Original Research Article

BIOCHEMICAL CHANGES IN STREPTOZOTOCIN-INDUCED DIABETIC RATS FED WITH HIGH CONCENTRATION OF *COLOCASIA ESCULENTA* FLOUR.

ABSTRACT

Background: An endocrine and metabolic disease of the pancreas such as Diabetes Mellitus (DM), is of Public health dimension responsible for 536.6 million cases in the globe. The treatment of DM takes lots of resources, making alternative treatment options like the utilization of medicinal plants like Colocasia Esculenta (CYN) a point of research, hence this study involving biochemical evaluation of streptozotocin-induced diabetic rats (SIDR) fed on high concentration of the flour. **Methodology:** CYN was processed into into pellets, dried in an oven at 60°C, and adequately stored for further use. Fourty-two male albino rats with weights ranging from 134 and 247 grammes, were purchased, acclimatized and induced with insulin resistance by the administration of 10% fructose diet, thereafter, the rats were made to develop type-2 diabetes mellitus (T2DM) by the intraperitoneal injection of streptozotocin. For 28 days, an intervention formulation consisting of 50:50% ratio of cocoyam flour and commercial rat feed, was administered at the end of which blood samples were collected from the slaughtered animals for various biochemical analyses. **Results & Discussion**: The active biological substances in the cocoyam flour included phenolics, D-stilbene, phthalate, and artemisinin, along with more antioxidant minerals than those found in usual rat meals. The formulation exhibited CAT activity of 7.9 units/min and DPPH of 53.2%. Poor glycemic control was suggested by the persistently elevated random blood glucose readings observed along the time trend. Although the results of the liver function tests were similar for the intervention and standard control, the formulation was more effective than metformin at reducing lipid peroxidation and in the hypolipidemic effects. **Conclusion:** Administration of high cocoyam flour concentration demonstrated comparable biochemical effects to the anti-diabetic drug metformin in SIDRs, despite its poor glycemic control. This suggests that cocoyam flour may be applied as a supplemental treatment for people with T2DM.

Keywords: Cocoyam flour, glycemic control, diabetic rats

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1. INTRODUCTION

Diabetes mellitus (DM) is responsible for 536.6 million cases in the world (10.5%) with a projected affected population of 783.2 million people by 2045 [1]. Various complications such as cardiovascular, renal and ocular diseases are among health effects of hyperglycemia brought on by pancreatic cell malfunction or inadequate insulin synthesis [2]. Cases of diabetes mellitus are rising faster in low-income countries—like Nigeria—than in high-income

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ones, with higher incidence, prevalence, and daily adjusted life years (DALYs) [3]. There are several challenges associated with managing diabetes, including those related to finances, labour, the infrastructure of healthcare, and managing complications [4]. For individuals impacted, this lowers quality of life, productivity, and life expectancy [5].

The high costs and complexity of managing diabetic complications pose a substantial challenge in countries with fragile healthcare systems and limited resources [6]. As a result, there is an urgent need to look into cost-effective techniques to reduce illness prevalence, severity, and complications while maximising available resources, particularly in developing nations. Integrating lifestyle changes, such as following suggested dietary patterns and increasing physical activity, as supplementary management techniques have been demonstrated to dramatically reduce risk factors, lowering the frequency of new cases, disease severity, and related comorbidities [7]. Various management strategies such as use of Diabetic Medical Diet Therapy have been introduced with promising results [8]. Other dietary interventions have been proven to aid diabetes mellitus treatment [9]. Among such dietary interventions is the use of plants and plant-based diets which has been championed by the World Health Organisation for the management of T2DM [10]. Bioactive substances with anti-inflammatory and antioxidant qualities are found in such therapeutic plants including cocoyam, whose *in vitro* and *in vivo*, activities are associated with immunomodulatory and antihyperglycemic effects [11, 12].

The bioactive compounds in plant food extracts include peptides, amino acids, flavonoids, and polyphenols, which stimulate pancreatic β-cells and hepatic enzymes to regulate blood glucose levels (13). Numerous investigations have demonstrated that the phytochemicals in cocoyam have hypoglycemic and antioxidant properties [14, 15]. Eleazu and colleagues [16] found that the mechanism behind this antidiabetic activity was associated with the suppression of acute pancreatitis and the delay or regulation of the starch-to-glucose conversion process. Many other medicinal plants such as extracts from the bulb of Allium sativum L, the leaf extract of Aloe vera, and the seed kernel of Mangifera indica, have

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been demonstrated to provide anti-diabetic properties [17]. This study aimed to evaluate the antidiabetic and other biochemical benefits of cocoyam flour, a plant-based diet, administered to diabetic rats.

