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Evaluation of Potential in Wonderful Kola (*Buchiolizia coreica*) Seed Extract on Streptozotocin Induced Type 2 Diabetes in Male Wister Rats

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Abstract

Diabetes mellitus is referred to as a metabolic disorder in which there is high glucose level in the blood as a result of insulin deficiency, resistance or both. Globally, it has been deducted that the adult population with diabetes will rise by 69% for the year 2030. Thus, Bucholzia Coriacea (B. Coriacea) a perennial plant belonging to the family capparidaceae and genus Bucholzia is popularly known as wonderful kola. It's also known as wonderful kola, its other name is called Garcinia kola .it has a long history of use in west Africa and central Africa, thus, the study on evaluation of potential in wonderful kola (buchiolizia coreica) seed extract on streptozotocin induced type 2 diabetes in male wister rats. **Material and Methods:** Fresh seeds of B. coriacea were plucked and washed with distilled water, the filtrate was concentrated using rotary evaporator and water bath. The extract was then weighed and stored in a refrigerator. 100g of crude extract and 1000mg of metformin was properly dissolved in 10ml of distilled water. The rats were carefully selected and separated into cages. 7 albino rats were used for normal control while 4 rats

were kept in each of the remaining cages, and 6 replications were obtained, the test was carried out carefully by injecting the alloxan into the rats intraperitoneally and infecting them with diabetes mellitus, the following sets were made: normal group, negative and positive control group, while three groups were for extracts dosage. With exception of the normal control, all the groups were induced with diabetes. The extract (stem bark of Mangifera indica) will be administered orally to the three set of groups separately (i.e., one extract to one set). Determination of Fasting Blood Glucose Level by Intestinal Glucose Absorption. **Results:** Treatment groups receiving methanol Wonder Kola seed extract showed varying degrees of improvement in these parameters compared to the negative control group. Notably, Group VI, receiving the highest dose of the extract, demonstrated the most significant reduction in urea levels, suggesting a potential protective effect on renal function. The study investigated the effects of Wonder Kola seed extract on serum electrolytes, urea, and creatinine levels in alloxan-induced diabetic albino rats. Notably, significant variations were observed in these biochemical parameters across the different treatment groups. The study assessed the effects of methanol Wonder Kola seed extract on liver enzymes (AST, ALT, ALP) and serum protein levels (total protein, albumin, total bilirubin, direct bilirubin). Significant variations were observed in these parameters among the treatment groups compared to the normal and negative control groups. Treatment with the extract led to notable reductions in liver enzyme levels, indicating potential hepatoprotective effects. **Conclusion:** The findings of this study demonstrate the potential pharmacological benefits of methanol Wonder Kola seed extract in managing diabetes mellitus and associated complications.

Keywords: Evaluation, Potential, Wonderful Kola, Buchiolizia Coreica, Seed Extract, Streptozotocin, Diabetes, Wister Rats

INTRODUCTION

Diabetes mellitus is referred to as a metabolic disorder in which there is high glucose level in the blood as a result of insulin deficiency, resistance or both (American Diabetes Association, 2009). Globally, it has been deducted that the adult population with diabetes will rise by 69% for the year 2030 (Shaw et al., 2010). Type 2 diabetes occurs when there is an advanced determent in insulin action (insulin resistance, IR), which proceeds to β-cell dysfunction due to the failed ability of pancreatic β-cells to compensate for insulin resistance (Srinivasan et al., 2005). The number of people suffering from diabetes worldwide is estimated to be 422 million and 80–90% of them from Type 2 diabetes

(Snowden, 2019). Sedentary lifestyle such as taking high-calorie containing food, lack of exercise, ageing are all risk factors for type two diabetes and hence conduce to the recent rising prevalence of obesity and T2D (Aude et al., 2004). Streptozotocin has been utilized broadly for induction of diabetes both type 1 diabetes and T2D in experimental animals (Szkudelski, 2001). Unfortunately, it lacks the ability to induce IR directly which is one of the pathogenesis of Type 2 diabetes, rather, it induces diabetes from direct pancreatic β-cells damage which resembles a typical Type 1 diabetes (Srinivasan et al., 2005).

