



COCONUT LIQUID AS DIETARY INTERVENTIONS FOR HYPERGLYCEMIC RATS

Hanaa H. Ehsayed¹, Hassan M. Sobhi² and Mona S. Kassem^{3*}

¹Department of Environmental Studies for the Nutritional Chemistry and Metabolism, National Nutrition Institute, Egypt.

²Department of Natural Resource, Faculty of Post Graduated African Studies, Cairo University, Giza, Egypt.

^{3*}Department of Animal Ecology of Post Graduated African Studies, Cairo University, Giza, Egypt.

Abstract

Coconut liquid is a natural beverage that contains several biologically active nutrients. Diabetes is a syndrome characterized by the loss of glucose balance due to various reasons. This study aims to evaluate nutrients effect of coconut liquid on hypoglycemic. The experimental animals were divided into four groups: normal control, normal rats induced with Streptozotocin (STZ) as diabetic control and diabetic rats treated with coconut liquid by two doses (100; 500 mg/kg diet) for four weeks. At the end of period assayed biological parameters (feed intake, body weight gain and feed efficiency ratio); diabetes markers (glucose, insulin, homeostasis model of assessment insulin resistance and homeostasis model of assessment beta pancreas cells); liver function (Alanine transaminase; aspartate transaminase and alkaline phosphates) and histological examination. The results indicate that significantly attenuated hyperglycemia as oxidative stress of STZ-induced diabetic rats and indicating the therapeutic coconut liquid.

Key words: Hyperglycemia - coconut liquid - Dietary Interventions.

Introduction

The world corroborative phytochemical remedies as they are economical; often, free from adverse side effects and containing polyphenols. Polyphenols may help prevent metabolic syndrome (Fujioka *et al.*, 2006) because these compounds are considered to be antioxidants (Martin and Appel, 2010).

Coconut water (CW) or liquid (CL) or milk (CM) from coconut fruit is a nutritious beverage (Anurag and Rajamohan, 2003). It contains low levels of carbohydrates, fats and calories (Yong, *et al.*, 2009). It has inorganic ions, amino acids, phytohormones, vitamins C and vitamin B, (Mohamad *et al.*, 2017) and a good source of minerals (Borse *et al.*, 2007) and (Omosho and Odeyemi, 2012). Yong *et al.*, (2009) reported that coconut juice has medicinal properties. Misra, (2016) mentioned that coconut sap is perfect for digestion, facilitates, clear urination and prevent jaundice. Coconut liquid has many health-elevate capabilities including anti-inflammatory (Rao and Najam, 2016), antibacterial properties (Mandal

et al., 2009), protects reproductive health (Kunle-Alabi, *et al.*, 2015) and beneficial effect on blood pressure/lipid levels (Bhagya *et al.*, 2010a).

Diabetes mellitus is a common metabolic disorder and is considered a major reason for death worldwide (Kim *et al.*, 2012). Rother, (2007), defines that in diabetes mellitus, the pancreas does not produce (type 1) or properly respond (type 2) to insulin, which leads to elevated glucose in the blood. Sendrayaperumal *et al.*, (2014) who indicated that chronic hyperglycemia, is associated with the dysfunction of bodies and the failure of some organs. Chen *et al.*, (2016) explained that there numerous hypoglycemic drugs have been synthesized for the remedy, but those drugs were restricted by aspect effects and high prices.

