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Shallot Fortified Noodles Downregulate Hyperglycemia and Oxidative Stress Biomarkers in Streptozotocin-Induced Diabetic Rats

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Abstract

Plant based diet rich in polyphenols and antioxidants contribute to averting and controlling ailments linked to oxidative stress (OS). Shallot is a bulb vegetable, sweeter and milder in taste than onions; they are regularly used for culinary purposes due to their subtle flavor. Shallot was incorporated into wheat flour for noodles production and fed to streptozotocin (STZ) – induced diabetic rats for a period of fourteen days. Effects of shallot fortified noodles on glycemia and carbohydrate hydrolyzing enzymes of rats were investigated. Oxidative impairment in rats' liver and kidney homogenates and the serum biomarkers of liver and kidney function tests were assessed. Results revealed that noodles mitigated the raised blood glucose levels in diabetic rats and notable decease was observed in the α-glucosidase and α-amylase activities. Similarly, the noodles enhanced the activities of antioxidant enzymes in liver and kidney homogenates, and reduced the TBARs levels. Noodles down regulated the serum alanine aminotransferase, aspartate transferase and alkaline phosphatase levels and up regulated the albumin levels. Shallot fortified noodles (10%) exhibited hypoglycemic effect, attenuate OS biomarkers, thereby hampering the complications of diabetes.

Keywords: Oxidative stress bio-markers; Shallot; Noodles; Diabetic rats

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INTRODUCTION

The predominance of diabetes (DM) is spreading globally at an endemic level, thereby becoming a public health matter. DM is a class of metabolic syndrome, identified with hyperglycemia caused by deformities in the secretion of insulin or its activity or both (Shah &Brownlee, 2016). Prolonged DM is connected with both microvascular and macrovascular complexities, with subsequent organ and tissue damage (Chawla *et al.,* 2016). Researchers have explained the fundamental molecular mechanism responsible for the progression of diabetes complexities or complications (Yaribeygi *et al.,* 2018; 2019), yet the specific pathophysiology is not implicit. However, oxidative stress (OS) has been acknowledged as one of the most important mechanism responsible for the progression of DM (Yaribeygi *et al.,* 2019).

OS is an occurrence initiated by the discrepancy in the massive expression and buildup of oxygen radicals (ROS) in the tissues as well as cells; and the capability of a biological system to neutralize or detoxify the metabolic by-products (Pizino *et al.,* 2017). It could also be referred to as the disruption in the balancing of prooxidant-antioxidant of the cell, in support of the prooxidant, and thus overwhelming the antioxidant capability of the cell (Niki, 2016) and finally the damage of tissues. It ensues from the increased creation or generation as well as the reduced displacement of oxidants by the antioxidant cellular defense. According to Pizzino et al. (2017), the ROS produced by the cells and tissues, as metabolic by-products, are hydrogen peroxide (H_2O_2) superoxide radicals ($O_2^{\bullet-}$), hydroxyl radicals ($^{\bullet}OH$) and singlet oxygen ($^1O_2$).It is worth mentioning, that ROS has both beneficial and harmful effects, they are involved in some regulatory activities in cells, and likewise, other normal metabolic processes are supported by some quantities of ROS (Gómez-Zorita*et al.,* 2012). Nevertheless, the unrestrained production of ROS is damaging; because they cause modification of the membrane structure and loss in the functionality of proteins, deoxyribonucleic acid (DNA) and enzymes, resulting in numerous diseases including insulin resistance, cancer, DM and cardiovascular *diseases* (Bardaweel *et al.,* 2018). Consequent to OS, the metabolic irregularities of DM is responsible for the overproduction of mitochondrial superoxide in the epithelial cells of the small and large capillaries and the cardiac muscle (Tangvarasittichai, 2015). Also, OS function as an intermediary between insulin resistance, the development to glucose intolerance and formation of DM. Hurrle & Hsu (2017) reported that, ROS influences several area or spots in the insulin receptor signal transduction causing a reduction in the expression of GLUT4 transporter in the cellular membrane and bringing about insulin resistance in the peripheral tissues.

However, the body has emplaced diverse defense schemes to offset or neutralize the consequences of uncontrolled free radicals and OS, these schemes involve endogenous antioxidant molecules which could be enzymatically or non-enzymatically based. Enzymatic endogenous antioxidants includes, catalase (*CAT),* superoxide dismutase (SOD) and glutathione peroxidase (GPX), known as the innate immune systems,

they provide the first barrier or line of defense antioxidant. The non–enzymatic endogenous antioxidants are glutathione, L-arginine, lipoic acid and coenzyme- Q10. Apart from these are dietary antioxidants sources (exogenous) which could either be of animal or vegetal (plant) source. Authors have reported different spices and herbs (vegetal sources) as rich sources of dietary antioxidants; these include garlic, basil, african pepper, black pepper, ginger, shallot and corn silk (Omoba *et al.,* 2019; Ademosun *et al.*, 2021; Adeyemo *et al.,* 2022; Rabi *et al.,* 2022). The health benefits of this exogenous antioxidant could be maximally exploited through nutrition

Shallot (*Allium ascalonicum*) is a spice, bulb vegetable used traditionally in cooking (Mohammadi-Motlagh *et al.,* 2011).It is abundant in flavonoids together with phenols, it exhibit anti-diabetic potentials and lowers the blood pressure (Mikaili *et al.* ,2013; Omoba *et al.,* 2022). Hydroxybenzoic acid has been identified as a major polyphenol in shallot (Sun *et al.,* 2019 ;Adeyemo *et al.,* 2022), and known for its hypoglycemic effect. High prevalence of diabetic complications in developing countries coupled with limited and expensive health care resources, calls for regular consumption of foods with these dietary antioxidants to assist in preventing OS and complications of DM.

Urbanization has integrated instant noodles as part of our daily meal especially in Sub-Saharan Africa, due to its convenience. It is universally acceptable and eaten, regardless of the age group, events and type of weather or climate. This therefore makes it a convenient carrier of dietary or nutritional antioxidant and might reduce the development of OS, DM and its complications upon regular consumption. Several authors have reported on the enrichment of noodles with plants/ vegetables and their by-products rich in dietary antioxidants such as spinach, shiitake, and chestnut (Susanti *et al.,* 2020; Wang *et al.,* 2020; Dulger-Altıner & Mete, 2020). There is little or no information about the effect of shallot fortified noodles on oxidative stress biomarkers despite the wide acceptance of noodle as our daily meal. This study therefore, aims to provide information on the influence of shallot fortified noodles on oxidative biomarkers in STZ-induced diabetic rats.

