International Journal of Advances in Nephrology Research

5(1): 98-103, 2022; Article no.IJANR.91280

Effect of Methanolic Stem Bark Extract of *Acacia nilotica* (Bagaruwa) on Some Renal Function Parameters in Alloxan Induced Diabetic Albino Rats

Kabiru Sirajo [a*], Zulkallaini Shehu [a], Ibrahim Mas'ud [b] and Musa Muhammad Dan-Ige [a]

[a] Department of Biochemistry, Sokoto State University, Sokoto, Nigeria.
[b] Department of Environmental Science, Islamic University in Uganda, Uganda.

Authors' contributions

This work was carried out in collaboration among all authors. Author KS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ZS and IM managed the analyses of the study. Author MMDI managed the literature searches. All authors read and approved the final manuscript.

Article Information

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Original Research Article

Received 02 July 2022
Accepted 04 September 2022
Published 27 September 2022

ABSTRACT

Background: Diabetes Mellitus (DM) is a complex metabolic disorder characterize by high blood sugar which gives rise to many complications including diabetic nephropathy. While there were enormous reports on the uses and efficacy of various medicinal plants, very few information are available on their safety and side effects while been used to treat certain ailment.
Aim: The aim of this study is to determine the effect of methanolic stem bark extract of *Acacia nilotica* on some renal function parameters in alloxan induced diabetic albino Rats.
Methodology: Thirty (30) young albino rats were grouped into six (6), comprising of five (5) rats per group. Diabetes was induced by single intraperitoneal injection of freshly prepared alloxan monohydrate and blood glucose level was determined forty eight hours (48 hrs) after injection. After induction of diabetes, Metformin and selected doses of *Acacia nolitica* extract were orally administered for 4 weeks after which serum biochemical markers were determined.
Results: *Acacia nilotica* and metformin decreased fasting blood glucose levels compared to diabetic control Group. No significant changes were observed in electrolytes level with the

**Corresponding author: E-mail: ksirajo2020@gmail.com;*

exception of urea and creatinine that significantly (P<0.05) decreased at 1200 mg/kg and 600 mg/kg respectively compared to control.
Conclusion: The present study revealed that, the plant extract possessed hypoglycemic effect and that it have nephrotoxic protection effect.

Keywords: Acacia nolitica; albino rats; diabetic mellitus; electrolytes; fasting blood sugar; metformin; stem bark.

1. INTRODUCTION

Diabetes Mellitus (DM) is one of the most common metabolic disorders of great concern all over the world. DM is caused due to lack of insulin or ineffective production of insulin in the pancreas and lead to abnormalities in carbohydrate, protein and lipid metabolism. A total of 463 million people were reported to have DM in 2019 and this number is predicted to rise up to 578 million by the year 2030 and 700 million by 2045 [1]. High blood sugar gives rise to many complications like diabetic retinopathy, diabetic nephropathy, atherosclerosis, hypercoagulability, cardiovascular diseases, coronary heart disease, abdominal obesity, hypertension, hyperlipidemia, cerebrovascular disease, coronary artery disease, foot damage, skin complications, alzheimer's disease, hearing impairment, and depression [1].

Diabetic nephropathy (DN) is one of the primary causes of death in diabetic people. DN is accompanied by basement membrane thickening, messengial cell growth, fibrosis, and podocyte death, all of which result in structural and functional problems [2]. Patients with diabetes who have functionally impaired renal cells have higher excretions of urine albumin, urea, uric acid, and creatinine, BUN, fluid retention, glomerular lesions, and lower glomerular filtration rate (GFR) [3]. In addition, oxidative stress and chronic hyperglycemia are two significant factors that contribute to the development of diabetic complications [4,5]. According to Young et al. [6], long-term exposure to hyperglycemia may cause early pathological changes in the kidneys that result in protein matrix accumulation, the development of renal hypertrophy, tubulo-interstitial changes, and an increase in the thickening of the tubular basement membrane. Furthermore, several metabolic abnormalities, oxidative stress, and advanced glycation end products (AGEs) raise the risk of developing diabetic nephropathy [7]. Vascular aging and damage are brought on by the interaction between AGEs and their receptors, which is directly related to the pathogenesis of DN. Chronic hyperglycemia also causes oxidative stress by raising the quantity of reactive oxygen species (ROS), which allows AGEs to develop. Therefore, changes in the aforementioned metabolic processes result in morphological and functional nephron aberration, which finally leads to DN [2]. According to Ekakitie, [8] there are several medicinal plants with anti-nephropathy potentials. Furthermore, studies suggested that medicinal plants improve DN by suppression of oxidative stress, inflammation and AGEs inhibition [2-10].