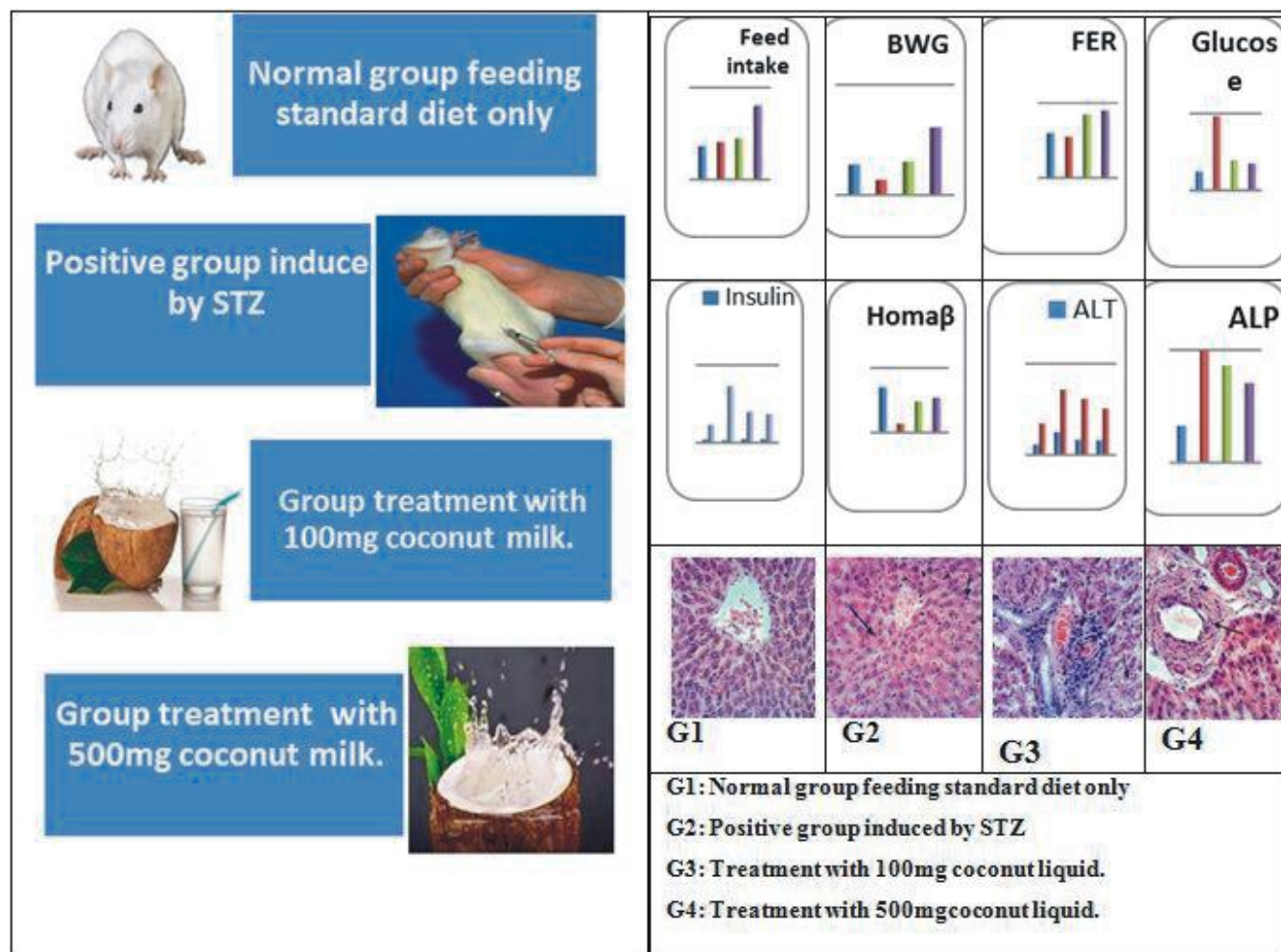
Thus the present study was done to investigate the effects of coconut liquid on oxidative stress in diabetic rats.

Materials and Methods

Materials

• Streptozotocin (STZ) was obtained from Sigma Chemicals Company.

**Author for correspondence* : E-mail: monakassem8080@yahoo.com



- Commercial fresh Coconut fruit was obtained from the local market. The coconut was broken carefully and the liquid endosperm was freshly collected and used for the experiment.

- All kits of the biological parameters were purchased from Morgan Chemical Company, Egypt.

- Diets: The standard diets were prepared according to the methods of Reeves *et al.*, (1993).

- Rats: Thirty-eight male albino rats 'Sprague-Dawley' strain weighing (105 ± 5 g) were obtained from the animal colony, Helwan Farm, Vaccine and Immunity Organization, Egypt.

Experimental design: Experimental rats were kept an individual in wire cages under hygienic conditions (standard lighting (12-h. light and 12-h. dark cycle); the room temperature was maintained at $25 \pm 2^\circ\text{C}$) throughout the experiment. Food and water were provided ad-libitum and checked daily. Rats fed on a standard diet for a week as adaptation before experimentation and approved from the National Nutrition Institute experimental animals unit. After that, the rats were divided into two main groups as follows:

- The first main group (8 rats) was fed on a standard diet as a healthy control group for four weeks.

- The second main group (30 rats) induces diabetes by Streptozotocin (50 mg/kg BW) dissolved in 0.1 M sodium citrate buffer, pH 4.5) was administered intraperitoneally injected comply with Ballester *et al.*, (2004). The pH was adjusted to 4.5 by the proper addition of concentrated NaOH/HCL using a calibrated pH meter. 0.1 M citrate buffer was prepared by dissolving 2.1 g of citric acid or 2.94 g of sodium citrate in 100 ml of distilled water. Rats with glucose levels >200 mg/dl were classified as diabetic.