Reports gotten from various studies showed that high fat or fructose diet induced insulin resistance in experimental animals but failed to induce hyperglycemia (Srinivasan et al., 2005; Wilson and Islam, 2012). In as much as giving animals a high fructose load alone can induce IR, several weeks may be required to achieve this. Hence, the cost and duration of the study will be high. More so, the animals can naturally develop nutritional tolerance when exposed to longtime feeding with fructose without developing signs and symptoms of IR and impaired glucose tolerance (Stark et al., 2000). Therefore, the search and development of a suitable Type 2 diabetes rat model that will boycott the setbacks experienced in using STZ as single agents to induce IR and Type 2 diabetes came into place. Interestingly, the model has been achieved through a combined effect of fructose and STZ. High fructose load induced IR while a low dose of STZ caused the initial β cell dysfunction and subsequently hyperglycemia (Wilson and Islam, 2012; Stalin et al., 2016). This model is a close replica of the natural history of T2D and its metabolic features in humans. More so, it is cheaper, readily available and useful for investigation various compounds. Plants have been used extensively for treatment of disease due to the fact that they can produce multifarious basic biochemical and organic substances such as carbohydrates, proteins, terpenes, steroids, alkaloids and glycosides (Andrews, 1982).

Bucholzia Coriacea (B. Coriacea) a perennial plant belonging to the family capparidaceae and genus Bucholzia is popularly known as wonderful kola (Joshua et al., 2023). It's also known as wonderful kola, its other name is called Garcinia kola .it has a long history of use in west Africa and central. The earliest record of its use dates back to the 17th century, when European traders brought it to Europe from Africa .in traditional medicine, wonderful kola is believed to have many benefits, including promoting digestive health, treating fever, and reducing inflammation, it is known as the energy seed.it is also been used as a stimulant and as a treatment for liver and kidney problems. Some research has shown that it may have anti-cancer, anti-bacterial and antimicrobial properties. Wonderful

kola improves blood sugar control and insulin sensitivity. (Mohammed et al., 2014). The aim of this research work is to determine the potential of the seed extract of wonderfull kola on hyperglycemic induced.

Figure 1: Wonderful Kola (*Buchholzia coriacea*)

Phytochemical constituent of Buchholzia coriecea (wonderful kola)

Bioactive constituents have been reported in seed of wonderful kola. Authors have reported the presence of alkaloids, saponins, tannins, flavonoids, oxalates, phytates cardiac glycosides, steroids, resins, carbohydrate, anthraquinone, glycosides in seed of wonderful kola (c Ibrahim and Nwachukwu et al., 2014; Obiudu et al., 2015; Okere and Ladeji, 2016; Umeokoli et al., 2016). Authors have variously reported that different extracts of wonderful kola have different effects depending on the specific bioactive ingredients.

In a quantitative determination of dried seed of wonderful kola, Ibrahim and Fagbohun (2012) and Izah et al., (2018) reported that methanol extract of wonderful kola has superior effect compared to ethanol extract with regard to alkaloids, glycosides, saponins, steroids, tannins, flavonoids and sugar content while ethanol extract is superior with regard to phenols and terpenes. Mbata et al. (2009) reported that both hot water and methanol extracts of wonderful kola seeds/leaves contain anthraquinone, whereas Umeokoli et al. (2016), Osadebe et al. (2011) reported that absence of anthraquinone. Ajayi et al., 2021 Nwankwo et al. (2019) reported the presence of phlobatannins, carbohydrates, proteins, tannins, saponins, alkaloids and flavonoids in leave of wonderful kola. Age is one of the essential considerations often made in determining bioactive constituents in plants. The

presence of phytochemicals/bioactive ingredients or compounds in plants is an indication that they have biological activity (Kigigha et al., 2018,). Ibrahim and Fagbohun (2012) considered alkaloids as the most efficient therapeutic constituents of plant. Alkaloids have some medicinal potential including central nervous system, stimulant, pain reliever, pyretic action, anesthetics in ophathalmology (Heikens et al., 1995). Izah (2018), Kigigha et al. (2015) reported that alkaloids have mechanisms to wade off pests including microorganisms. Probably due to the pain-relieving potentials of alkaloids, it can be used as analgesics. Ojelere (2014), Ibrahim and Fagbohun (2012), Izah etal., (2018) reported that derivatives of alkaloids can be used as analgesic, and antispasmodic.

The presents of phenol compounds in plants are an indication of its pesticidal properties. Typically, phenolic compounds are used for disinfection, and it also remain a standard which other bacteria are compared (Ibrahim and Fagbohun, 2012). Phenol compounds can easily oxidize to form phenolate ion, an electron acceptor (Ibrahim and Fagbohun, 2012). Flavonoids which is an example hydroxylated phenolic compounds help plants to resist disease causing microbes (Opoku and Akoto, 2015; Epidi et al., 2016a, b). Probably due to this, it has anti-oxidant, anti-microbial and anti-tumor properties (Osuntokun and Oluwafoise, 2015; Epidi et al., 2016a, b), anti-allergies, anti-inflammation, platelet aggregation, free radicals, anti-ulcer and hepatoxins potentials (Ibrahim and Fagbohun, 2012).