MATERIALS AND METHODS

Chemicals and Materials

Streptozotocin (STZ) used was obtained from Sigma-Aldrich Co. (St. Louis, MO, USA), while the acarbose employed was obtained from Glenmark Pharmaceuticals Europe Ltd. (Watford, UK). Roche - AccuChek Active Blood glucose meter was purchased from Roche Diagnostics GmbH, (Mannheim, Germany). Other reagents used are of analytical grade and distilled water was used in the study.

Shallot bulb and wheat flour were purchased from major suppliers at *Shasha* and *Erekesan* markets in Akure, Nigeria. The shallot bulbs were validated at the Department of Crop, Soil, and Pest Management of The Federal University of Technology, Akure, Nigeria. Albino Wistar male rats were procured from the animal house of the Faculty of Veterinary Medicine, University of Ibadan, Nigeria.

Preparation of Samples

Preparations of shallot flour and noodles

Flour was obtained from shallot by using the technique of Setyadjit et al. (2017). Shallots were washed and allowed to drain, sliced into smaller sizes and oven dried for a period of 7days at 45°C with the aid of a forced air circulating oven(Plus11 Sanyo Gallenkamp PLC, Loughborough, Leicestershire, UK), and pulverized with a laboratory grinder (Model KM 901D; Kenwood Electronic, Hertfordshire, UK) into fine powder. The fine powder was packed in an air tight, properly fastened container, and kept at room temperature (~ 27°C) awaiting usage.

The shallot fortified noodles was formulated by employing the technique described by Anggraeni & Saputra, (2018) with slight modifications. Preparation was done by using composite flour at an inclusion of shallot to wheat flours at 0, 3:97, 5:95, 7:93, and 10:90% respectively. The mixture of 100g of composite flour, guar gum (0.5g), sodium hydrogen carbonate (0.2g), carboxymethyl cellulose (0.5g) and 40 mL of water was kneaded until smooth. The dough was then allowed to rest for 10 minutes, after which, dough was rolled into sheets (sheeting) with a thickness of 1.6 mm and manually cut into thin slices. The slices were dried for 12 h at 45°C, cooled, and stored (27 ±3^{o}C) in a water proof container.

Administration of Streptozotocin to Experimental Rats, Preparation of Tissue Homogenates and Serum

Albino wistar rats (48 in number) weighing 150 g – 200 g, confined (in cages), were made to adapt to the experimental conditions (temperature 25± 3^{o}C; RH 60 – 70%; with 12 h light/dark cycle), for two weeks. Rats were fed with rat pellets and water was provided, during the period. Experimental study was approved by the Federal University of Technology, Akure, School of Agriculture and Agricultural Technology ethical committee (FUTA/SAAT/2020/024). The animal study was conducted in line with the ethical guiding principles of the United State (US) National Institute of Health (NIH)**.** The baseline blood glucose levels of the experimental rats were taken prior to the administration of STZ (data not published). Experimental rats were caused to fast overnight before the initiation of diabetes. STZ (freshly prepared) via chilled citrate buffer of 0.1 M and pH 4.5 was injected intraperitoneally (i.p) at a single maximum dose of 60 mg/kg of body weight as reported by Hasanein & Shahidi (2011), excluding the control group which was given citrate buffer only. High blood glucose levels were established in the experimental rats after 72 h, by determining the blood glucose test via tail tipping, making use of a glucometer. Experimental rats having blood glucose reading of≥ 250 mg/dl were considered diabetic and were arbitrarily distributed into eight clusters or sets consisting of six (6) experimental rats each and used for the study. The sets are:

Set I: Experimental rats induced with citrate buffer (pH 4.5) and nurtured with basal diets (NC).

Set II: Diabetic induced experimental rats nurtured with normal basal diet (STZ-Induced)

Set III: Diabetic induced experimental rats that were orally given acarbose (25

mg/kg body weight, with basal diet (STZ+ACA)

Set IV: Diabetic induced experimental rats nurtured with 0% shallot (Noodles made from 100% wheat flour).

Set V: Diabetic induced experimental rats nurtured with 3% shallot (Noodles made from 970g and 30 g shallot flour).

Set VI: Diabetic induced experimental rats nurtured with 5% shallot (Noodles made from 950g wheat and 50g shallot flour).

Set VII: Diabetic induced experimental rats nurtured with 7% shallot (Noodles made from 930g wheat and 70g shallot flour).

Set VIII: Diabetic induced experimental rats nurtured with 10% shallot (Noodles made from 900g wheat and 100g shallot flour).

Water and feed were given *ad libitum* and the blood glucose of the experimental rats assessed for the fourteen (14) days period of study at 3 days intervals. A synthetic antidiabetic drug (acarbose) was used as the control (standard) drug, for a period of the study. Experimental rats were fasted on the fourteenth (14th) day and were sacrificed by cervical dislocation. The serum was collected inside EDTA vessels, through cardiac (heart) puncture using syringe but the organs (liver and kidney) were swiftly removed, cleaned in 0.9% icy saline solution and mopped up using a filter paper (ash free).

Tissue Homogenate Preparation

Harvested organs (liver and kidney) were homogenized individually to obtain crude enzymes. Homogenization (using a Teflon homogenizer) of the tissues was done in an icy saline phosphate buffer (0.1M, pH 7.4) at 1/5 w/v with nearly 1200 rev/min. The slurry of tissues (homogenates) was then centrifuged (3000 rpm for 10 min) resulting in a low-speed filtrate(fluid), stored frozen and the pellets were discarded prior to analysis.

Serum Preparation

The entire blood gathered through cardiac puncture within the EDTA vessels was centrifuged (3000 rpm for 10 min) to set apart the serum. Isolated serum was drained into normal sample bottles and refrigerated for further analysis.

Biochemical Assays (*In vivo*)

α-Amylase and α-Glucosidase activities assay

Inhibitory effect of shallot fortified noodles on the activity of α-amylase was carried out as described by Worthington (1993), while the inhibitory effect on α-glucosidase activity was carried out using the method reported by Zhang et al. (2007).

Determination of Enzymatic Antioxidant Assay

The activity of superoxide dismutase (SOD) in the tissue homogenates was ascertained using the procedure of Misra & Fridovich (1972), the catalase activity (CAT) was also measured according to the procedure of Sinha (1972). The Glutathione-S-Transferase (GST) activity of the tissue homogenates was investigated according to the procedure of Habig et al. (1974), by employing 1-chloro-2, 4-dinitrobenzene (CDNB) as substrate.