- The rats in the second main group were divided into (3 subgroups): Subgroup (1): diabetic rats fed on standard diet as a positive control group. Subgroup (2&3): diabetic rats fed on standard diet subjoin with 100 mg and 500 coconut liquid /kg diet according to Preetha *et al.*, (2012) for four weeks.

At the end of the period, the rats have fasted overnight and then sacrificed after anesthesia and blood samples were collected from the hepatic portal vein. The serum was separated in Eppendorf tube at -20°C until

analysis. Besides the liver of every rat was removed by carefully dissection, washed in saline (0.9%), dried by filter paper then weighed and so the portion from that place in 10% formalin for histopathological examination.

Methods

Biological evaluation: Animals and diet were weighed twice a week. At the end of the experiment calculated for them as a mean and standard error for each group.

Body weight gain = final body weight - initial body weight

Feed efficiency ratio (FER): Calculated according to Manjula *et al.*, (2016) as follows:

Feed efficiency ratio = Body weight gain (g) per day / Feed intake (g) per day

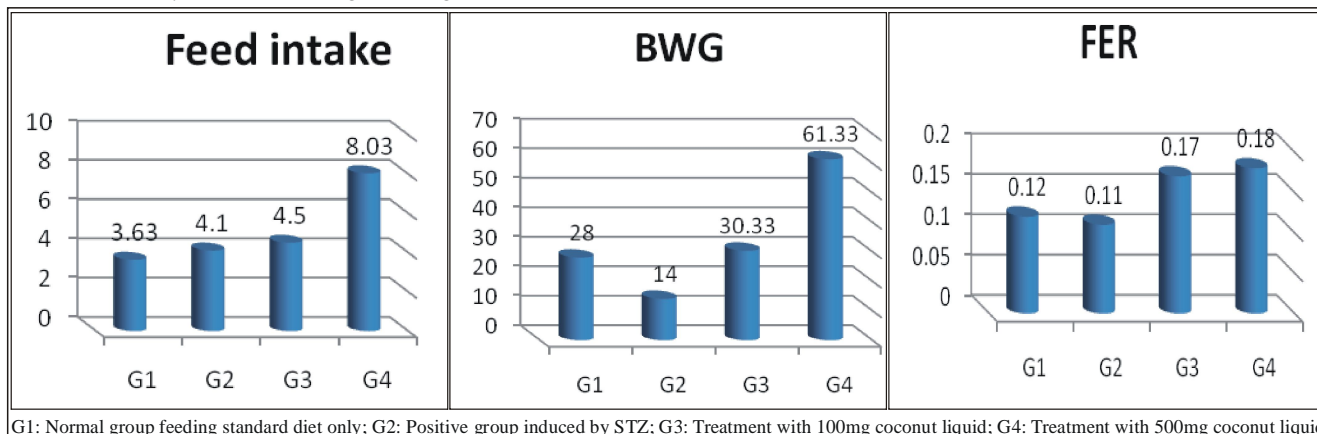
Biochemical analysis: Determined Glucose by the BIOMED kit was according to Trinder, (1969). Fasting serum insulin level was measured using the ultrasensitive rat insulin ELISA kit were determined using standard techniques by Lipina *et al.*, (2015). Determination of insulin resistance by the homeostasis model assessment – insulin resistance (HOMA-IR) and HOMA-β cell calculated as the following formula: $HOMA-IR = \text{insulin } (\mu\text{U/mL}) \times \text{glucose (mg/dl)} / 405$. $HOMA-\beta = [20 \times \text{fasting serum insulin } (\mu\text{IU/l})] / [\text{fasting serum glucose (mmol/l)} -$

3.5] according to Niemczyk *et al.*, (2013) and Matthews *et al.*, (1985). Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) were assayed by spectrometer appropriate to Reitman and Frankel, (1957) Method. Alkaline phosphatase was determined by method of Powell and Smith, (1954).

Statistical Analysis: The obtained data were statistically analyzed using computerized SPSS (the statistical package for social science). Effects of different treatments were analyzed by one way ANOVA (Analysis of variance) test followed by post hoc least significant difference analysis (LSD) $P < 0.05$ was used to indicate significance between different groups according to Snedecor and Cochran, (1967).