The hot taste of wonderful kola seed is probably due to the presence of tannin (Ibrahim and Fagbohun, 2012). Tannin is highly toxic to microbes. Tannins also play essential role in wound healing including varicose ulcers, hemorrhoids, frostbite and burns (Ibrahim and Fagbohun, 2012; Kigigha et al., 2015;). Saponin helps to inhibit sodium ion efflux by blockage of the entrance of the sodium ion out of the cells (Ibrahim and Fagbohun, 2012). The presence of saponin suggests that the plant could be used as cough suppressant. Many other bioactive constituents of plants also have medicinal potentials.

Scientific validation of wonderful kola

In the scientific validation of the medicinal potency of wonderful kola, several species of microbes including bacteria (gram positive and negative) and fungi have been studied. Also, in the non- microbial caused disease condition, organisms such as rat and mice have been widely used as experimental organisms.

Anti-microbial Studies have variously shown that wonderful kola seed contain antimicrobial (antibacterial and antifungal) activities (Izah etla., 2018). Furthermore, the antimicrobial properties have been widely attributed to bioactive components (Kigigha et al., 2015) such as alkaloids and tannins. Studies have indicated that seed of wonderful kola is sensitive to both gram positive and gram-negative organisms.

Antioxidants

Antioxidants are essential in maintaining optimum cellular functions in humans (Akinyede et al., 2021). According to Akinyede et al. (2021), humans have evolved highly complex antioxidant systems that work together to protect the body from aging and pathogenesis of age-related disorders such as cancer, hypertension, atherogenesis, alzheimer and parkinson disease. Antioxidants also play essential role in detoxifying some toxicant in the human body. Adisa et al. (2011) also reported that seed extract of wonderful kola has antioxidant activity. Nwaehujor et al. (2012) reported that reported that methanol fruit extract of wonderful kola possesses antioxidant activities. Adisa et al. (2011) demonstrated that ethanol and butanol seed extracts of wonderful kola is has antioxidant activity. The anti-oxidant potency of wonderful kola may be associated to the presence of n-Hexadecanoic acid, hexadecanoic, 15-methyl-, methyl ester, (Z)-Docos-13-enoic acid, 9,12-Octadecadienoic acid and 9,12 Octadecadienoyl chloride (Z, Z).

Hyperlipidemia, Anti-Hypercholesterolemic And Anti-Atherogenic Activity

Oluchi et al. (2017) described hyperlipidemia as an anomalistic increase of lipids in the blood, abundance of triglycerides and cholesterol. This is due to uneven rise in lipoproteins that play essential role in the transportation of lipids in the blood, branded as hyperlipoproteinemia (Oluchi et al., 20170. Biswas et al. (2017), Oluchii et al. (2017) reported that hypercholesterolemia is the most prevalent variety of dyslipidemia that could predispose an individual to cardiovascular diseases such as atherosclerosis, and pancreatitis. Botanicals such as wonderful kola have demonstrated clinic efficacy for the management of hyperlipidemia using male wistar rats as test organisms (Oluchi et al., 2017). Hypercholesterolemia is a condition characterized with high level of cholesterol in the blood (Obode and Adebayo 2020) and it's the major cause of atherosclerosis (Obode and Adebayo 2020). According to Obode and Adebayo (2020), atherosclerosis is a major cause of chronic non –infectious diseases such as stroke and some other cardiovascular. Hypercholesterolemia has the tendency to predispose an individual to hypertension and

cardiovascular diseases (Edijala et al., 2005). The disease is basically cause by both genetic and environmental factors. Botanicals have showed to have positive effect towards its management. Obode and Adebayo (2020) demonstrated that ethanolic seed extract of wonderful kola contain anti-hypercholesterolemic agent using rat as experimental organisms. Obode and Adebayo (2020) reported that ethanolic seed extract of wonderful kola has anti-atherogenic activity which the authors attributed to the presence of flavonoids, saponins and plant sterols. Furthermore, anti-hypocholesterolemic potentials of wonderful kola may be associated to the presence of n-Hexadecanoic acid, 9,12-Octadecadienoic acid and 9,12 Octadecadienoyl chloride (Z, Z).