Lipid Peroxidation Assay

The procedure of Ohkawa et al. (1979) was employed to determine the lipid peroxidation assay via the formation of thiobarbituric acid-reactive species (TBARS) through an acid heating reaction.

Serum Biomarkers of Liver Function.

The serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined following the procedure of Reitman & Frankel, (1957). Serum alkaline phosphatase (ALP) activity was determined using the improved structured procedure recommended by Deutsche Gessellschaft fur Klinische Chemie (Rec. GSCC DGKC) (1972). Serum albumin concentration was measured by employing the procedure of Weiss et al. (1965) as modified by Doumaset al. (1971).

Kidney Function Test

The levels of serum creatinine and urea were assessed by employing the modified Jaffe method of Spierto et al. (1979) as well as the Urease-Berthelot procedure of Blass et al. (1974) respectively.

Statistical Analysis

Data obtained were statistically analyzed using Graphpad prism (version 6.0 GraphPad Software Inc.; San Diego, CA, USA) as well as Statistical Package for Social Sciences (SPSS) version. 20.0 (SPSS Inc., Quarry Bay, Hong Kong). Data (triplicate readings) were expressed as means ±standard error of mean. Mean values were evaluated using one-way analysis of variance (ANOVA) and significance difference (adjudged at $p < 0.05$) within means were determined using Duncan‘s Multiple Range Test (DMRT).

RESULTS

Blood Glucose Concentration of STZ-Induced Diabetic Rats Fed with Shallot Fortified Noodles

Administration of STZ ($60mgkg^{-1}$) caused a significant elevation of the experimental rat’s blood sugar to $\geq 200mgdL^{-1}$ (except the NC group), as seen in Figure 1. Significant reduction was observed in the blood sugar levels of rats (from $\geq$ 400 mgL^{-1} to $\leq$ 120 mgL^{-1}) after the treatment with shallot fortified noodles. The highest decrease (76%) was observed in rats fed with 10% shallot fortified noodles followed by 7% (74% decrease), while 62% decrease was observed in rats treated with STZ + ACA. Feeding the diabetic rats with shallot fortified noodles (especially 7 and 10%) lessen the blood sugar of the rats after the 14 days.

Effects of Shallot Fortified Noodles on α-Glucosidase and o-Amylase Activities of STZ-Induced Diabetic Rats

Influence of shallot fortified noodles on the activities of intestinal α-glucosidase as well as pancreatic α-amylase in streptozotocin -induced diabetic rats are shown on Fig 2a and b. Drastic increase were observed in the activities of the intestinal α-glucosidase (about 3-fold increase) and pancreatic α-amylase (13-fold increase) of the untreated (STZ-induced) in contrast with the NC rats. Administration of shallot fortified noodles resulted in remarkable decrease of 17 – 66% in the α- glucosidase activities (Fig 2a) and

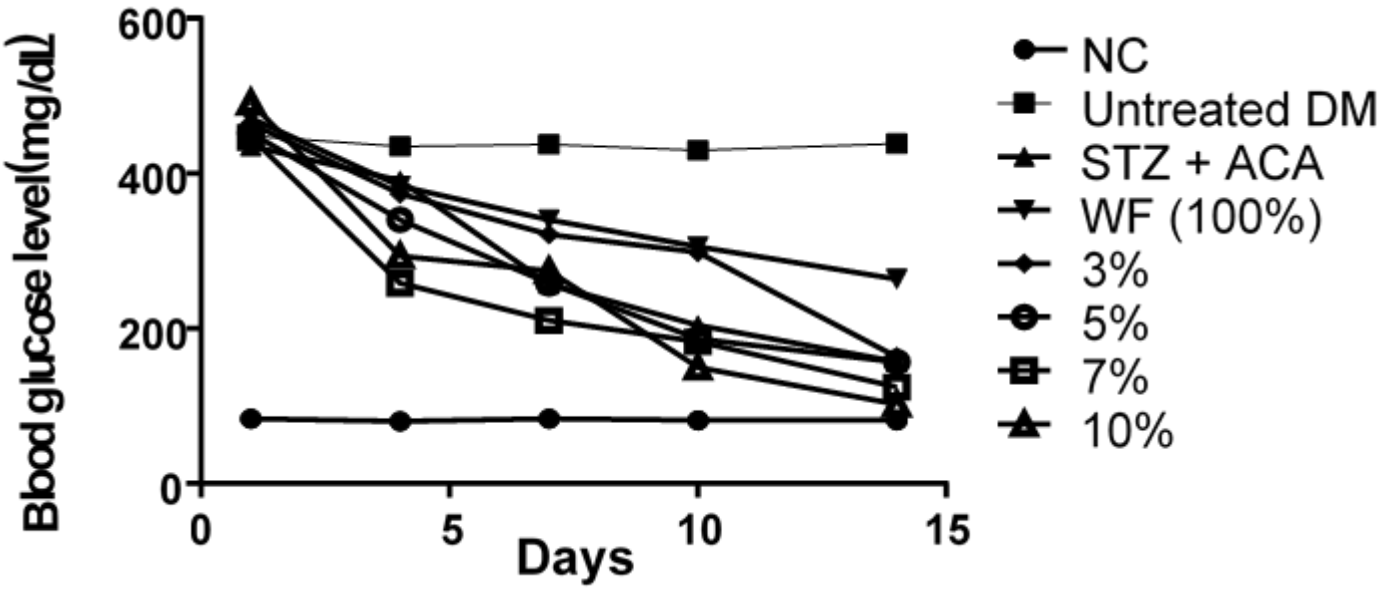
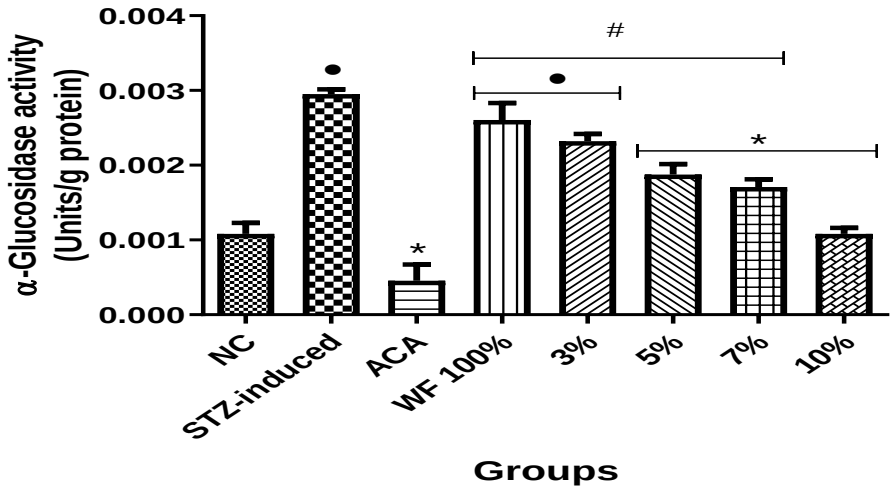