Acacia nilotica known as ''Bagaruwa'' in Hausa language of Northern Nigeria is a proverbial, medium sized tree and broadly scattered in tropical and subtropical countries [11]. The stem bark extract of *Acacia nilotica* have been reported to contain wide range of phytochemicals, among which are flavonoid, triterpenes, alkaloids, cardiac glycosides, carbohydrate, anthraquinone, unsaturated steroids and saponins [3]. Different parts of the plant have been shown to possessed, vasoconstriction, antibacterial, anti-hypertensive, hypoglycemic, anti-inflammatory, antitumor, antifungal, anti-trypanosomal, Antidiarrheal, Antihyperlipidemic and anthelmintic activity [12-20].

Therapeutic evaluation of medicinal plants has recently witnessed a growing interest amongst researchers worldwide [21]. While there were enormous reports on the uses and efficacy of various medicinal plants, very few information are available on their safety and side effects while been used to treat certain ailment. Therefore, the aim of this research work is to investigate the effect of methanolic *A. nilotica* stem bark extract on six renal function parameters in alloxan induced diabetic albino rats.

2. MATERIALS AND METHODS

2.1 Plant Collection and Authentication

Stems barks of *A. nilotica* were collected from Sokoto south local government area of Sokoto

State, in May 2020. It was authenticated in the botany unit, Biology department of Sokoto State University. The collected sample was cut into small pieces and air dried at room temperature for four weeks. It was then ground into fine powder by a mechanical grinder, followed by sieving through a 40 mesh sieve. The grounded sample was packed in clean dry plastic air tight bag.

2.2 Preparation of Plant Extract

One hundred grams (100 g) powder of the plant sample was later extracted in 90% methanol (600 ml) for 72 h. The extracts were filtered using clean cloth and Whatman No. 1 filter paper. The filtrate was concentrated in vacuum at 30^{o}C and stored in sterile sample containers at 40^{o}C until further use.

2.3 Experimental Animals

Thirty (30) healthy adult, both sexes albino Rats weighing 120-145g were used in the study. They were obtained from the Animal Research Centre (ARC) of the Ahmadu Bello University (ABU), Zaria, Nigeria. The animals were allowed to acclimatize for a period of two weeks in the animal house at the department of Biochemistry in Sokoto State University, Sokoto, prior to the study. The rats were housed in polypropylene cages, maintained under standard laboratory conditions. The animals were maintained on 12 h light, dark cycle, and fed with standard mice pellets.

The total of thirty (30) albino rats were grouped into six (6), comprising of five (5) rats per group (n = 5). The groups were as follows:

Group 1: (Normal control) received distilled water only.

Group 2: (Diabetic control) received Alloxan monohydrate without treatment.

Group 3: (Positive control) Received conventional drug (Metformin 250mg/kg)

Group 4: Test group (*A. nilotica*, 300mg/kg)

Group 5: Test group (*A. nilotica*, 600mg/kg)

Group 6: Test group (*A. nilotica*, 1200mg/kg)

The animals were fasted for 8 hours, but allowed free access to water. Diabetes was induced experimentally by single intraperitoneal injection of freshly prepared alloxan monohydrate (150 mg/kg) in group 2 - 6. Forty eight hours after injection, blood glucose was determined using glucose analyzer model with glucometer strips. Rat with blood glucose level above 2000 mg/L (>11.1 mmol/L), were considered diabetic and suitable for use in the study. After induction of diabetes, Metformin and selected doses of *A. nilotica* extract were orally administered for 4 weeks.

2.4 Estimation of Serum Biochemical Markers

At the end of the 28 day treatment period, the rats were fasted overnight, anaesthetized with chloroform and then decapitated. Blood samples were collected via cardiac puncture into non-EDTA tubes. It was allowed to coagulate, before centrifugation and the serum separated was used for biochemical analysis. Using corresponding commercially available diagnostic kits, spectrophotometric estimations of Fasting Blood glucose (FBG), Electrolytes (Na^{+}, K^{+} Cl^{-}, and HCO^{3-}), Urea and Creatinine were performed as primary markers of diabetic nephrotoxicity.

2.5 Statistical Analysis

The results were expressed as the Mean ± SD (n=5). The results were statistically analyzed using Statistical Package for Social Science (SPSS) version 20. One-way ANOVA was used followed by Duncan's test for parametric multiple comparisons between the control and the treatment groups. Differences were considered significant at $p<0.05$.