2. MATERIAL AND METHODS

Collection and Preparation of the Plant Food Material

The roots of a variety of cocoyam (*Colocasia Esculenta*) identified with the accession number NCe 005, was adequately processed and pelletized before storing them in an airtight container for future use.

Experimental Animals

Fouty-two (42) male albino rats weighing between 134 and 249 grammes were procured, and divided into set of four, tagged, A, B, C, and D. Each set had ten rats, identified by a permanent marker numbered 1–10. Weekly weights of the rats were kept, while food and drink were administered ad libitum for one week for acclimatization to occur. All laboratory animals were cared for following established procedures [18].

Induction of Insulin Resistance Using Low Fructose Diet

Low fructose diet (10%) was made by dissolution of 30 grammes of fructose in 300 millilitres of water and administered to the rats for one week, to achieve insulin resistance.

Induction of Type 2 Diabetes Mellitus using STZ

The rats were fasted overnight on the sixth day of the administration of 10% fructose diet, and their blood glucose levels were measured to establish normoglycemia. All normoglycemic rats except the normal control group of nine rats, were given intraperitoneal injections of Streptozotocin (STZ) by dissolving 1 g in 50 mL of freshly prepared sodium citrate buffer solution, using the formula for giving extracts to experimental animal subjects [19, 20]. Before beginning the experimental feeding procedures, blood samples were taken from the treated rats' tail veins at 72 hours and day 12 after STZ exposure and tested for blood glucose levels using a blood glucose meter (Acu-check activeR). The hyperglycemic rats were randomly assigned to the standard control, negative control, and intervention groups. All the groups

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received treatment for 28 days. Groups A and B received commercial rat feed and water only, Group C received metformin at 200 mg/kg, as 0.002 ml per Kg body weight orally daily using an oral dispenser, and Group D received a blend of Colocasia esculenta flour and commercial rat feed at 50:50 ratio [21].

The groups were as follows:

Group A: Standard Control

Group B: Normal Control

Group C: Negative Control

Group D: STZ-induced diabetic rats administered with *Colocasia Esculenta* (Cocoyam) flour intervention feed

Biochemical Analysis

a. Estimation of blood glucose, lipid profile, liver function, kidney function and myocardial function tests

After 28 days, the rats were given an overnight fast, and their final body weights recorded. The blood glucose levels were determined using a glucometer (Acu-check activeR). The triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were determined with Randox test diagnostic kits [22]. The levels of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol were also determined using Frieddewald *et al* formula [23]. The assessment of liver function parameters (serum bilirubin, total protein, serum glutamate oxaloacetate transaminase, ALT, and serum glutamate pyruvate transaminase, AST), as well as kidney and cardiac function (urea and creatinine), was carried out under the protocol described by Jin and colleagues [24].

b. Estimation of Antioxidant Mineral Analysis

The analysis of antioxidant minerals, including zinc, copper, magnesium, and manganese, was conducted using the Atomic Absorption Spectrophotometer (AAS) (Analyst 200, Perkin Elmer, Wallham, MA, USA).

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c. Determination of antioxidant activities (DPPH)

The 2, 2-Diphenyl 1-picrylhydrazyl (DPPH) Free Radical Scavenging Activity was determined by spectrophotometric analysis. We followed the steps that Oulai and associates described [25]. The antioxidant was computed using the sample extract's potential for free radicals.

d. Estimation of antioxidant enzyme system [Superioxide dismutases (SOD), Catalase, (CAT), GLuthathione Peroxidase (GPx), Reduced and Oxidized Glutathione (GSH) and Glutathione-S-Transferase (GST)] Activities.

A superoxide scavenging activity was carried out according to the modified NBT reduction approach proposed by Lalhminghlui and Jagetia [26], with a pure DMSO control employed to measure the mixture's absorbance at 560 nm and ascorbic acid (AA) serving as the reference standard for the percentage calculation to evaluate the free radical scavenging ability. The catalase activity was measured using a spectrophotometric method of Mukhtar and colleagues [27].

The quantification of glutathione peroxidase activity was done using erythrocyte hemolysate under Paglia and Valentine's criteria [28], and the findings were expressed in mg/gHb, while the reduction and oxidation of glutathione were quantified using the protocol described by Beutler and colleagues [29]. The calibration curve, which was made using GSH solutions at various concentrations, was used to translate the absorbance of the samples into concentrations. The GSH levels in erythrocytes were normalised to the haemoglobin value and expressed as mg/g GSH/Hb. mg/g was employed in the final results report.

e. Estimation of Lipid peroxidation

The lipid peroxidation test method created by Ohkawa and colleagues [30] was employed to determined lipid peroxidation which was recorded as MDA free radical scavenging activity.