Anti-fertility

Fertility is the natural tendency to produce offspring. Fertility rate is the number of offspring born per mating pair within a given population. In recent times, fertility issues are becoming a major challenge in some part of the world. Some botanicals have demonstrated the potentials to be used as anti-fertility agents. Obembe et al. (2012) demonstrated that seed extracts of wonderful kola have anti-fertility effects in male rats and indicated that epididymis is the most probably site of action.

Anti-helminthic

Helminths are invertebrates characterized by elongated, flat or round bodies and are generally called worm. The parasite has several types including flukes (trematodes), tapeworms (cestodes), roundworms (nematodes) etc. Botanicals have been used to managing helminthes. Nweze and Asuzu (2006) reported that seed of wonderful kola have anti-helmintic properties. Nwankwo et al. (2019) demonstrated that the leaves of wonderful kola are effective against Fasciola hepatica, Phertima posthuma and Taenia solium. red-Jaiyesimi, et al. (2011) reported that ethanolic seed extracts of wonderful kola have larvicidal action against Haemonchus contortus and Heligmosomoides polygyrus. Fred-Jaiyesimi et al. (2011) reported chloroform and methanol seed extracts of wonderful kola have anti-helmintic potentials against Eudrilus eugeniae (earthworm) and Bunostomum phlebotomum (cattle hookworm).

MATERIALS AND METHODS

Collection of Seed Materials

The Seed

Fresh seed of wonderful kola (buchholzia coriacea) were purchased from Wukari market, Wukari Taraba state, Nigeria and were authenticated in the department of biochemistry at federal university Wukari, Taraba, Nigeria.

Preparation of The Seed Materials

Fresh seeds of B. coriacea were plucked and washed with distilled water. The sliced seeds were spread on a clean mat in a well-ventilated room with regular turning to enhance even drying and avoid decaying. The sliced seeds were shade-dried for 10 weeks. The shade dried sliced seeds were pulverized with an electric blender and a known weight (800 g) of the pulverized B. coriacea seeds were macerated in 70% ethanol (700 ml) and allowed to stand for 24 h. The mixture was separated with Whatman No. 1 filter paper. The filtrate was concentrated using rotary evaporator and water bath. The extract was then weighed and stored in a refrigerator.

Equipment and Materials

Weighing balance, syringes (1ml, 2ml, 5ml, 10ml) Buchholzia coriacea seed extract, distilled water, animal feed (Top feed), cages, formaldehyde, drinking bottles, alloxan, measuring cylinder, cotton wool, methylated spirit, hand gloves, reagent bottles, methanol.

Extract Preparation

100g of crude extract taken into a conical flask, and 100ml of distilled water was added to the sample and mixed to form a solution.

Preparation of Standard Drug (Metformin)

1000mg of metformin was properly dissolved in 10ml of distilled water.

Breeding of Animals (Albino Rats)

Samples used for this work were 27 disease-free (healthy) albino rats which were purchased at Yola, Adamawa State. The rats were carefully selected and separated into cages. 7 albino rats were used for normal control while 4 rats were kept in each of the remaining cages, and 6 replications were obtained. The test was carried out carefully by injecting the alloxan into the rats intraperitoneally and infecting them with diabetes mellitus. The rats were

maintained under standard laboratory conditions and were allowed free access to standard diet and water ad libitum (as often as necessary). They were also allowed to acclimatize for 24 hours and feeding was done regularly.

Experimental Design

After the albino rats were randomly divided into different groups, the following sets were made: normal group, negative and positive control group, while three groups were for extracts dosage. With exception of the normal control, all the groups were induced with diabetes.

The extract (stem bark of *Mangifera indica*) will be administered orally to the three set of groups separately (i.e., one extract to one set) as shown in Table 1 below for 14 days.

Statistical Presentation and Processing

Every data collected in the course of this work was statistically presented, processed and analysed to the best of standards.

Method of Data Collection

Collection of data was done at interval of 7 days (1 week) after the administration of the first treatment dose in the albino rates. Parameters were duly collected and analysed.

Method of Data Analysis

Data collected were subjected to Analysis of Variance (ANOVA) using the Statistical Package for the Social Sciences (SPSS) for test of hypothesis for the final results, discussion and conclusion in statement of facts of this research work.

Determination of Fasting Blood Glucose Level

The rats were allowed free access to food and water and housed at relatively constant room temperature. Food was withdrawn from all groups 18 h prior to the start of experiment and blood was obtained from the tail vein of rats for glucose concentration which was determined through a quantitative glucose oxidase method using a glucometer stripe plus glucose monitoring system. The instructions provided by the kit manufacturer were essentially followed.