Results and Discussion

Fig. 1, illustrated that there were significant differences for FI, BWG and FER within all groups. The highest value of all biological parameters showed in a group (4) which treatment with 500 mg/kg diet from coconut liquid after induces diabetes. Dose-dependent response of coconut aqueous on STZ induced diabetic rats were evaluated and found that 500 mg/kg diet of coconut liquid was effective in increased FI and BWG when compared to another dose (100mg/kg diet) in rats.



G1: Normal group feeding standard diet only; G2: Positive group induced by STZ; G3: Treatment with 100mg coconut liquid; G4: Treatment with 500mg coconut liquid.

Fig. 1: Biological parameters (FI); (BWG) and (FER) for normal; diabetic and diabetic treatment with coconut liquid groups.

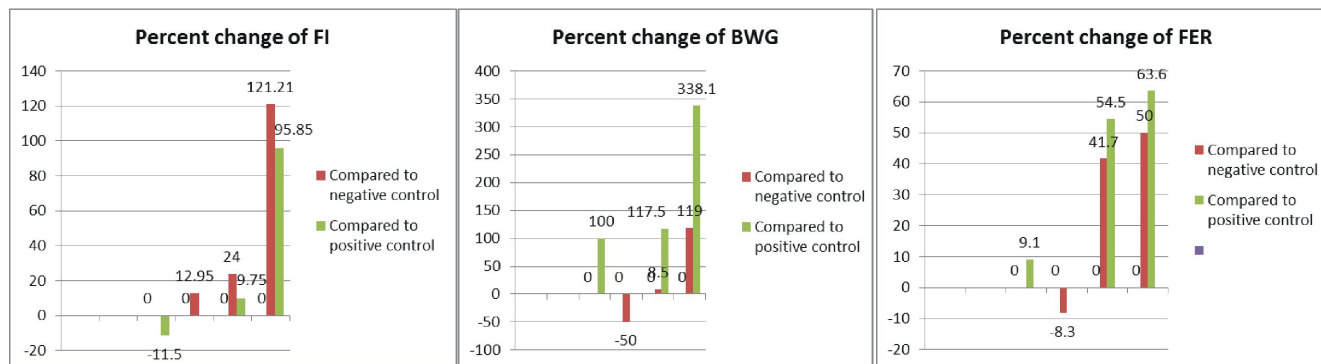
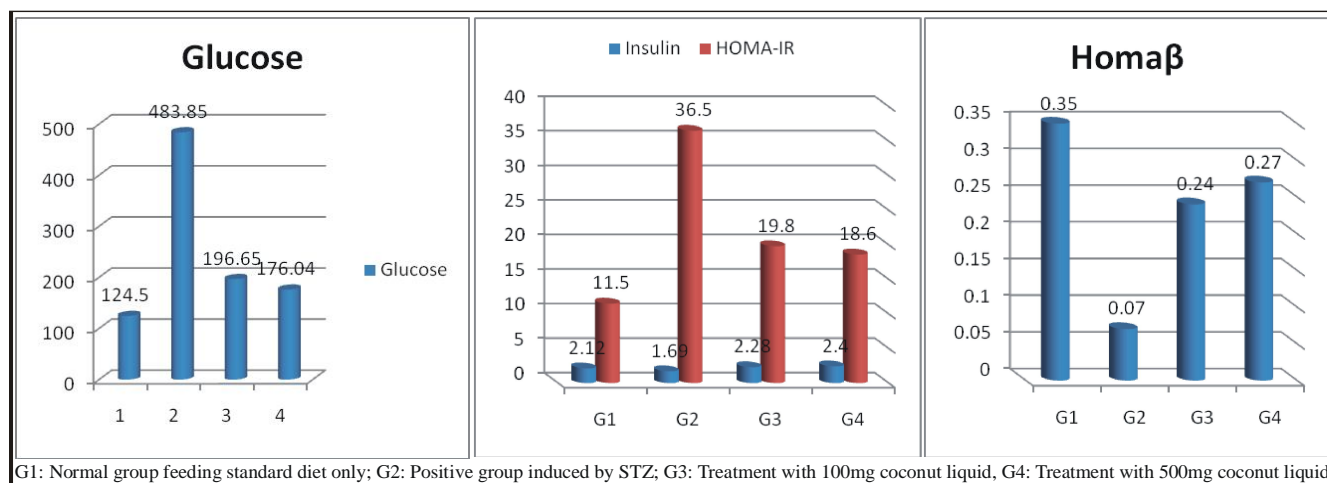


Fig. 1b: Percent change of Biological parameters (FI) ;(BWG) and (FER) for normal; diabetic and diabetic treatment with coconut liquid groups.