Quantitative Analysis of Bioactive compounds using Gas chromatography-Mass Spectrometry (GC-MS).

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After ten grammes (10 g) of cocoyam flour were added to 2.5 L of methanol and allowed to mix for 48 hours, a soxhlet apparatus was used to extract the filtrate for three hours at 500C. To search for phytochemical components in the extract, mass spectrometry (MS; 5975B MSD) and gas chromatography (GC; Agilent 6890N) were employed.

Statistical Analysis

The results were then gathered and expressed as the standard error of the mean (SEM) of triplicate for eight rats in each group using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) version 20.0. The statistical significance of the mean difference was assessed using Tukey's post-hoc test, with a significance level of $P<0.05$. A one-way analysis of variance (ANOVA) was used to compare the means.

3. RESULTS AND DISCUSSION

1.0 Antioxidant Mineral Composition & Antioxidant Activities

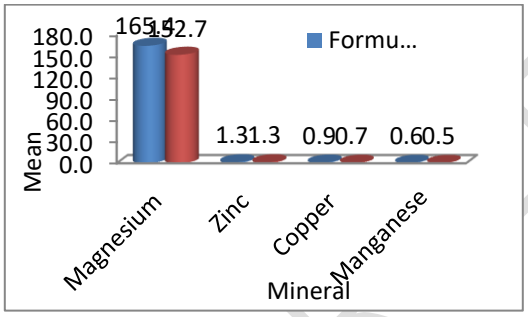

Figure 1: Antioxidant Mineral Compositions of the Cocoyam Flour

Figure 1 showed that the Cocoyam flour formulation was higher in magnesium, copper and manganese concentration when compared to the commercial rat feed.

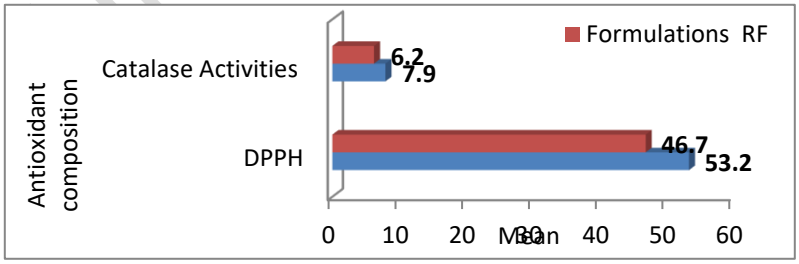

Figure 2: Antioxidant Activities of the Cocoyam Flour

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The DPPH and CAT activities were higher in the cocoyam flour formulation when compared with the commercial rat feed.

2.0: Effect on Blood Glucose

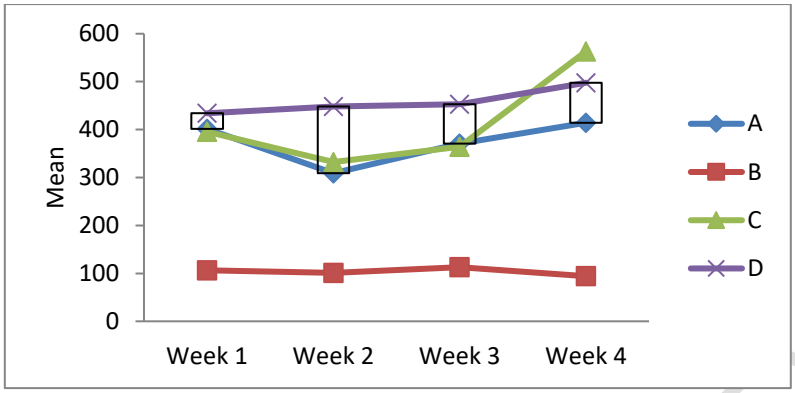

Figure 3: Effect on Blood Glucose over time

Figure 3 showed that the rat group fed on the cocoyam flour (Group D) had poor random blood glucose control when compared to the standard control (Group A) over time.