Figure 1: Blood Glucose Concentration of Streptozotocin-Induced Diabetic Rats Fed with Shallot Noodle Samples
Key: NC (Normal Control); Untreated DM (Induced rat without treatment); STZ+ACA (induced rat with antidiabetic drug-acarbose); WF (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

a



b

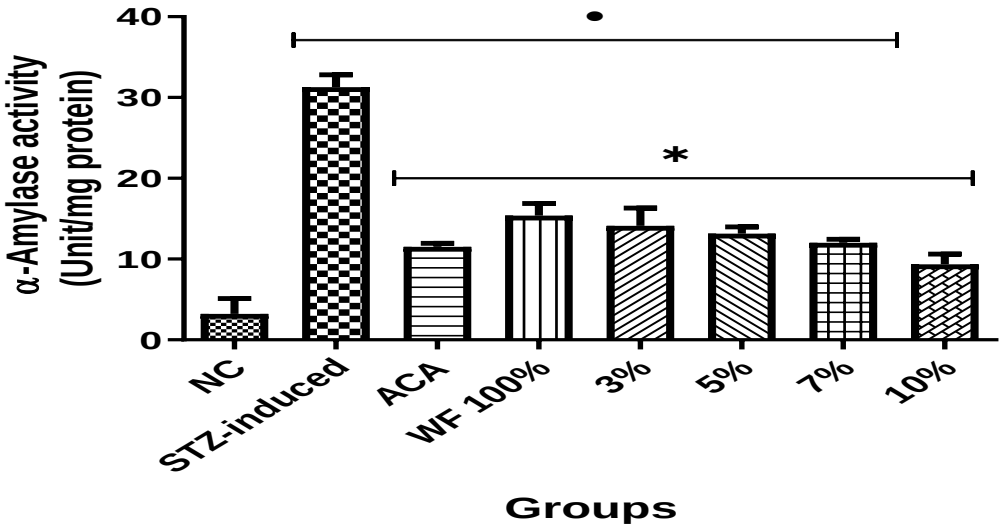


Figure 2: (a) Effects of different % inclusion of shallot on α-glucosidase activity, and (b) α-amylase activity in the Pancreas of streptozotocin induced rats

Values represent mean ± standard deviation (n = 6 rats per group).

●Mean values are significantly different (P < 0.05) vs Normal control.

*Mean values are significantly different (P < 0.05) vs STZ treated group.

#Mean values are significantly different (P < 0.05) vs STZ+ACA treated group

Key: NC (Normal Control); STZ-induced (Induced rat without treatment); ACA (induced rat with antidiabetic drug-acarbose); WF 100% (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

56 – 75% decrease in α-amylase activities (Fig 2b) in comparison to STZ-induced. The inhibition actions of the shallot fortified noodles on α-glucosidase and α-amylase activities, occurred in a concentration dependent manner, as 10% shallot fortified noodles demonstrated the highest percentage inhibition in both activities (Fig 2a and b).

Effects of Shallot Fortified Noodles on Enzymatic Antioxidant Activities of Tissue Homogenates of STZ-Induced Diabetic Rats

Significant reductions of 72% and 79% were observed in the SOD activities of liver and kidney homogenates (Fig. 3a& b), while, 88 and 96% reductions were noticed in the CAT activities of liver and kidney homogenates (Fig. 3c& d), upon induction with STZ, compared to NC. Feeding the STZ induced (diabetic) rats with shallot fortified noodles increased the activities of SOD and CAT in the tissues. About 2 to 3 fold increases was

recorded in the liver, while, 5 to 7 fold increase was noticed in the kidney homogenates for the SOD activities in comparison to STZ- induced. Also, for the CAT activities, 6 to 8 fold increase was observed in the liver, and 5 to 6 fold increases in kidney homogenates, compared to STZ-induced.