G1: Normal group feeding standard diet only; G2: Positive group induced by STZ; G3: Treatment with 100mg coconut liquid, G4: Treatment with 500mg coconut liquid.

Fig. 2: Glucose, Insulin, HOMA-IR and HOMA β for normal; diabetic and fed on coconut liquid groups.

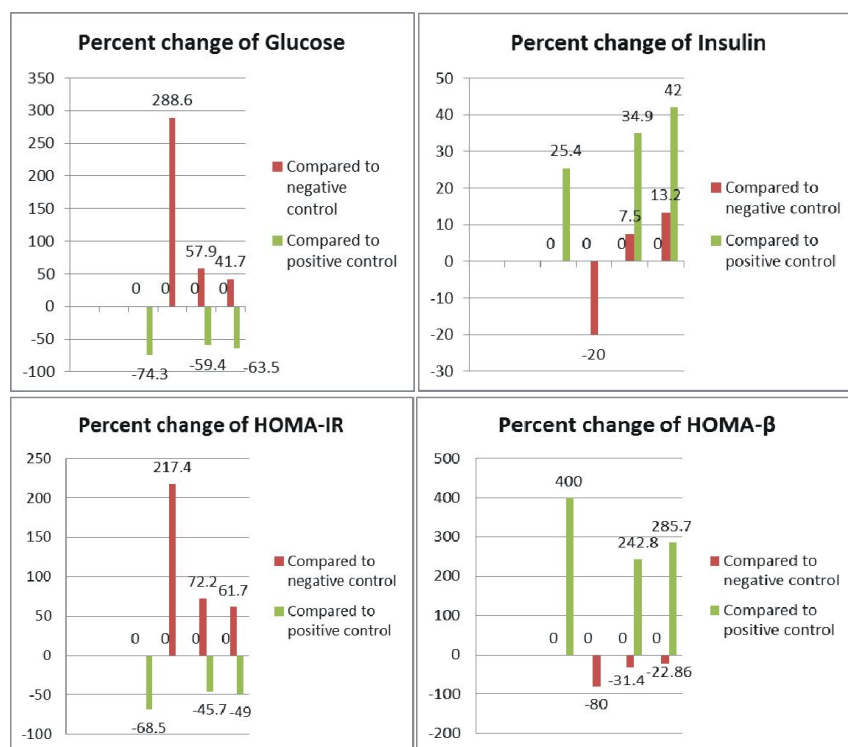


Fig. 2b: Percent change of Glucose, Insulin, HOMA-IR and HOMA β for normal; diabetic and fed on coconut liquid groups

While there were non-significant differences for FER within two group's intake both doses. This due to a coconut liquid contains bioactive compounds like vitamins, proteins, minerals, amino acids, etc. The richness of macro- and micronutrients in coconut liquid possess many medicinal properties, including antioxidant and palatability (Mohamed *et al.*, 2017). In the same figure observed the STZ induced diabetic rats effective in decreased BWG and FER but FI was higher than normal rats. The findings showed that a decrease of BWG which was lined with finding Dekel *et al.*,(2009) who found the weight loss of up to 40% within 2 weeks of STZ injection in their high dose model. Nagarchi *et al.*, (2015) when induced

diabetes mellitus in adult Westar rats by Streptozotocin deduced the body weight decreased. They explained that BW loss of the animals' injurious effects of STZ which caused the alkylation of DNA and produced hyperglycemia. Present observations are in agreement with the findings of Zafer, (2009), Habibuddin *et al.*, (2008) and Lee *et al.*, (2008). The increase in FI was explained by Pai *et al.*, (2006) who found in diabetic rats that taste cells innervations were significantly reduced. These findings showed that taste impairment in diabetic may be due to neuropathy defects and/or morphological changes in the bulbous nerve endings on the tongue.

In experimental animals, Streptozotocin (STZ) is widely used to induce insulin-dependent diabetes mellitus (Fadillioğlu *et al.*, 2008). The direct result of STZ in the diabetogenic is representative in damage to the

pancreatic beta cells resulting in degranulation and forfeit of the capability to secrete insulin (Gu, *et al.*, 1997).