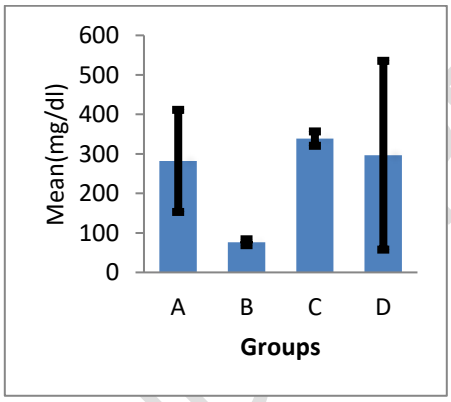

Figure 4: Fasting Blood Glucose Level on the Day of Sacrifice

Figure 4 showed that Group D rats fed on cocoyam flour had approximate fasting blood glucose values with the rats on standard treatment (Group A) on the 4th week of intervention.

3.0 Biochemical Changes

3.1: Oxidative Stress Markers

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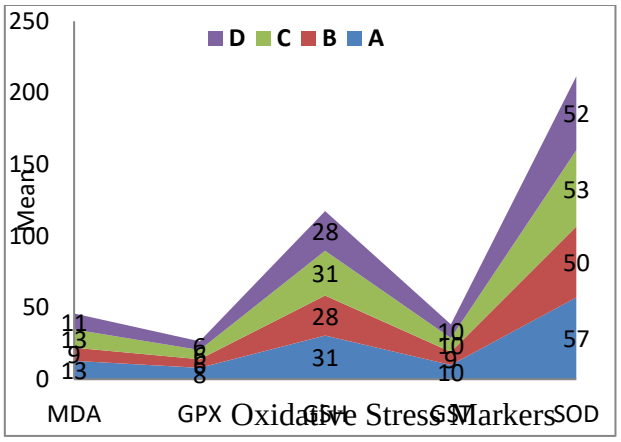

Figure 5: The Oxidative Stress Markers in the Various Groups

Figure 5, showed that the oxidative stress marker, MDA, value was least in the normal control and cocoyam-administered groups just like the values of the antioxidant enzyme, SOD.

3.2: Inflammatory Markers

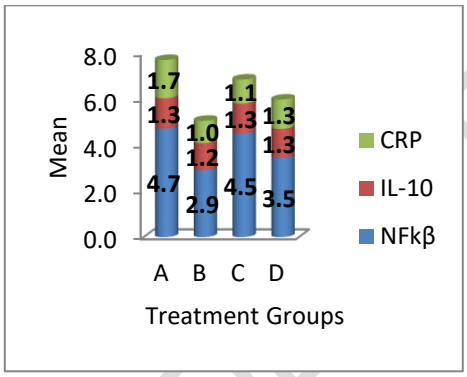

Figure 6: Result of the Inflammatory Biomarkers of the Various Groups.

Figure 6 showed that the Group D rats fed on cocoyam flour had comparable mean values of the IL-10, CRP and NFkB with the normal control.

3.3: Serum Bilirubin and Protein Levels

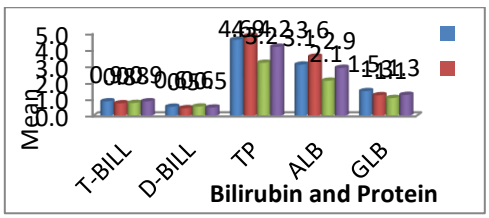

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Figure 7: Result of the Serum Bilirubin and Protein Levels

Figure 7 showed that the direct bilirubin values were similar for Group D and normal control.

3.4: Serum Lipid Profile

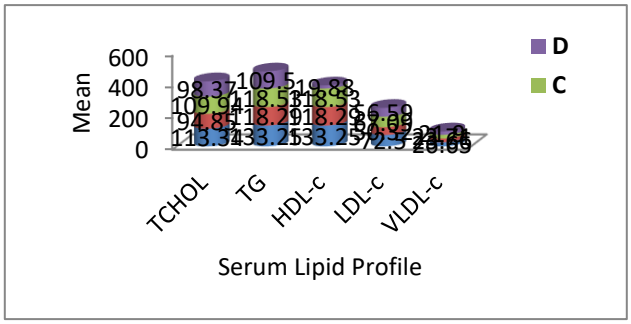

Figure 8: Result of the Groups` Serum Lipid Profiles

Figure 8 showed that the total cholesterol, triglyceride and LDL-C mean values were lowest in the normal control and group fed on cocoyam relative to the standard control.

3.5: Renal Functions

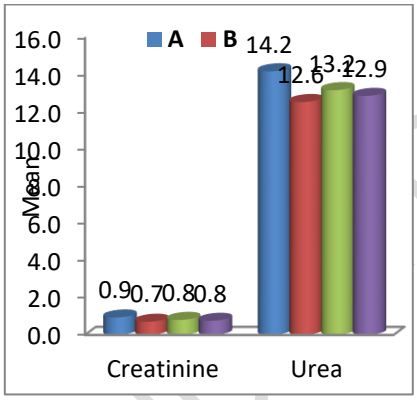

Figure 9: Result of the Urea and Creatinine of the various Groups

Figure 9 revealed that the mean urea values in group D and the normal control were the least comparable, much better than values obtained from the standard control.