Determination of Intestinal Glucose Absorption

To evaluate the effect of fasting duration on intestinal absorption of glucose, the method described by Odukanmi et al 2022, was used. The rats were allowed free access to food and

water and housed in a relatively constant room temperature. Food was withdrawn from the animals prior to the experiment and they were anesthetized with ketamine (75 mg/kg body weight). The trachea was slit opened to allow animals breathe spontaneously. Through a midline laparotomy, the intestinal segments of about 20 cm long were identified for consistency after separating the intestine into 2 major segments. The proximal segment was distal to the ligament of Treitz (Jejunum) while the distal end was just proximal to the ileocecal junction (ileum). The segments were open at both ends then to permit gentle irrigation with Ringers solution. The excess fluid was removed by gently forcing air under low pressure through the segments. The distal end of each segment was then ligated and 4 mL of Ringers solution containing 4.4 g of glucose was infused into each segment through the proximal ends. The proximal open ends were then ligated and the intestinal segments were returned to the abdominal cavity, and were sutured. The temperature of each animal was maintained with a heating lamp. The initial glucose concentration was noted and samples were collected at intervals of 60 minutes from each animal. The glucose concentrations were analysed through a quantitative assay (Glucose Oxidase) method using Fine test glucose monitoring system. Each study lasted for 1 hour, at the end of which the two segments were drained of their content and dried with a filter paper. Weights of each intestinal segment were determined and amount of glucose absorbed per gram of intestinal segment was evaluated. The difference between the initial glucose concentration and the final glucose concentration was divided by the factor of their respective weight in gram.

RESULTS

1 Result Presentation and Description

This describes the experiment's results, which demonstrated the extract's impact on various organs, by measuring the blood's levels of some biochemical parameters

Table 1: Effect of Buchiolizia Coreica Seed Extraction Blood Glucose

Groups	**Day 1**	**Day 3**	**Day 7**	**Day 14**
Normal Control	5.65 ± 0.19^{a}	5.76 ± 0.21^{a}	5.74 ± 0.16^{ab}	5.25 ± 0.22^{ab}
Negative Control	23.78 ± 0.30^{d}	24.73 ± 0.58^{d}	25.37 ± 1.93^{d}	27.07 ± 0.51^{d}
Positive Control	6.23 ± 0.47^{a}	5.49 ± 0.37^{a}	5.41 ± 0.33^{a}	4.78 ± 0.18^{a}
100 mg/kg	18.09 ± 1.00^{c}	6.22 ± 0.28^{b}	6.55 ± 0.53^{b}	5.77 ± 0.67^{b}
200 mg/kg	14.30 ± 0.80^{b}	5.77 ± 0.40^{a}	5.07 ± 0.61^{a}	5.68 ± 0.19^{b}
400 mg/kg	22.29 ± 0.56^{d}	18.38 ± 0.72^{c}	17.19 ± 0.55^{c}	14.51 ± 0.39^{c}

Values are presented as Mean ± SD. Values with different superscript across group indicates a significant ($p<0.05$) difference.

Table 2: Effect of *Buchiolizia Coreica* Seed Extraction Hepatic Marker Enzymes

GROUPS	ALT (U/I)	AST (U/I)	ALP (U/I)
Normal Control	20.00 ± 0.41[a]	35.09 ± 2.07[a]	80.21 ± 0.44[a]
Negative Control	58.11 ± 0.42[d]	60.60 ± 1.12[d]	255.80 ± 1.12[d]
Positive Control	29.98 ± 0.12[b]	38.00 ± 2.18[b]	80.69 ± 1.49[a]
100 mg/kg	40.00 ± 0.22[c]	48.00 ± 1.11[c]	98.22 ± 1.11[c]
200 mg/kg	31.00 ± 0.12[b]	46.09 ± 1.81[c]	86.99 ± 1.01[b]
400 mg/kg	28.99 ± 0.31[b]	38.15 ± 2.00[b]	87.00 ± 1.12[b]

Values are presented as Mean ± SD. Values with different superscript across group indicates a significant ($p<0.05$) difference.