Statistical results in fig. 2, showed that the diabetic group (G2) elevated blood glucose value with significant differences when compared to other groups. These results were harmony with finding observed by Nagarchi *et al.*, (2015) who concludes that STZ at 50mg/kg BW induces diabetes and marker higher glucose levels in the diabetic rats than normal animals. On the other hand treatment of diabetic groups with coconut liquid, 100and 500 mg /kg diet (G3 & G4) showed a significant reduction of blood glucose when compared to diabetic control, but it did not reach normal control. These previous results due to the

aqueous part of the coconut, containing vitamins C and B, as an antioxidant scavenging free radicals (Mohamad *et al.*, 2017).

Fig. 2, observed that the insulin value in the second group (G2), which was injected with STZ showed lower than the normal rate in the first group with significant differences. The previous findings observed that may due to the beta cells of the pancreas have a low antioxidative defense capacity, thus the generation of ROS by STZ leads to the death or degranulation of these cells. This is possible due to the reduction product of the reaction, dialuric acid, which generates hydrogen peroxide, superoxide radicals and hydroxyl radicals. In the third and fourth groups, which fed on coconut liquid (100; 500mg/kg diet) the level of insulin increased at a rate close to a normal level. Besides, a study was done by Salihi *et al.*, (2009) illustrated that the coconut water has a significant lowering effect in alloxan-induced diabetes. Supporting the former report by Misra, (2016) who was conformance the nutrient-rich coconut liquid has a low Glycemic Index and its antioxidant properties. It is possible that the beta cells respond to oxidative stress might have been enhanced thus enabling the cells to carry out their

function of insulin production. Consequently, this increase in insulin production will lead to reduced blood glucose.

The homeostasis model assessment-estimated insulin resistance (HOMA-IR) may constitute a useful method not only for diagnosing insulin resistance but also for follow-up during the treatment of patients. Continuous infusion of glucose HOMA-IR is thought to reflect essentially hepatic insulin resistance (Bonora *et al.*, 1999). In the same fig. 2 can be noted that the group infected with diabetes by STZ increased the ratio of HOMA- IR compared to other groups. The highest value in HOMA-IR of STZ injection agreement with Juncheng *et al.*, (2011) who found the group fed normal diet administered with STZ alone, increased glucose and insulin. Increase fasting glucose is a direct result of insulin resistance because of decreased sensitivity to the glucose-lowering effect of insulin. In fig. 2 found that both groups fed on 100 or 500 mg of coconut liquid/kg diet reduced the proportion of HOMA IR. These decreases in the HOMA-IR values suggest that treatment with coconut aqueous caused by diet. Chitturi *et al.*, (2002) observed a significant decrease in blood sugar and insulin levels, that positively affecting the HOMA-IR values.

Deterioration β -cells (glucose- and lipotoxicity), leading to gradual wastage of these cells by increased glucose levels and increased levels of free fatty acids due to insulin resistance, (Saltier and Kahn, 2001) .

HOMA- β cells values in fig. 2 clear that the ratio for the second group injected with STZ was lower than the first group. In addition, the group fed 100 mg of coconut liquid/ kg diet showed betterment in HOMA β . As for the fourth group a noticeable amelioration, this is close to the first natural group. These

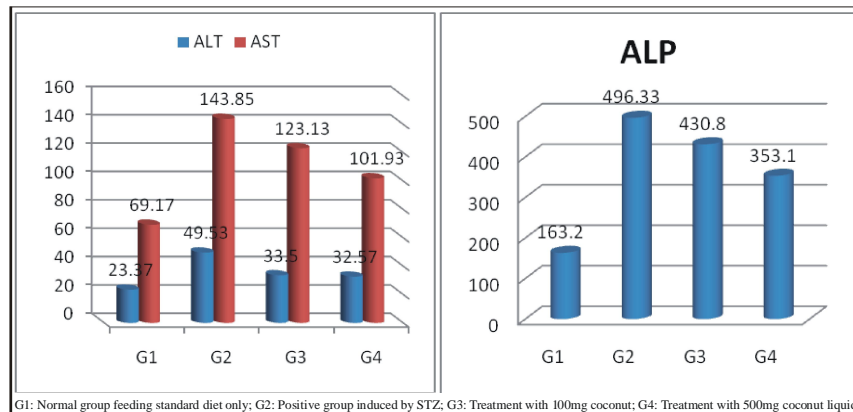


Fig. 3: Liver function (ALT; AST and ALP for normal; diabetic and diabetic treatment with coconut liquid groups