3.6 Cardiac Function Texts

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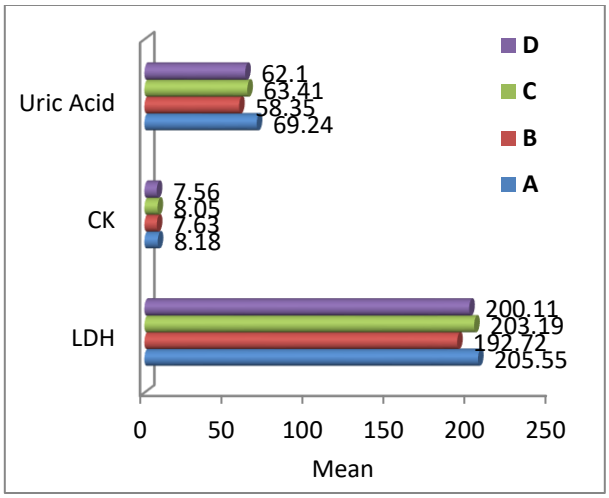

Figure 10: Result of the LDH and CK for the Groups

Figure 10 revealed that the LDH mean values of the rats in Group D fed on cocoyam flour and that of the normal control had the least and comparable values for the CK and uric acid.

DISCUSSION

1.0 Antioxidant Compositions & Activities

The GC/MS analysis revealed that the cocoyam formulation contained different bioactive compounds such as benzofuran, 2,3-dihydro-, dihydroartemisinin, 10-O-(t-butyloxy)-, phenol, 2,6-dimethoxy, E)-Stilbene, 2-Methoxy-4-vinylphenol, and dibutyl phthalate. The results aligned with earlier research that documented the presence of polyphenolic compounds like 3-5-di-t-butyl phenol, and fatty acid derivatives like octadecanoic acid, in cocoyam [16], with such compounds possessing hypoglycemic and antioxidant activities [14, 15]. Various concentrations of antioxidant minerals such as Zinc (1.30 mg/100 g), copper (0.86 mg/100 mg), manganese (0.61 / 100 mg), and magnesium (165.36 mg/100 mg) were also found in the cocoyam flour formulation, with the mean values being statistically significant variations between the values obtained from the conventional rat meal and the

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cocoyam formulation. Notably, the cocoyam formulation has higher concentrations of all four (100%) antioxidant minerals. Variations in the mineral contents of several cocoyam types, such as Zn, Cu, Mn, and Mg, have been noted in earlier studies [31]. For instance, Coronell-Tovar and colleagues [32] reported that the Mg, Cu, and Mn values in cocoyam corm flour were 0.72 mg/g, 6.90µg/g, and 4.42 µg/g, respectively, while Wada and colleagues [31] reported that the Zn, Cu, Mn, and Mg contents in green cocoyam were 3.06 mg/100g, 1.04 mg/100g, 2.48 mg/100g, and 78.77 mg/100g, Mn, and Mg, respectively. The presence of bioactive compounds and antioxidant minerals in cocoyams helps them scavenge free radicals. The cocoyam formulation's DPPH activity in this investigation was 53.21%, a significantly higher value than the conventional rat meal's 46.02% (Figure 2). Different scholars have reported the antioxidant capacity of cocyam plant extract [33, 34, 35], with polyphenols adduced to be responsible for such activity [16, 34].

The CAT activity of the flour formulations and commercial rat feed was 7.07 and 6.15 units/min, respectively, indicating a 15% increase of CAT activity in cocyam compared to the (Figure 2). The antioxidant enzyme catalase plays a critical role in preventing oxidative damage brought on by elevated levels of reactive oxygen species. Superoxide dismutase (SOD) facilitates the conversion of the highly reactive superoxide anion into O_2 and, subsequently, the less reactive species H_2O_2, which is further converted to water by the enzymatic processes of catalase or glutathione peroxidase.