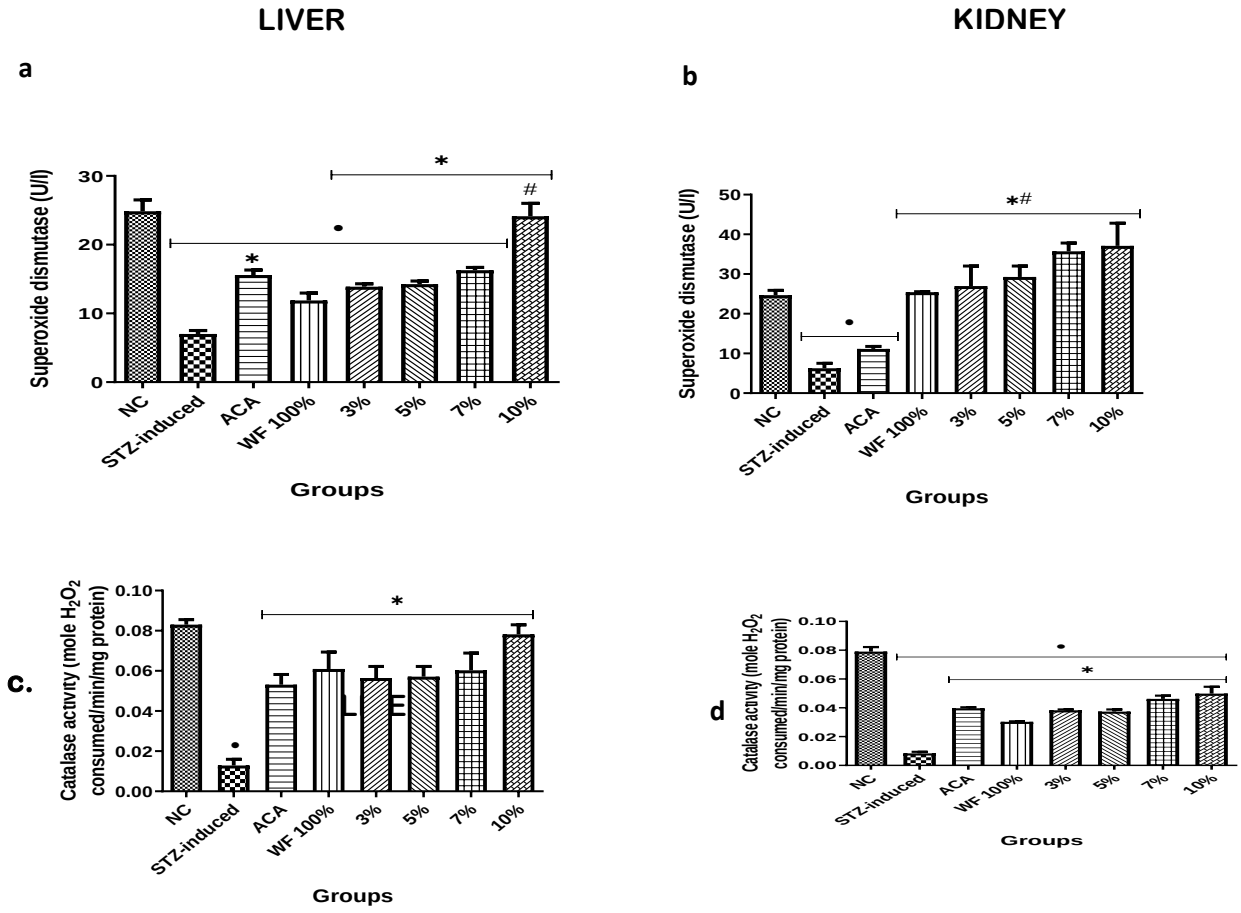


Figure 3: Effects of different % inclusion of Shallot on (a) Superoxide Dismutase (b) Catalase activities

Values represent mean ± standard deviation (n = 6 rats per group). ●Mean values are significantly different ($P < 0.05$) vs Normal group.

*Mean values are significantly different ($P < 0.05$) vs STZ treated group.

#Mean values are significantly different ($P < 0.05$) vs STZ+ACA treated group

Key: NC (Normal Control); STZ-induced (Induced rat without treatment); ACA (induced rat with antidiabetic drug-acarbose); WF 100% (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

Effects of Shallot Fortified Noodles on Glutathione-*S*-Transferase (GST) Activity and Lipid Peroxide Level in Homogenates (Liver and Kidney) of STZ-induced Diabetic Rats

Inducement with STZ resulted in 69% and 77% reduction in the activities of GST (liver and kidney homogenates respectively) as compared with the NC rats (Fig. 4a &b).Feeding with shallot fortified noodles significantly increased ($p < 0.05$) the GST activities in liver and kidney, as it occasioned 59-63% increase in liver and 63-67% increase in kidney, in comparison to the STZ-induced rats.

Induction with STZ prompted significant ($p < 0.05$) increases of 53% and 71% in the TBARs levels (liver and kidney) as compared with the NC group (Fig. 4c & d). Treatment with the shallot fortified noodles caused 56 - 67% significant reduction in the TBARs level in the liver homogenate (Fig. 4c) and 44 - 55% reduction in the kidney homogenates in comparison to the STZ – induced, with sets treated with10% shallot fortified noodles having the highest reduction in both homogenates (liver and the kidney).

Effects of Shallot Fortified Noodles on Activities of Alanine Aminotransferase, Aspartate Transferase, Alkaline Phosphatase and Albumin Levels in the Serum of STZ-induced Diabetic Rats

As observed in Fig 5 a - c, there were significant increases ($P < 0.05$) in the activities of serum alanine aminotransferase (ALT), aspartate transferase (AST) and alkaline phosphatase (ALP) of STZ-induced rats compared to NC, with percentage increases of 217% (ALT), 500% (AST) and 167% (ALP) respectively. The treatment with the shallot fortified noodles resulted in 34 -64% decrease in ALT, 22- 24% decrease in AST and 40 – 64% decrease in ALP as against DM rats. Significant reduction ($P < 0.05$) of 73% was noticed in serum albumin level upon inducement with STZ in comparison to NC (Fig 5d). Treatments (ACA, WF100% and the shallot fortified noodles) up regulated the serum albumin level as against the DM group. ACA and WF100% up regulated the serum albumin by 33% and 100%, while the shallot fortified noodles exhibited upward regulations ranging from 117 to 208% in the serum albumin as against the DM group. Consumption of 7 and 10% shallot fortified noodles brought serum albumin to normal range of 34 -54mg/ml.

Effects of Shallot Fortified Noodles on Serum Creatinine and Urea of STZ-induced Diabetic Rats

Figures 6a & b revealed that inducement with STZ significantly increased the Creatinine level in STZ induced rats by 300%as against NC (Fig 6a). Treatments with shallot fortified noodles occasioned substantial reduction in creatinine levels when compared to STZ-induced rats. ACA resulted in 44% reduction; WF100% caused 50% reduction while the shallot fortified noodles caused 63 -81% reduction with 10% having the highest reduction. Revealing that feeding rats with shallot fortified noodles were more effective in down regulating the creatinine levels than other treatments (ACA and WF100%). Treatment of rats with 5%, 7% and 10% shallot fortified noodles was not significantly different from NC.