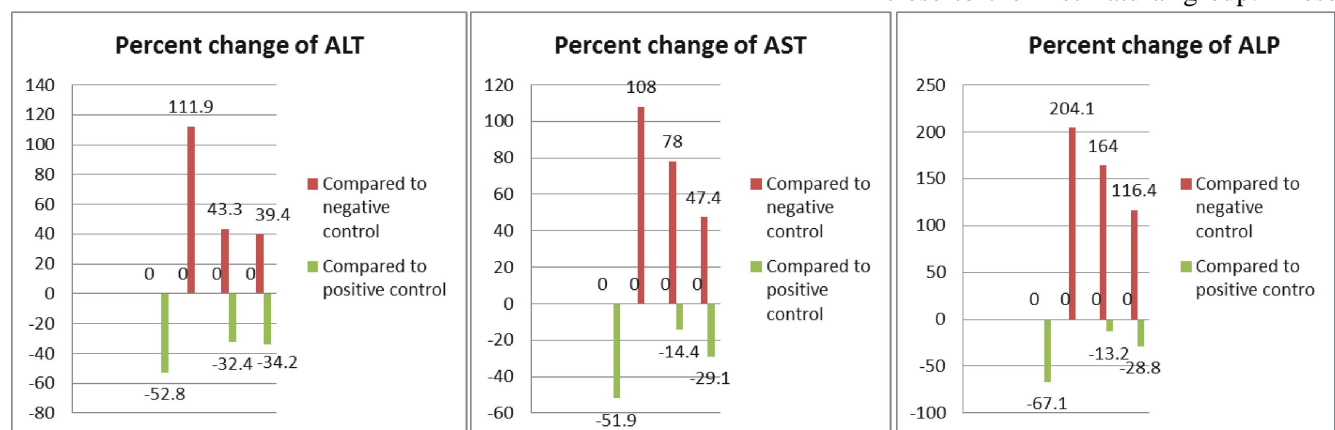


Fig. 3b: Percent change of liver function (ALT; AST and ALP for normal; diabetic and diabetic treatment with coconut liquid groups.

results concluded that coconut liquid has a significant improvement in the HOMA- β ratio and progressed blood sugar. The protective effects of coconut liquid against oxidative stress in STZ-induced diabetic rats may be due to the presence of biologically active components in it. Coconut liquid revealed that it contains L-arginine which important modulators of glucose metabolism and insulin sensitivity. L-arginine is reported to possess anti-glycation and anti-peroxidative potential in diabetes. L-arginine also can regenerate pancreatic β -cells and reduce STZ - induced pancreatic damage in diabetic rats (Stancic *et al.*, 2012). Coconut liquid (CL) contained: Ascorbic acid and minerals like (potassium, magnesium, calcium and manganese) according to Owu *et al.*, (2006). Jean *et al.*, (2009) who reported indicating that the administration of vitamin C reduces plasma glucose and improves the basal metabolic rate in STZ induced diabetic rats. Khassaf, *et al.*, (2003) found vitamin C increases SOD activity, provides anti-inflammatory action and it can directly scavenge singlet oxygen, superoxide and hydroxyl radicals. Magnesium, one of the minerals present in CL is anti-hyperglycemic potential and it can reduce free radical generation (Vasdev and Stuckless, 2010). Serum potassium levels affect insulin secretion by pancreatic β -cells and dietary potassium intake is significantly associated with the risk of contracting diabetes mellitus (Chatterjee *et al.*, 2010). Potassium supplementation in hypoglycemic patients corrected the defects of insulin release in response to glucose loads (Reno *et al.*, (2013).

Manganese, another important mineral present in CL, also possesses protective effects against diabetes (Walter *et al.*, 1991).

Findings in fig. 3 can be indicated to liver function; Alanine aminotransferase (ALT); aspartate aminotransferase (AST) and alkaline phosphates (ALP) were higher in the second group induced with STZ than first group (normal control). In the third group, fed CL was 100 mg/kg di *et al.*, T, AST and ALP values decreased. In the fourth group, fed on 500 mg/kg diet of CL, the ratio was close to the average of the normal control group. Coconut liquid resulted in the reduction of the level of AST, ALT and ALP. These data are consistent with the results obtained by Effiong and other, (2010) who can be observed that CL is rich in the B vitamins; which have a role to play in the maintenance of liver cells integrate. Serum concentrations of liver function marker enzymes, ALT, AST and ALP induced diabetic rats were elevated this may be due to leaking out of enzymes from the tissues and induce the liver injury by free radical mechanism; Coconut liquid treatment regulated the activity of ALT and AST in the liver (DeFronzo, 1999). Ravikumar *et al.*, (2010) and Preetha, *et al.*, (2013a) found that elevated levels of ALP in diabetes may be due to extensive damage to the liver by the alloxan-induced diabetic rats. Treatment with coconut liquid induced diabetic rats caused a decline in the ALP level. In diabetic rats, mature CL treatment showed significant beneficial effects along.