2.0 Effect on Blood Glucose

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The study concluded that there were notable differences in the average random blood glucose (RBG) levels between the groups ($F= 13.963$, $p<0.001$) and that these differences changed steadily from the first to the fourth week with a positive trend. The group administered with cocoyam formulation exhibited a consistent upward trend in RBG values over time, higher than the normal, standard, and diabetic controls Figure 3), suggesting that cocyam given at high concentration did not control random blood glucose (Figures 3 and 4). These results are not in conformity with other studies on the hypoglycemic effects of cocoyam flour. Prior research by Eleazu and colleagues showed that feeding lower doses of cocoyam flour to STZ-induced diabetic mice for three to four weeks reduced blood glucose levels by 38% to 58.75% [15, 16]. Even though phenolics and artemisinin are bioactive chemicals with known antidiabetic properties, the formulations' observed hyperglycemic effects could be the result of antioxidants' pro-oxidative properties at higher dosages [36, 37].

3.0 Biochemical Activities

a. Effect on Oxidative Stress Markers

Oxidative stress resulting from Diabetes mellitus affects the body's antioxidant reserves thereby causing imbalance in the antioxidants and reactive oxygen species (ROS) ratio [38], reduced redox ratio [39] and reduction in the concentration of the scavenging enzymes catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD) [40]. Protein glycation that leads to higher products of lipid peroxidation including carbonyls, malondialdehyde (MDA), and advanced glycation end products (AGEs), in T2DM plasma. [41]. When antioxidants are given, these products of lipid peroxidation are reduced [42]. In this study, the normal control

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group's MDA mean value of 9.29 mg/g, compared to that of the negative control group of 12.65 mg/g, meant an increase of peroxidation in the negatie control group, by 36.06% (Figure 5). This finding was in tanderm with recent reported works that documented an increased MDA level in hyperglycemia and diabetes mellitus [42]. The group treated with cocoyam flour displayed a decreased MDA value (11.28 mg/g) in comparison to the normal control group (12.77 mg/g), with the difference being statistically significant. Since this value in group D was far better than in the standard control, the implication was that cocoyam had higher potency in amelioration of lipid peroxidation than metformin, the antidiabetic drug. This contradicts the results of other studies [42]. The findings of our investigation in streptozotocin (STZ)-induced diabetic rats may have been influenced by the fact that metformin toxicity at certain doses can result in oxidative stress, which in turn increases lipid peroxidation and, in this case, MDA levels [43]. The levels of the antioxidant enzymes GSH, GST, and SOD rose relative to the normal control, but none of the groups' increases were statistically significant (Figure 5). This outcome is consistent with some earlier studies that found diabetic patients on antidiabetic drugs having higher levels of GSH, catalase, and antioxidants than those not receiving medication [42].

b. Effect on Inflammatory Biomarkers

Important mediators of leucocyte recruitment in both acute and chronic inflammation are soluble cytokines [44]. Serum, plasma, and tissues contain proinflammatory cytokines such as the c-reactive proteins, interleukins (IL)-1α, IL-1β, IL-2, IL-6, IL-8, IL-12, tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFNγ) [45]. Anti-inflammatory (IL-4, IL-5, IL-10, and Transforming growth factor β1 (TGF-β) are

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also present in these tissues but tresults from one tissue cannot be used interchangeably [46]. The activation of the nuclear factor kappa B (NF-kB) results in overexpression of the proinflammatory cytokines [47]. In this study, the mean average values of CRP and NFkB. showed significant differences among the groups (Figure 6). The CRP levels in the cocoyam flour intervention group (1.28 ng/ml) were greater than those in the normal control group (0.97 ng/ml) but lower than those in the standard control group (1.67 ng/ml) (Figure 6). The high potency of the bioactive compounds in the cocoyam flour resulted in the reduced inflammatory response as shown by the lower CRP and NFkB values. Comparing the NFkB levels of the diabetic rats fed cocoyam (4.46 x 10-6 mg/g), normal control (2.91 x 10-6 mg/g), negative control (4.51 x 10-6 mg/g), standard control (4.73 x 10-6 mg/g), and other groups revealed an identical trend with statistically significant differences. Similarly, compared to the negative and normal controls, the IL-10 levels in the cocoyam flour intervention group were statistically significantly lower (Figure 6).