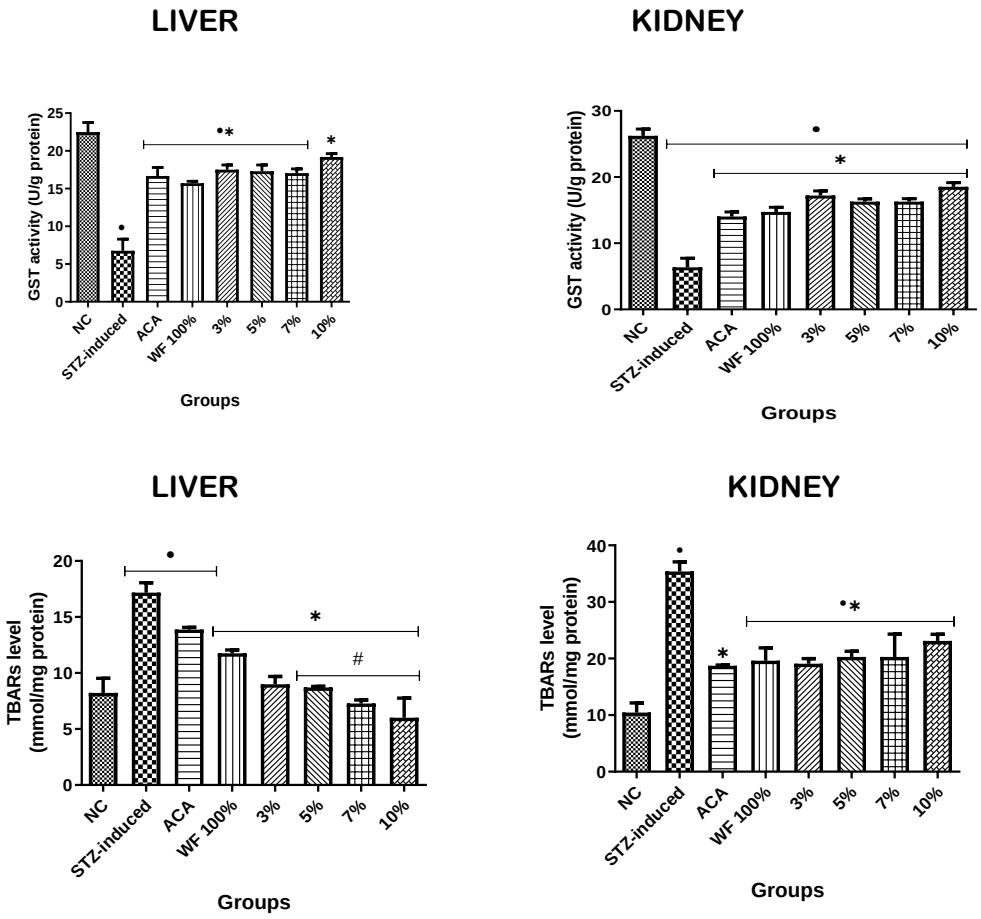


Figure 4: Effects shallot noodles on (a) glutathione-*S*-transferase (GST) activity and (b) lipid peroxide level in liver and kidney of STZ induced diabetic rats

Values represent mean ± standard deviation (n = 6 rats per group). ●Mean values are significantly different (P < 0.05) vs Normal group.

*Mean values are significantly different (P < 0.05) vs STZ treated group.

#Mean values are significantly different (P < 0.05) vs STZ+ACA treated group

Key: NC (Normal Control); STZ-induced (Induced rat without treatment); ACA (induced rat with antidiabetic drug-acarbose); WF 100% (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

The level of urea increased appreciably in STZ – induced rats by exhibiting 163% increase as against NC group (Fig 6b). Treatment with acarbose (ACA) brought about a drastic reduction of 67% in comparison to STZ- induced, while the WF100% resulted in 19% decrease. The treatment with shallot fortified noodles caused 33-67% reduction in urea level in comparison with STZ- induced, with 10% shallot noodle having the highest percentage reduction (67%). Treatment with 10% shallot

noodle down regulated the urea level to value lower than the urea value of the NC rats (8mg/ml).

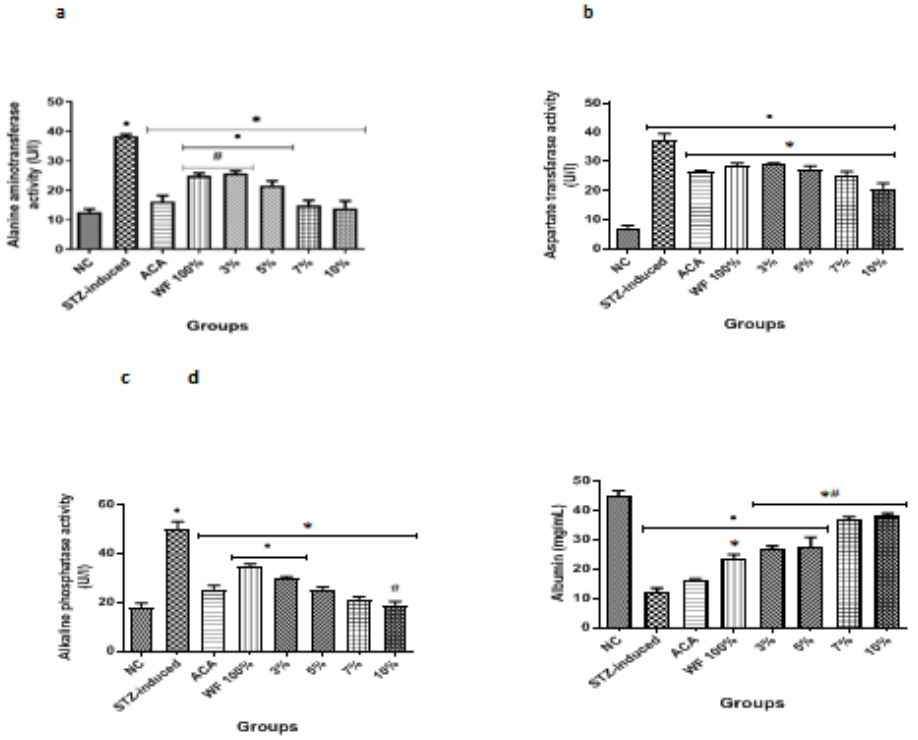


Figure 5: Effects of shallot noodles on activities of (a) Alanine aminotransferase activity (b) Aspartate transferase activity (c) Alkaline phosphatase activity (d) Albumin level in the s erum of streptozotocin induced rats

Values represent mean ± standard deviation (n = 6 rats per group).

●Mean values are significantly different ($P < 0.05$) compared to Normal group.

*Mean values are significantly different ($P < 0.05$) compared to STZ treated group.