Table 3: Effect of *Buchiolizia coreica* Seed Extraction Serum Proteins/Bilirubin

GROUPS	TB (µmol/L)	DB (µmol/L)	TP (g/dL)	ALB (g/dL)
Normal Control	4.58 ± 0.27[a]	3.29 ± 0.12[a]	14.13 ± 0.55[c]	10.83 ± 0.10[d]
Negative Control	15.62 ± 0.09[d]	8.41 ± 0.10[d]	10.95 ± 0.37[a]	6.13 ± 0.05[a]
Positive Control	8.10 ± 0.17[c]	4.42 ± 0.12[b]	14.42 ± 0.26[c]	9.82 ± 0.18[c]
100 mg/kg	7.00 ± 0.20[b]	6.01 ± 0.11[c]	10.90 ± 0.42[a]	6.09 ± 0.12[a]
200 mg/kg	7.11 ± 0.22[b]	4.00 ± 0.09[a]	12.50 ± 0.66[b]	8.00 ± 0.13[b]
400 mg/kg	6.99 ± 0.18[b]	4.66 ± 0.14[b]	12.90 ± 0.45[b]	9.90 ± 0.10[c]

Values are presented as Mean ± SD. Values with different superscript across group indicates a significant ($p<0.05$) difference. *Key: TB: total bilirubin, DB: direct bilirubin, TP: total protein, ALB: albumin*

Table 4: Effect of *Buchiolizia coreica* seed extraction Serum Electrolytes Urea Creatinine (SEUCR) Parameters

Groups	Urea(mg/dl)	Cr(mg/dl)	Na^+(mmol/L)	K^+(mmol/L)	Cl^-(mmol/L)	$HCO3^-$ (mmol/L)
I	42.96 ± 0.20[a]	1.35 ± 0.18[a]	135.20 ± 2.00[a]	5.36 ± 0.30[a]	87.65 ± 5.07[a]	22.50 ± 1.60[d]
II	70.03 ± 0.18[e]	2.50 ± 0.21[d]	160.82 ± 3.90[d]	7.87 ± 0.61[d]	126.76 ± 5.72[f]	9.20 ± 0.52[a]
III	56.62 ± 0.18[d]	1.52 ± 0.22[a]	138.00 ± 1.90[ab]	4.98 ± 0.23[a]	100.11 ± 4.80[b]	19.50 ± 2.00[c]
IV	50.75 ± 0.19[c]	1.60 ± 0.16[a]	140.00 ± 2.80[b]	6.43 ± 0.52[b]	116.90 ± 6.87[e]	18.02 ± 1.80[b]
V	46.72 ± 0.21[b]	1.54 ± 0.20[a]	139.22 ± 2.80[ab]	6.31 ± 0.21[b]	110.54 ± 3.90[d]	18.42 ± 1.90[b]
VI	43.15 ± 0.20[a]	1.53 ± 0.19[a]	150.11 ± 3.00[c]	5.90 ± 0.38[ab]	108.03 ±6.81[c]	18.77 ± 1.65[bc]

Values are presented as Mean ± SD group. Values with different superscript across group indicates a significant ($p<0.05$) difference. *Key:*

Cr: creatinine, Na^+: sodium, K^+: potassium, Cl:chloride, HCO_3^-: bicarbonate

1. Effect of *Buchiolizia coreica* seed extract on blood glucose

The results presented in Table 4.1 demonstrate significant ($p<0.05$) variations in blood glucose levels among the different groups over the course of the study. Notably: Normal Control Blood glucose levels remained relatively stable throughout the study period, with slight fluctuations observed on different days. Negative Control group, consistently exhibited markedly elevated blood glucose levels compared to the normal control group across all days. Blood glucose levels for positive control group remained consistently lower compared to the negative control group. While groups receiving 100 mg/kg, 200 mg/kg, and 400 mg/kg Groups different doses of Buchiolizia coreica seed extract displayed varied blood glucose levels across the study days. Notably, higher doses (200 mg/kg and 400 mg/kg) showed a trend of decreasing blood glucose levels over time, with the most pronounced reductions observed on day 14.

2. Impact of buchiolizia coreica seed extract on ALT Activity

From the data in table 4.2, a significant ($p\leq0.05$) divergence in ALT levels was observed across the groups. Group II (58.11 ± 0.42) and groups IV (40.00 ± 0.22), V (31.00 ± 0.12), and VI (28.99 ± 0.31) displayed marked differences compared to the normal control group I (20.00 ± 0.41). Notably, groups I, III, IV, V, and VI exhibited significant differences in ALT levels compared to the negative control group II.

3. Impact of buchiolizia coreica seed extract on AST Activity

Table 4.2 indicates that, when compared to the normal control group I (35.09 ± 2.07), which received only distilled water, group II (60.60 ± 1.12), the negative control group that received only alloxan,group III (38.00 ± 2.18), the positive control group,and group IV (48.00 ± 1.11), group V (46.09 ± 1.81) and V (38.15 ± 2.00) showed a significant ($p\leq0.05$) difference in AST levels. And significant ($p\leq0.05$) difference was observed when all groups are compared with group II. But there was no significant difference between group III and group VI, group IV and group V.