3. RESULTS AND DISCUSSION

The results from this study show that the FBG level in non-DM group was invariable throughout the experimental period and the FBG level before the treatment was significantly higher among the groups compared with non-DM groups (Table 1). After treatment the mean value for the final fasting blood glucose (FFBG) in DM control group was significantly higher compared to non-DM control group (Table 1). However, the level of FBG in *A. nilotica* stem bark extract treated groups decreased compared with diabetic controls. Similarly metformin treated group significantly decreases when compared with diabetic control.

The results are similar to those of Niyodusenga, Bukachi [9] who reported the glucose lowering effect of *A. nilotica* in diabetic rats. He suggested that, the hypoglycemic activity of *A. nilotica* extract possibly occurs by stimulating the activity of the β cells of the pancreas and/or due to its insulin like action on insulin sensitive cells.

Adebayo et al. [22] and Yakubu et al. [23] revealed that assessing the level of excretory metabolites such as urea, creatinine and electrolyte levels can be implored as a reliable tool to evaluate renal function.

There was no significant change in the serum sodium, potassium, chloride and bicarbonate levels in the groups administered the *A. nolitica* stem bark extract at tested doses compared to diabetic control (Table 2). However, there was a significant decrease ($P<0.05$) in the serum urea and creatinine levels in the groups administered with *A. nolitica* stem bark extract at 1200 mg/kg and 600 mg/kg doses respectively, compared to diabetic control (Table 2). This result is not in agreement with that of Tanko et al*.* [24] who reported a significant increase in the levels of sodium and chloride with no significant change in urea, creatinine and potassium by leave aqueous extract of *A. nilotica* at 1000 mg/kg. Similarly, Abdulhamid, [21] observed significant changes in the level of sodium, potassium and creatinine. This implied that different solvents may have different capacity to extract secondary metabolites that are important for blood related functions. On the other hand, different parts of medicinal plants could have different concentrations of such metabolites necessary for its medicinal roles.

It was reported that, changes in serum potassium level usually alternate with those of sodium [25]. Conversely, our result shows that, the serum level of both potassium and sodium did not significantly change, compared to control.

Table 1. Effect of stem bark extract of *A. nolitica* on fasting blood glucose level of experimental rats

Parameters	Normal Control	Diabetic Control	Positive Control	300 mg/kg	600 mg/kg	1200 mg/kg
Intial FBG (mMol/L)	4.26 ± 0.53$^{\#}$	8.16 ± 0.60*	7.76 ± 0.31	8.42 ±1.23*	8.58 ±1.09*	8.42 ± 0.63*
Final FBG (mMol/L)	4.31 ± 0.69$^{\#}$	8.92 ± 0.74	6.38 ± 0.59**	7.36 ± 1.35	6.16 ± 0.78**	4.66 ± 0.67$^{\#}$

Values are mean ± SD. Values followed by the same superscript are not statistically different (P<0.05)

Table 2. Effect of *A. nolitica* stem bark extract on electrolyte, urea and creatinine levels of experimental rats

Parameters	Normal Control	Diabetic Control	Positive Control	300 mg/kg	600 mg/kg	1200 mg/kg
Na^+ (mMol/L)	138.60±2.79	138.40±7.54	144.80±6.30	137.60±7.50	135.60±9.15	138.20±6.06
K^+ (mMol/L)	4.24±0.49	3.48±0.43	3.80±0.93	3.76±0.86	3.04±0.68	4.34±0.57
Cl^- (mMol/L)	99.80±3.83	96.20±7.29	99.01±5.70	93.20±4.87	90.40±2.97	96.01±8.80
HCO^{3-} (mMol/L)	27.20±3.27	28.00±4.69	24.40±5.32	27.20±1.92	25.60±3.58	26.40±3.58
Urea (mMol/L)	4.00±0.89	6.10±0.65	4.96±0.38	4.46±0.70	4.60±0.95	4.66±1.04*
Creatinine (mg/dl)	0.44±0.20	1.02±0.13	0.70±0.26	0.68±0.16	0.62±0.15*	0.60±0.22

*Values are mean ± SD (n=5) *statistically different from diabetic control (P<0.05)*

4. CONCLUSION

The present study showed that methanolic stem bark extract of *A. nolitica* produced hypoglycemic effect in alloxan-induced diabetic rats, at the dose tested. Moreover, the plant extract cause slight decrease in the level of electrolytes after treatment at selected doses with significant decrease in urea and creatinine.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

The authors thank Sokoto State University Management for providing necessary facilities to carry out the research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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