#Mean values are significantly different ($P < 0.05$) compared to STZ+ACA treated group

Key: NC (Normal Control); STZ-induced (Induced rat without treatment); ACA (induced rat with antidiabetic drug-acarbose); WF 100% (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

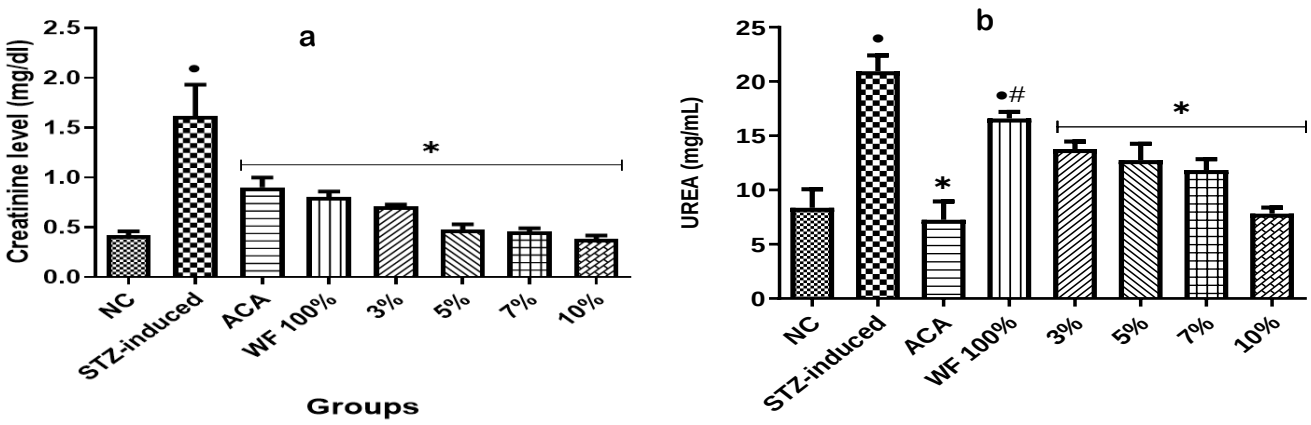


Figure 6: Effects of shallot noodles on (a) serum creatinine (b) urea levels of streptozotocin induced rats
Values represent mean ± standard deviation (n = 6 rats per group).
●Mean values are significantly different (P < 0.05) compared to Normal group.
*Mean values are significantly different (P < 0.05) compared to STZ treated group.
#Mean values are significantly different (P < 0.05) compared to STZ+ACA treated group

Key: NC (Normal Control); STZ-induced (Induced rat without treatment); ACA (induced rat with antidiabetic drug-acarbose); WF 100% (induced rat fed with 100% wheat flour); 3% (induced rat fed with 30 g shallot and 970 g wheat flour noodles); 5% (induced rat fed with 50 g shallot and 950 g wheat flour noodles); 7% (induced rat fed with 70 g shallot and 930 g wheat flour noodles); 10% (induced rat fed with 100 g shallot and 900 g wheat flour noodles).

DISCUSSION

Enhancing the antioxidant status of foods through the use of vegetables and spices have been confirmed to be effective in the control of hyperglycemia and the aftermath oxidative damage (Unuofin, &Lebelo, 2020). Shallot is been utilized extensively as spice or vegetables in food preparations and conventional medicine due to envigorating abilities (Adeyemo *et al.*, 2022).In this research, the inducement of rats with STZ caused elevation of blood glucose concentration ($\geq$ 400 $mgL^{-1.}$), thus implying the diabetic state of the rats. STZ is a known diabetogenic compound which destroys the pancreatic β cells by prompting swift irrevocable necrosis on the pancreatic β cells, causing hypoinsulemia and hyperglycemia (Qinna,&Badwan, 2015). However, the blood glucose reduction observed after feeding rats with shallot fortified noodles might be attributed to some flavonols in the shallots (quercetin, diallyl disulfide) as reported earlier to ameliorate diabetic condition (Jung *et al.*, 2011).This corroborate the findings of Omoba et al. (2022) in which the hypoglycemic properties exhibited by shallot amaranth based snacks, was attributed to dietary fibres and phytochemicals (flavonoids) in the shallots. Flavonols are a subclass of flavonoids, acknowledged to have numerous positive health benefits. They exhibit hypoglycemic abilities via the inhibition of carbohydrate hydrolyzing

enzymes activities, controlling uptake of glucose, the secretion and signaling of insulin as well as removal of adipose (Vinayagam& Xu, 2015).

Inhibition of the carbohydrate hydrolyzing enzymes activities is frequently used in evaluating antidiabetic activities, since the procedure for digestion of carbohydrate to disaccharides is initiated by the pancreatic α - amylase. The disaccharide is catalyzed by intestinal α - glucosidase to monosaccharides causing an exaggerated upsurge in blood sugar after meal. Feeding the rats with shallot fortified noodles inhibited the activities of these enzymes and impedes the release of glucose from starch, with consequent decrease in the absorption of glucose by the intestine. The inhibitory activities exhibited by the shallot fortified noodles could be accredited to the innate phytochemicals (polyphenols). Sittisartet al. (2017) identified the polyphenols in shallots as kaempferol, gallic acid, apigenin, and quercetin, with proven α-amylase and α - glucosidase inhibiting properties (Martinez-Gonzalez, et al., 2019). The shallot fortified noodles might be valuable food for managing DM

In a non - diabetic condition, superoxide anions ($O_2^{\bullet-}$) and hydroxyl radicals ($^{\bullet}OH^{-}$) are generated in minute quantities, along with hydrogen peroxide (H_2O_2) though not a free radical (but capable of damaging cells at low quantity).According to Mushtaq et al. (2015), these generated free radicals are swiftly removed by innate antioxidant defense mechanisms, principally enzymes [catalase (CAT),Glutathione-S-transferase (GST), superoxide dismutase (SOD), and glutathione(GSH)]. While in a diabetic condition, OS is often activated by the increased and or uncontrolled generation of these free radicals as well as severe reduction in antioxidant cellular defense enzymes. In this present research, induction of the experimental rats with STZ, dwindled the levels of these innate enzymes in the homogenates (liver and kidney) of the induced rats (Fig 3a – d; Fig 4a and b). The reduced activities of these enzymes may perhaps cause a superfluous release of superoxide anions ($O_2^{\bullet-}$) and hydrogen peroxide (H_2O_2), with subsequent generation of hydroxyl radicals ($^{\bullet}OH^{-}$). These further originates lipid peroxidation initiation and propagation, with their causal upsurge OS in a diabetic state and its complications (Augustine*et al.*, 2021). However, the administration of shallot noodle enhanced the activities of the enzymes and consequently eased OS. These observations are similar to the results of other studies in which shallot or shallot extract treatment improved the actions of these innate defense antioxidant enzymes (Wongmekiat et al., 2008). Preceding work support our observations that consumption of shallot or shallot incorporated diets improves type 2 diabetes milletus and its complications (Omoba *et al*., 2022). Furthermore, the strong protection of shallot against OS and cell damage might be attributed to the incidence of sulphur compounds namely diallyl disulfide, N-acetylcysteine, diallyl sulfide and S-ethylcysteine (Omidifar *et al.*, 2020). Hajian et al. (2018) similarly, ascribed the sturdy anti- diabetic activities of Persian shallot to the large amount flavonoids and saponin in the shallot.