4. Impact of buchiolizia coreica seed extract on ALP Activity

The findings from table 4.2 revealed a significant ($p \leq 0.05$) variation in ALP levels among the groups. Group II (255.80 ± 1.12) and groups IV (98.22 ± 1.11), V (86.99 ± 1.01), and VI (87.00 ± 1.12) exhibited marked differences compared to the normal control group I (80.21 ± 0.44), with the exception of group III. All groups demonstrated a significant ($p \leq 0.05$) divergence in ALP levels compared to the negative control group II.

5. Impact of buchiolizia coreica seed extract on Total Protein Activity

Table 4.3's results showed that there was a significant ($p<0.05$) difference in the groups' TP levels. In comparison to the normal control group I (14.13 ± 0.55), the results indicated a significant ($p<0.05$) difference in TP level for groups II (10.95 ± 0.37), IV (10.90 ± 0.42), V (12.50 ± 0.66), and VI (12.90 ± 0.45). However, no significant ($p<0.05$) difference was found between group III (14.42 ± 0.26 c) and group I. Additionally, when comparing the groups (I, III, V, and VI) to the negative control group (II), there is a significant ($p<0.05$) difference. There was no discernible difference ($p<0.05$) between groups II and IV.

6. Impact of buchiolizia coreica seed extract on Albumin Activity

The results from table 4.3 indicated significant ($p<0.05$) differences in AB levels among the groups. Groups II (6.13 ± 0.05) and IV (6.09 ± 0.12) showed marked differences compared to the normal control group I (10.83 ± 0.10). However, no significant ($p<0.05$) difference was observed between groups II and IV, or between groups III and VI.

7. Impact of buchiolizia coreica seed extract on Total Bilirubin Level

The findings from table 4.3 revealed significant ($p<0.05$) differences in TB levels among the groups. Groups II (15.62 ± 0.09 d), III (8.10 ± 0.17 c), IV (7.00 ± 0.20), V (7.11 ± 0.22), and VI (6.99 ± 0.18) exhibited marked differences compared to the normal control group I (4.58 ± 0.27a). Significant ($p<0.05$) differences were observed for all groups compared to the negative control group II, while no significant ($p<0.05$) difference was observed between groups IV, V, and VI.

8. Impact of buchiolizia coreica seed extract on Direct Bilirubin Level

From table 4.3, significant ($p<0.05$) differences in DB levels were observed among the groups. Groups II (8.41 ± 0.10 d), III (4.42 ± 0.12 b), IV (6.01 ± 0.11), and VI (4.00 ± 0.09) exhibited significant differences compared to the normal control group I (3.29 ± 0.12). Significant ($p<0.05$) differences were observed for all groups compared to the

negative control group II, with no significant difference observed between groups III and VI.

9. Impact of buchiolizia coreica seed extract on Urea Levels

Group II, the negative control (70.03 ± 0.18 e), exhibited the highest urea levels, significantly different from the other groups. Group VI (43.15 ± 0.20 a), the treatment 3 group, showed the lowest urea levels, which were significantly different from those of group II. Groups III, IV, and V demonstrated intermediate urea levels, with no significant differences observed among them.

10. Impact of buchiolizia coreica seed extract onCreatinine (Cr) Levels

Similar to urea levels, Group II displayed the highest creatinine levels (2.50 ± 0.21 d), significantly different from the other groups. Groups III, IV, and V showed lower creatinine levels compared to the negative control, with no significant differences observed among them. Group I, the normal control, exhibited the lowest creatinine levels (1.35 ± 0.18 a).

11.Impact of buchiolizia coreica seed extract on Sodium (Na+) Levels

Group II (160.82 ± 3.90 d), the negative control, demonstrated the highest sodium levels, significantly different from the other groups. Group III (138.00 ± 1.90 ab), the positive control, exhibited sodium levels significantly lower than those of the negative control but higher than those of the treatment groups IV, V, and VI, which showed intermediate levels. Group I showed the lowest sodium levels (135.20 ± 2.00 a).

12. Impact of buchiolizia coreica seed extract on Potassium (K+) Levels

Consistent with the pattern observed in other parameters, Group II (7.87 ± 0.61 d) showed the highest potassium levels, significantly different from the other groups. Groups III, IV, V, and VI displayed lower potassium levels compared to the negative control, with no significant differences observed among them. Group I showed the lowest potassium levels (5.36 ± 0.30 a).

