC-2030D), and preserved for subsequent analyses.

Preparation of crude extract

Crude extracts of *N. laevis* and *A. digitata* leaves were obtained by the method outlined by Mbagwu *et al*. [11]. Pulverized leaf material (100 g) was cold macerated for 72 hours in

400 mL of 70 % ethanol, with periodic agitation. After maceration, the mixture was filtered through Whatman No. 1 filter paper. A water bath maintained at 40 °C was used to concentrate the filtrate and yield the crude extract in dry form.

Quantitative phytochemical analysis

Quantitative phytochemical analyses of the crude extracts were carried out using standard methods; flavonoids [13], phenol [14], tannin and saponins [15], alkaloid [16].

Acute oral toxicity study of *N. laevis* and *A. digitata* leaf extracts

Acute oral toxicity assessment of the crude extracts was conducted following the Organisation for Economic Co-operation and Development (OECD) Guideline 423 [17]. A limit test was performed using a single dose of 2000 mg/kg bodyweight. Prior to administration, the animals were fasted overnight. In the initial phase, two rats were assigned to separate treatment groups: Group 1 received *N. laevis* extract (2000 mg/kg b.w.), while Group 2 was administered *A. digitata* extract at the same dosage. Close observation was maintained for the first 30 minutes post-administration, followed by periodic monitoring over four hours. Following confirmation of survival in these test animals, four additional animals per group received same dosage. All animals were subsequently monitored for 24 hours for any sign of toxicity or mortality, after which the LD_{50} was determined.

Experimental Animals

Wistar rats with an average body weight of 150 g were obtained from the Department of Biochemistry, Federal University of Technology Minna. Prior to experimentation, all animals underwent a seven-day acclimatization period under controlled laboratory conditions, maintained at 24 ± 2°C with a 12-hour light/dark cycle. Throughout this period, the rats had ad libitum access to food and water. Experiments with the animals were conducted in compliance with the principle of laboratory animal care (NIH Publication No. 85-23, 1985).

Induction of experimental diabetes

Diabetes mellitus was experimentally induced in Wistar rats using alloxan monohydrate according to the method described by Azad and Sulaiman [18]. Bodyweights and fasting blood glucose levels were recorded prior to induction. Overnight-fasted animals received a single injection of a freshly prepared alloxan solution at a dose of 150 mg/kg bodyweight via the intraperitoneal route. Blood samples were obtained by tail puncture 72 hours post induction and a glucometer (Exactive Vital) was used to check the blood glucose levels. Animals having blood glucose concentration greater than 200 mg/dL were used for the study.

Evaluation of *in vivo* antihyperglycaemic activities of *N. laevis* and *A. digitata* leaf extracts

Wistar rats were divided into nine experimental groups (A-I), each containing four animals housed in individual cages. First, animals were fasted over the night and then blood glucose readings were taken. Afterwards, treatments with the crude extracts were administered orally using gastric cannula. Treatments were administered daily for 28 days. Throughout the treatment period, daily administrations were

performed according to the following regimen: Group A (Normal Control): 0.1 mL distilled water, Group B (Diabetic Control): 0.1 mL distilled water, Group C (Standard Treatment): Metformin (100 mg/kg b.w.), Groups D-F: *N. laevis* extract (100, 200, and 400 mg/kg b.w. respectively), Groups G-I: *A. digitata* extract (100, 200, and 400 mg/kg b.w. respectively). Blood glucose levels and bodyweights were estimated on a weekly basis to determine the most active crude extract.

Data analysis

All data were processed using SPSS Statistics (Version 22) with one-way analysis of variance. For group comparisons, Duncan's post hoc test was used. Results were presented as mean values ± standard error of the mean (SEM). A probability threshold of $p < 0.05$ served as the criterion for establishing statistical significance in all analyses.

RESULTS

Quantitative phytochemical compositions of *N. laevis* and *A. digitata* leaf extracts

The phytochemical composition of *N. laevis* and *A. digitata* leaf extracts are presented in Table 1. *N. laevis* had a significantly higher ($p < 0.05$) phenol, tannins and saponins content than *A. digitata.*

Table 1: Quantitative Phytochemical Compositions of *N. laevis* and *A. digitata* Leaf Extracts

Sample	Phenol (mg/g)	Flavonoids (mg/g)	Alkaloids (mg/g)	Saponins (mg/g)	Tannins (mg/g)
N. laevis	8.65 ± 0.01^{b}	12.01 ± 0.01^{a}	8.05 ± 0.01^{a}	11.63 ± 0.02^{b}	7.41 ± 0.01^{b}
A. digitata	7.33 ± 0.01^{a}	22.12 ± 0.01^{b}	12.07 ± 0.01^{b}	7.59 ± 0.01^{a}	6.98 ± 0.01^{a}

Data are presented as mean values ($n = 3$) ± standard error of the mean. Different superscripts down a column denote statistically significant difference at $p < 0.05$.