Insulin resistance and hyperinsulinemia were found to be strongly correlated with CRP levels by Nakano and colleagues [48]. This research validates prior investigations that discovered higher CRP levels in individuals with diabetes mellitus compared to those without the condition [50]. Additionally, the study discovered that diabetic rats had higher CRP levels. The presence of bioactive compounds such as artesinins, stilbenes and phenolics might have been responsible for the anti-inflammatory properties of the cocoyam flour as earlier reported by previous studies [49, 51, 52].

c. Effect on Liver Enzymes and Liver Proteins

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Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT) are raised in liver cell damage and hepatic insulin resistance [53, 54], with ALT specic for liver disease [54]. AST can be raised in other disease condition such as liver, mitochondria, among others and hence is less specific [55]. In diseases of the pancreas, kidney, and liver GGT is elevated [56, 57]. In chronic inflammatory cases such as oxidative stress, GGT, glutathione absorption, and the possible development of Type 2 Diabetes Mellitus are linked [58]. In this study, the AST value of 0.788 mg/g in the normal control outperformed the standard control (0.86 mg/g), negative control (0.83 mg/g), and intervention group (0.81 mg/g), though the values were not significantly different. However, none of the groups' ALT measurements demonstrated any appreciable differences. It is possible that the raised levels of ALT, AST, and GGT may be arising from the accumulation of fat in the liver fat due to insulin resistance, dyslipidemia, metabolic syndrome, and Type 2 Diabetes Mellitus since fatty liver raises liver enzymes [59]. Yazdi and colleagues found a positive correlation between elevated liver enzymes and body weight, along with other elements of the metabolic syndrome [60, 61].

The group given cocoyam flour in this study, had lower liver enzyme levels than the negative control group, demonstrating that even at greater dosages, the cocoyam formulation has hepatoprotective effects on diabetic rats. Such preventative benefits of cocoyam flour pellets on diabetic rats have previously been shown [16]. There were no significant differences in total liver protein (TP) levels between the groups in this study, possibly because the liver enzyme ALT and the oxidative stress markers GST,

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GSH, and SOD were unaltered, preventing a major shift in TP levels. Nonetheless, there was a substantial difference in total blood protein levels between diabetes and normal control groups.

d. Effect on Bilirubin

When haem are catabolized, bilirubin, an antioxidant agent, is produced [62] and the presence of such compounds, results in risk reduction for metabolic syndrome and chronic illnesses [63]. When the level of bilirubin is moderately raised, its physiological benefits for disease prevention and management manifests [64] and are linked to the antioxidative and anti-inflammatory qualities [65]. In this study, the mean bilirubin levels were not significantly different among the groups but the total and direct bilirubin levels were significantly lower in the standard control group (Figure 7). Comparative to the normal control group, the group given cocoyam flour had comparable total and direct bilirubin levels, indicating that both antidiabetic medications and cocoyam flour were beneficial (Figure 7). Wang and colleagues [66] observed a higher concentration of direct bilirubin in persons with Type 2 Diabetes Mellitus (T2DM), although serum levels of bilirubin subtypes are enhanced in cases of impaired fasting glucose and the initiation of new T2DM. If T2DM is sustained, the level of bilirubin drops, because hyperglycemia produces oxidative stress, which boosts the activity of heme oxygenase-1, an enzyme that increases bilirubin production and raised serum levels. With the prolongation of the hyperglycemia, more reactive oxygen species are released leading to increased bilirubin consumption and, eventually, lower bilirubin levels [67]. Studies have found lower serum bilirubin levels in diabetic patients [65], indicating prolonged hyperglycemia.

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e. Effect on Serum Lipid Profile

In the present investigation, there were no statistically significant differences in triglyceride or very low-density lipoprotein levels but the Total cholesterol levels varied significantly between groups, with the normal control group having the lowest amount (94.85 mg/dl). The group administered with cocoyam flour, had a lower value (98.37 mg/dl) than the normal control (113.34 mg/dl) and negative control (109.94 mg/dl) (Figure 8). The levels of high and low-density lipoproteins followed comparable trajectories; those who received the cocoyam formulation had mean values of 19.88 and 56.59 mg/dl and mg/dl, respectively (Figure 8).

The low-density lipoprotein levels in this group were 75.20 mg/dl, while the high-density lipoprotein levels were 133.25 mg/dl (Figure 8). These results were less than what was seen in the normal control group. These findings revealed that the cocoyam formulation outperformed metformin, the antidiabetic medication used in group B, in terms of hypolipidemic effects in diabetic rats. Dyslipidemia, characterised by elevated levels of low-density lipoproteins (LDL), decreased levels of high-density lipoproteins (HDL), and elevated triglyceride levels, is frequently linked to Type 2 Diabetes Mellitus (T2DM). Increased plasma triglyceride levels induce HDL to break down, lowering HDL levels and increasing LDL levels. Low HDL and hypertriglyceridemia increase fatty acid levels, leading to insulin resistance and β-cell dysfunction. Lipid profiles have been shown to improve with the administration of extracts with strong antioxidant capabilities like polyphenols. Taurine-treated diabetic rats showed improved lipid profiles, as evidenced by lower levels of triglycerides, cholesterol, and LDL and increased levels of HDL [67]. Cocoyam flour extract