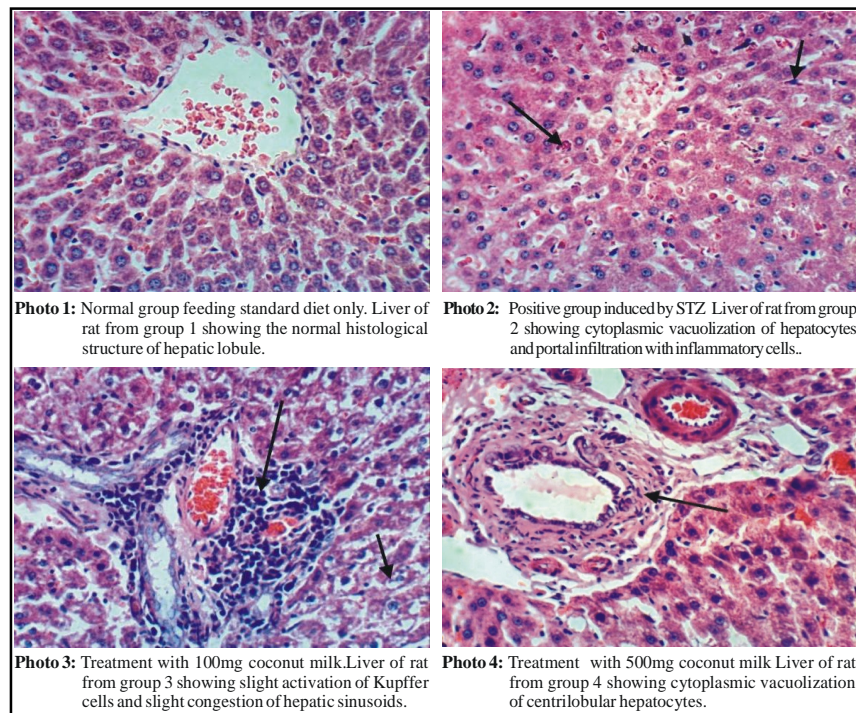


Fig. 4: Histological examinations for normal; diabetic and diabetic treatment with coconut liquid groups.

Histology

Photo 1, showed the normal histological structure of hepatic lobule in the (Normal group feeding standard diet only) but photo 2, showed Liver of rat from group 2 showing cytoplasmic vacuolization of hepatocytes and portal infiltration with inflammatory cells (Positive group induced by STZ). Photo 3, Liver of rat from group 3 (treatment with 100mg CL) has showing slight activation of Kupffer cells and slight congestion of hepatic sinusoids. In the photo 4, it is clear improvements in the cells and lack of congestion and cytoplasmic vacuolization of centrilobular hepatocytes (group treatment with 500mg CL). Gopal *et al.*, (2014) pathologically, the liver's histological structure was normal in the control group (group 1). Liver in the diabetic rats has complete (severe) destruction of hepatocytes in

severe congestion with nuclear condensation, loss of hepatic lobules and congested hepatic inflammation. Loku and Rajamohan, (2003) found that the group fed tender coconut water (6ml/100g BW) after induced liver by CCl₄: showing normal lobule, no fatty change and necrosis are seen, mild atrophy of hepatocytes is indicating by prominent insides. Another study showed that the histological changes in diabetic rats were restored to near normal when treatments with coconut liquid (Reno and Leland, 1999). Bhagya *et al.*, (2010a), showed the liver architecture is normal with cords of hepatocytes with normal cytoplasm and central nuclei no abnormal features. Control + CW treated group: no hepatic damage and fatty infiltration the liver architecture the same as normal. Group fed high fructose liver of rats showed degenerative changes hepatocellular damage, inflammatory infiltration and cytoplasmic vacuolization (spherical vacuoles) accumulated with lipids. Group fed fructose + CW treated: rats showed no hepatocellular damage and inflammatory infiltration with lower lipid accumulation.

Conclusion

The present study demonstrated that CL is effective in attenuating oxidative stress *via* the up-regulation of the antioxidant status in STZ induced diabetic rats, which shows the therapeutic potential of CL

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