Acute oral toxicity of *N. laevis* and *A. digitata* leaf extracts

Observations from acute oral toxicity study indicate no acute toxicity of the plant extracts. *N. laevis* and *A. digitata* leaf extracts both had an LD_{50} greater than 2000 mg/kg b.w. as no death was recorded up to the 2000 mg/kg bodyweight of the administered extracts. There was also no evident change in physical appearance and activities of the experimental animals during the study period.

Antihyperglycaemic activity of *N. laevis* and *A. digitata* leaf extracts on alloxan-induced diabetes in rats

The anti-hyperglycaemic activities, represented as mean fasting blood glucose (FBG) levels, of *N. laevis* and *A. digitata* leaf extracts on alloxan-induced diabetes in rats are presented in Figure 1. The extracts showed a dose-dependent decrease in FBG levels over the four-week period. At the end of the treatment period, the standard drug, metformin showed the highest percentage reduction (64.93 ±2.43 %) in FBG levels by lowering the blood glucose levels from 258.43

± 7.05 to 90.63 ± 6.95 mg/dL. However, this was not significantly different ($p < 0.05$) from the percentage reduction in FBG levels obtained for *N. laevis* (400mg/kg b.w.) treated group (57.42 ± 2.69 %) (Table 2).

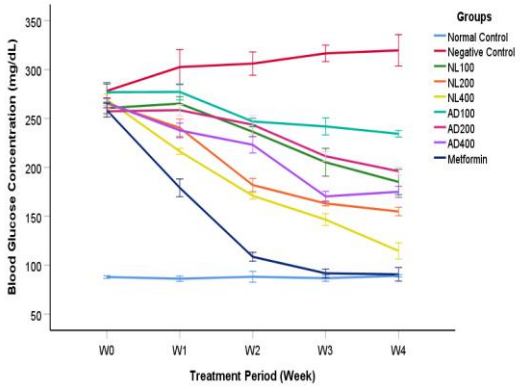

Figure 1: Effect of *N. laevis* and *A. digitata* Leaf extracts on Fasting Blood Glucose Levels of Alloxan-induced Rats

NL100, NL200, NL400: *N. laevis* administered at 100, 200 400 mg/kgb.w. AD100, AD200, AD400: *A. digitata* administered at 100, 200 400 mg/kgb.w. Metformin: 100 mg/kgb.w. Metformin

Table 2: Percentage Decrease in FBG Levels of Alloxan-induced Rats after Four Weeks of Treatment with *N. laevis* and *A. digitata* Leaf extracts

Treatment Group	Percentage Decrease in FBG Level (%)
Normal Control	No significant change
Negative Control	-14.84 ± 4.44[a]
Metformin	64.94 ± 2.43[f]
NL100	28.70 ± 6.58[cd]
NL200	41.61 ± 1.84[e]
NNL400	57.47 ± 2.69[f]
AD100	15.18 ± 2.51[b]
AD200	23.79 ± 1.86[bc]
AD400	34.10 ± 2.85[de]

Data are presented as mean values (n = 4) ± standard error of the mean. Different superscripts down a column denote statistically significant difference at $p < 0.05$.

NL100, NL200, NL400: *N. laevis* administered at 100, 200 400 mg/kgb.w. AD100, AD200, AD400: *A. digitata* administered at 100, 200 400 mg/kgb.w. Metformin: 100 mg/kgb.w. Metformin

Effect of *N. laevis* and *A. digitata* leaf extracts on bodyweights of alloxan-induced rats

Changes in bodyweight of the treatment groups over the course of the treatment period are shown in Figure 2. All induced animals recorded a decrease in their bodyweights in the first week post induction with alloxan monohydrate. At the end of the treatment period, all treated groups recorded a slight increase in bodyweight. However, the Negative Control group recorded a steady weight loss.