13. Impact of buchiolizia coreica seed extract on Chloride (Cl-) Levels

Group II (126.76 ± 5.72 f), the negative control, exhibited the highest chloride levels, significantly different from the other groups. Groups III, IV, V, and VI demonstrated lower chloride levels compared to the negative control, with no significant differences observed among them. Group I showed the lowest chloride levels (87.65 ± 5.07 a).

14. Impact of buchiolizia coreica seed extract on Bicarbonate (HCO3-) Levels

Similar to other parameters, Group II (9.20 ± 0.52 a) showed the highest bicarbonate levels, significantly different from the other groups. Groups III, IV, V, and VI displayed lower bicarbonate levels compared to the negative control, with no significant differences observed among them. Group I showed the highest bicarbonate levels (22.50 ± 1.60 d).

DISCUSSION

Alloxan is cytotoxic to β-cells in pancreatic islets of Langerhans, leading to reduced insulin release and glucose consumption by body tissues (Bahar, 2017). Alloxan is a known diabetogenic drug used to induce Type 2 diabetes in animals. It operates by triggering necrosis of pancreatic beta cells by the formation of free radicals (Etuk 2010), resulting in metabolic derangements such as a rise in blood glucose levels. Administration of high dose Alloxan to the rats, significant increase blood glucose level (hyperglycemia), Treatment with methanol Wonder Kola seed extract led to significant reductions in fasting blood glucose levels in alloxan-induced diabetic rats. This effect was particularly pronounced in groups receiving higher doses of the extract, suggesting a dose-dependent antidiabetic effect, this is in agreement with Okolo (2016), who in his work deduced that Treatment of alloxan-induced diabetic mice with the crude extracts of B. coriacea seed brought down the raised blood glucose levels significantly ($P = 0.043$) in a dose-dependent manner. The ability of the extract to lower blood glucose levels highlights its potential as an adjunct therapy for managing diabetes mellitus.

Serum creatinine and urea are well-established indicators of Glomerular Filtration Rate (GFR), which is the first stage in producing urine. It is the process by which the kidneys filter excess fluid and waste items from the blood into the kidney's urine collecting tubules, allowing them to be removed from the body (Lapshak et al., 2016). The study investigated the effects of Wonder Kola seed extract on serum electrolytes, urea, and creatinine levels in alloxan-induced diabetic albino rats. Notably, significant variations were observed in these biochemical parameters across the different treatment groups.

Group II, serving as the negative control, exhibited the highest levels of urea and creatinine (azotaemia), sodium (hypernatremia), potassium (hyperkalaemia), chloride(hyperchloremia), and reduced bicarbonate(acidosis), indicating the detrimental impact of alloxan-induced diabetes on renal function and electrolyte balance. Conversely,

treatment groups receiving methanol Wonder Kola seed extract showed varying degrees of improvement in these parameters compared to the negative control group. Notably, Group VI, receiving the highest dose of the extract, demonstrated the most significant reduction in urea levels, suggesting a potential protective effect on renal function. Anionye (2019) indicated in his contribution that increased creatinine levels in diabetes patients could be caused by reduced nephron function. The study further proposed that elevated urea levels in diabetes mellitus patients could be due to a reduction in the kidney's filtration function, resulting in the accumulation of waste products inside the system. Also, changes in serum Na+ and K+ levels have been linked to impaired renal function (Mohammmed et al., 2017).

Chronic mild elevations of transaminases are frequently found in type 2 diabetes and often reflect underlying insulin resistance (Harris, 2005). ALP is a membrane bound enzyme while ALT and AST are cytosolic enzymes. These enzymes are highly concentrated in the liver and kidney and are only found in the serum in significant quantities when the cell membrane becomes leaky and even completely ruptured. The study assessed the effects of methanol Wonder Kola seed extract on liver enzymes (AST, ALT, ALP) and serum protein levels (total protein, albumin, total bilirubin, direct bilirubin). Significant variations were observed in these parameters among the treatment groups compared to the normal and negative control groups. Treatment with the extract led to notable reductions in liver enzyme levels, indicating potential hepatoprotective effects. Furthermore, alterations in serum protein levels suggest a modulatory effect on hepatic function and protein metabolism.

CONCLUSION

The findings of this study demonstrate the potential pharmacological benefits of methanol Wonder Kola seed extract in managing diabetes mellitus and associated complications. The extract exhibited favorable effects on serum electrolytes, renal function, liver enzymes, serum protein levels, and antibacterial activity. Moreover, significant reductions in fasting blood glucose levels were observed, indicating promising antidiabetic properties. These findings support the traditional use of Wonder Kola seed extract in folk medicine and warrant further investigation into its therapeutic mechanisms and clinical applications

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Conflict of Interests

All authors have none to declare.

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