The degree of lipid peroxidation in the extract of fleshy tissues and cells and or blood serum

is measured by TBARs, which is a product of lipid peroxidation. The noticeable substantial increase in TBARs as noticed in the homogenates (liver and kidney) of the STZ - induced rats in relation to the normal control (NC) is expected as lipid peroxidation is usual of diabetes. TBARs therefore, is a signal to peroxidation and invariably OS. Our results substantiates the study of Gomathi et al. (2014) where, elevated TBARs levels were reported for extracts of tissues and biological fluids of STZ- induced diabetic rats. Nevertheless, the treatment with shallot fortified noodles reduced the level of the TBARs close to the control in both liver and kidney homogenates, implying that shallot fortified noodles ameliorates the production of free radicals. The observed biological activities of the shallot fortified noodles might be accredited to the phytochemical constituents of the shallots (total phenol, allicin, pyruvic acid and quercetin) as identified by Bhosale, et al. (2022) and Adeyemo et al. (2022).

ALT, AST and ALP are perhaps amid the frequently used liver injury markers. ALT and AST however, prompts the conveyance of an amino group in the alanine cycle for the formation of pyruvate and glutamate. ALT exists in the liver at a denser concentration than other tissues (kidney, heart and muscle cells). Subsequent to the occurrence of hepatocellular injury, the ALT drips out from the hepatocytes (liver cells) into the blood. Comparable to ALT, AST is initiated in the cytoplasm of the liver cells and other tissues, but the ALT is a more precise and detailed marker in liver disease than AST. In the current study, the administration of STZ increased the activities of these liver injury markers in the serum, this is an indication of a disorder or disruption in the integrity of the hepatic cells (diabetic liver injury) and hepatic failure as a result of the administration of the STZ. The increased level of these enzymes also indicated gluconeogenesis (Visweswara Rao et al., 2013). Gluconeogesis is a metabolic pathway; with consequent production of glucose from non-carbohydrate carbon substrates. It happens usually in the liver and kidney in the course of extended starvation or overnight fasting, and makes available glucose to the brain and the red blood cells. Our observation corroborates the animal study reported by Safhi et al. (2019) of elevated levels of these hepatic enzymes in the serum of the experimental rats induced with STZ.As seen in Fig 5 a and c, feeding the experimental rats with shallot fortified noodles decreased the serum hepatic enzymes in the rats to close to the control, specifically in rats fed with 10% shallot noodle, implying reduction in gluconeogenesis. Shallot noodle (especially 10%) might be able to protect the hepatocytes from hyperglycemia induced liver injury.

The serum albumin influences the vascular porousness or permeability and transports several molecules; it also traps free radicals (Roche*et al.,* 2008; Park *et al.,* 2014). Similarly, it plays pivotal role by controlling the serum osmotic pressure. The decreased serum albumin level in STZ induced experimental rats is a signal to the pathogenesis of some diseases (diabetes, cardiovascular diseases and some neurodegenerative diseases) linked to OS. Diabetic condition brings about a reduction in albumin concentration (Chen *et al.*, 2016),

if not managed through the application of insulin, might result in hypoalbuminemia. The decrease in albumin might be caused by high excretion of albumin from the urine attributed to diabetic nephropathy (Stehouwer, 2002)and or low hepatic production of albumin (Park *et al.,* 2014).Consumption of shallot noodle increased the serum albumin close to the normal control (NC) especially with 7 and 10% shallot fortified noodles. This agrees with the observation of Javad, et al. (2012), where Persian shallot extract increased serum albumin, by stimulating insulin secretion, and the insulin produced induces the integration of amino acids into proteins (Mansour *et al.,* 2002). Similarly, Chen,et al. (2016) reported that insulin stimulate the production of albumin in the liver by activating the gene transcription. In the liver, insulin stimulates the production of protein and lipid synthesis but stops gluconeogenesis, all these might reflect as increased serum albumin in the rat model after the treatment with shallot fortified noodles.

The degree of creatinine and urea in the serum, revealed the efficacy of the kidney (the glomerular filtration rate). High amount of serum creatinine and urea levels as indicated in STZ induced rats compared to the normal rats is an indication of kidney disease (Wang *et al.,* 2012). However, feeding the rats with shallot fortified noodles reversed the effect of the STZ, this was revealed by the significant reduction in the levels of serum creatinine and urea in fed rats to close to normal (Fig 6a and b). Ability of the shallot fortified noodles might be accredited to quercetin (a major flavonoid in shallot) known for its ability to enhance renal function in STZ induced rats with diabetes nephropathy by impeding the excessive production of transforming growth factor-β1(TGF-β1) and connective tissue growth factor (CTGF) in the kidney (Hu*et al.,* 2021) . TGF-β1 is a main profibrotic growth factor, initiated in acute kidney injury and it is linked with cellular responses that lead to the advancement of chronic kidney disease while, the CTGF is a chief umpire of tissue fibrosis.

CONCLUSION

Our study confirmed that the developed shallot fortified noodles exhibited blood glucose lowering potential at a concentration dependent manner and impedes the activities of intestinal α-amylase and pancreatic α-glucosidase in STZ – induced diabetes rats. The shallot fortified noodles raised the level of the innate defense antioxidant enzymes (SOD, CAT, GST) and lowered peroxidation of lipid by reducing the levels of TBARs in tissues (liver and kidney) homogenates. Hepatoprotective and renoprotective abilities of shallot fortified noodles were further revealed by their ability to reduce the serum hepatic enzymes and increase the serum albumin. Finally, the biological activity of shallot noodles in reducing OS consequent to hyperglycemia and attenuating diabetes complications was established, with 10% shallot fortified noodles been the most effective, and could be employed as functional food in attenuating OS biomarkers, as well as diabetes complications.

AUTHORS' CONTRIBUTION

The study was formulated and supervised by OSO. AGS and TDA carried out the research, processed the experimental data, and wrote the first draft of the manuscript. FJFA, read the draft while OSO supervised and reviewed the manuscript.

CONFLICT OF INTEREST

The authors declared that, there is no conflict of interest.

ETHICAL APPROVAL

This study contains ethics of approval and Protocol from by the Federal University of Technology, Akure, School of Agriculture and Agricultural Technology ethical committee (FUTA/SAAT/2020/024).

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