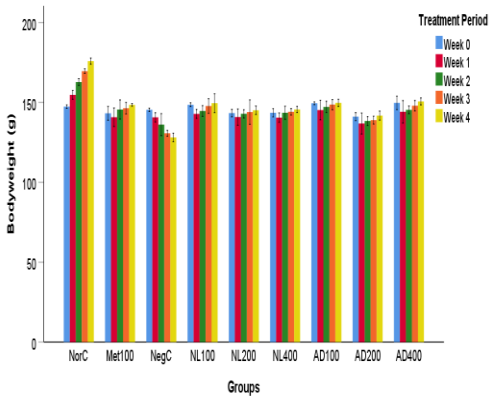

Figure 2: Bodyweight Changes of Alloxan-induced Rats after Treatment with *N. laevis* and *A. digitata* Leaf extract

NL100, NL200, NL400: *N. laevis* administered at 100, 200 400 mg/kgb.w. AD100, AD200, AD400: *A. digitata* administered at 100, 200 400 mg/kgb.w. Metformin: 100 mg/kgb.w. Metformin

DISCUSSION

The quantitative phytochemical analysis of *N. laevis* and *A. digitata* leaf extracts revealed significant differences in the concentrations of phenols, saponins, tannins, flavonoids and alkaloids. These variations may be as a result of differences in the secondary metabolism of these plants, which could be influenced by genetic, environmental, and physiological factors. Antihyperglycaemic study revealed *N. laevis* and *A. digitata* possessed antihyperglycaemic activities as evident by the dose-dependent decrease in blood glucose concentrations of the induced rats. This is consistent with the findings of Ajah *et al*. [19] and Mbagwu *et al*. [11], who reported the antihyperglycaemic potentials of *N. laevis* leaf extracts. Ebaid *et al*. [20] reported an improved lipid profile and a significant decrease in the blood glucose concentration of rats induced with streptozotocin after six weeks of treatment with methanolic leaf extract of *A. digitata*. *N. laevis* demonstrated a significantly higher antihyperglycaemic activity than *A.digitata*.

The reduction in blood glucose concentration following the administration of the extracts may be linked to the presence of bioactive phytochemicals in these plants. Certain phytochemicals have been reported to regulate glucose metabolism through multiple mechanisms. Ghorbani [21] reported that flavonoids improve glucose uptake and insulin sensitivity, while phenolic compounds protect pancreatic beta cells from oxidative damage, thereby improving insulin secretion [22]. Tannins and saponins, which were found in higher concentrations in *N. laevis*, have been reported to inhibit carbohydrate-digesting enzymes like α-glucosidase and α-amylase, delaying glucose absorption in the intestine [23]. This mechanism is similar to that of conventional antidiabetic drugs like acarbose, which slow down glucose release into the bloodstream. Polyphenols and flavonoids have been reported to increase glucose uptake in certain cells via the activation of AMP-activated protein kinase (AMPK), which is an important regulator of blood glucose levels [24]. Reports have shown that flavonoids have the ability to actively scavenge free radicals and lower inflammatory markers such as TNF-α and IL-6 [25], indirectly contributing to improved glucose homeostasis. Al-Ishaq *et al*., [26] suggested that flavonoids inhibit gluconeogenic enzymes, leading to decreased blood glucose levels. The higher antihyperglycaemic effect of *N. laevis* compared to *A. digitata* recorded in this study may be attributed to several factors, including

differences in phytochemical composition, bioavailability of active compounds, mechanisms of action, and interaction with various pathways of glucose metabolism.

Insulin deficiency disrupts normal glucose metabolism and forces the body to break down proteins and fats to meet its energy demands, leading to weight loss. The reversal of alloxan-induced weight loss following treatment with *N laevis* and *A. digitata* extracts can be attributed to enhanced insulin secretion, improved glucose utilisation, and reduced protein and fat catabolism [27], leading to restoration of muscle mass and fat stores. By improving glucose utilisation, the body is able to derive energy from glucose, reducing reliance on protein and fat stores for energy production, thus preventing further weight loss and promoting recovery.

CONCLUSION

This study revealed *N. laevis* and *A. digitata* lowered blood glucose levels in alloxan-induced rats. The antihyperglycaemic activity, presented as percentage reduction in FBG levels, of *N. laevis* administered at 400 mg/kgbw (57.42 $\pm$ 2.69 %) was not significantly different from the standard drug, Metformin (64.93 $\pm$2.43 %). This observed effect may be attributed to the presence of various bioactive compounds in the plant extracts. These findings suggest that *N. laevis* hold promise as a natural, cost-effective, and efficient alternative for managing diabetes and its complications.

Authors Contribution

KAY and UMB conceptualized the study. KAY, AAN, BMB, and UMB designed the study. ES and UMB participated in laboratory work and data collection. ES and GR performed the data analysis; ES, UMB, AAN, and BMB interpreted the data. ES prepared the first draft of the manuscript, reviewed by UMB and KAY. All authors contributed to the development of the final manuscript and approved its submission.

Disclosure of Conflict of Interest

Authors have declared that they have no competing interests.

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