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contains phenolic compounds which coud be responsible for its hypolipidemic effect in this study.

f. Effect on Renal Function

The correlation between kidney damage and uncontrolled type 2 diabetes, as well as elevated serum creatinine and urea levels, highlights the significance of prompt intervention in halting the advancement of end-stage renal failure [68, 69]. The study's findings on creatinine mean values between groups showed no significant difference ($P<0.05$) (Figure 9). However, the normal control group's mean urea levels were much lower (12.55 mg/dl) than those of the other groups (Figure 9). The mean urea readings (13.03 mg/dl) of the cocoyam formulation group were considerably lower than those of the standard and negative control groups (14.20 mg/dl and 13.19 mg/dl, respectively) (Figure 9). In diabetic rats, the cocoyam formulation outperformed the anti-diabetic medicine in terms of kidney protection. The study's findings revealed that diabetic controls had greater levels of urea and creatinine than normal controls, which is consistent with previous research that found diabetic rats with STZ-induced renal failure had higher levels of urea, creatinine, and uric acid than controls [70]. Compared to the standard and negative control groups (69.24 mg/dL and 63.41 mg/dL, respectively), the mean uric acid levels in the diabetic rats fed with cocoyam were considerably lower (Figure 10). This demonstrates that metformin is not as effective as cocoyam flour at protecting the kidneys of diabetic rats. The increased plasma uric acid levels in chemically induced diabetic rats are similar to those found in diabetic controls [71].

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The polyphenol content of cocoyam has been connected to the formulation's beneficial benefits on diabetic nephropathy [72, 73]. Polyphenols can reduce TGF-β expression and matrix-degrading enzymes, including MMP-2/MMP-9, in hyperglycemia-induced renal injury (characterised by extracellular matrix buildup, glomerular fibrosis, and renal failure) [74]. Inhibiting TGF-β and matrix-degrading enzymes can help control diabetic renal failure by reducing inflammation, fibroblast development, and fibrosis [75, 76]. In STZ-induced diabetic rats treated with a polyphenol mixture, leukocyte infiltration and necrotic cell count were reduced and the kidney structure was maintained [70].

g. Effect on Cardiac Function

Creatine kinase (CK) is an essential enzyme involved in the production of adenosine triphosphate during muscle contractions [77]. Certain muscle activities and metabolic syndrome lead to an increase in CK concentration [78]. According to Frank and Finsterer [79], higher levels of CK and lactate dehydrogenase (LDH) in type 2 diabetes are useful predictors of the disease's cardiac complications since they are markers of heart damage. Advanced glycated end products (AGEs), which have cardiotoxic implications such as cardiac fibrosis, are generated as a result of chronic hyperglycemia, which might trigger the fibrotic response [80].

In this study, the mean values of CK and LDH showed no significant differences between the groups, indicating that the different types of interventions among the rat groups, in this study, did not affect these enzyme levels (Figure 10). According to Kotb and colleagues' findings [81], there were no discernible differences in the levels of CK and LDH between T2DM patients on metformin and healthy controls,

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contradicting another study [78] which reported a little increase in CK levels or subclinically raised CK in the T2DM patients [78, 79]. The reasons for these varying findings may be due to the duration of the hyperglycemia. Asmat and colleagues have shown that prolonged exposure to high glucose makes cells, particularly cardiac cells, vulnerable to glucose toxicity [82]. This could account for the lack of significant variations in mean LDH and CK levels across groups. Comparative analysis of the duration of hyperglycemic stress on the Kotb and colleagues study and this research showed, a duration of four and eight weeks, respectively, periods considered not long enough for cardiac toxicity by the high blood glucose and hence the reported normal CK and LDH levels.

4. CONCLUSION

Cocoyam flour delivered in significant doses to STZ-induced diabetic rats did not appear to effectively manage blood glucose levels. Nonetheless, it has similar biochemical effects as conventional antidiabetic drugs like metformin do. Furthermore, even at high concentrations, cocoyam flour appears to prevent lipid peroxidation in people with diabetes. The research results indicate that diabetes patients should be encouraged to take cocoyam, especially given its potential benefits in lowering the risk of diabetic hepato-renal injury. In addition, more research is needed to discover how cocoyam impacts diabetes complications and how it interacts with other anti-diabetic medicines.

CONSENT

Not applicable

ETHICAL APPROVAL

Ethical approval number RSU/FBMS/REC/23/032, was obtained from the faculty of basic medical sciences, college of medical sciences, rivers state university, Port Harcourt, Nigeria.

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