Original Article

# Extracts of *Hunteria umbellata* reverses the effect of streptozotocin-induced pancreatic islet-cell destruction

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## Abstract

The use of extracts of plant parts in the treatment and/or management of diabetes mellitus has formed the basis of health care in most African countries. The aim of this study was to investigate the possible effect of oral administration of extracts *Hunteria umbellata* (HU) leaves and seeds on streptozotocin- induced pancreatic $\beta$-cell damage. Twenty four (24) adult wistar rats were selected into two control group (negative control group A and positive control group B) and two treatment groups (C & D) each containing six animals each (n= 6 per group). Rats in the positive control group (B) were giving intraperitoneal injection of with 50 mg/kg body weight of Streptozotocin (STZ) prepared with 0.05M Citrate buffer solution while the negative control group A rats were injected with a corresponding volume of Citrate buffer without STZ. Rats in the treatment groups were treated with 250 mg/kg body weight aqueous extract of seeds of *Hunteria umbellata* (group C) and 250 mg/kg body weight aqueous extract of leaves of *Hunteria umbellata* (group D) respectively. Blood samples were taken by repeated needle puncture of their tail tip vein every 72 hours at the end of a 12 hrs fasting. Fasting blood glucose was determined using a fine test glucometer and compatible glucose test strips. Rats were sacrificed by cervical dislocation on the 15$^{th}$ day and the pancreas was accessed and dissected out through a midline incision of the anterior abdominal wall of the rats. The pancreas was fixed in 10% buffered formal saline for routine histological examination. 5ml blood samples were collected in heparin coated tubes for serum anti-oxidant estimation. Results obtained showed that HU seeds and leaves extracts significantly ($P$ < 0.05) increased Superoxide dismutase (SOD) and Catalase (CAT) activities and decrease in the activity of Thiobarbituric acid reactive species (TBARS) when compared streptozotocin injected rats. Histological sections showed marked distortion, vacoulation of the central part of the Islet. Treatment with Hunteria umbellata seed and leaf extracts reversed the cytoarchitectural distortion of pancreatic Islet cells caused by Streptozotocin. This suggests that extracts of HU seeds and leaves posses antidiabetic potential.

**Key words:** *Hunteria umbellata*, streptozotocin, pancreatic Islet, cytoarchitectural distortion

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## INTRODUCTION

Intracellular actions of streptozotocin (STZ) result in changes of DNA in pancreatic $\beta$-cells comprising its fragmentation (Yamamoto *et al.,* 1981; Morgan *et al.,* 1994). Recent experiments have proposed that the main reason for STZ-induced $\beta$-cell death is the alkylation of DNA (Delaney *et al.,* 1995; Elsner *et al.,* 2000). The alkylation activity of STZ is related to the nitrosourea moiety especially at the O$^6$ position of guanine. After STZ injection to rats, different methylated purines were found in tissues of these animals (Bennett and Pegg, 1981). STZ is a nitric oxide (NO) donor and NO is found to bring damage to

pancreatic $\beta$-cells (Morgan *et al.,* 1994; Kroncke *et al.,* 1995). The participation of NO in the cytotoxic effect of STZ was confirmed in several experiments (Turk *et al.,* 1993; Kroncke *et al.,* 1995). Pancreatic $\beta$-cells exposed to STZ manifested changes characteristic for NO action that is, increased activity of guanylyl cyclase and enhanced formation of cGMP (Turk *et al.,* 1993). STZ is however not a spontaneous NO donor (Kronke *et al.,* 1995). This molecule is liberated when STZ is metabolized inside the cells, but NO synthase is not required (Kronke *et al.,* 1995). On the other hand, the lowering of NO concentration in pancreatic islet cells by inhibition of inducible forms of NO synthase partially counteracted DNA cleavage induced by STZ (Bedoya *et al.,* 1996). A similar result can be attained by NO scavengers (Kroncke *et al.,* 1995). However, the result of several experiments provide the evidence that NO is not the only molecule responsible for the cytotoxic effect of STZ. STZ was found to generate reactive oxygen species (ROS), which also contributes to DNA fragmentation and evoke other deleterious changes in the cells (Takasu *et al.,* 1991; Bedoya *et al.,* 1996). The formation of superoxide anions results from both STZ action on mitochondria increase activity of xanthine oxidase. It was demonstrated that STZ inhibits the Krebs cycle (Turk *et al.,* 1993) and substantially decreases oxygen consumption by mitochondria (Nukatsuka *et al.,* 1990). Augmented adenosine triphosphate (ATP) dephosphorylation increases the supply of substrate for xanthine oxidase ($\beta$-cells posses` high activity of this enzyme) and enhances the production of uric acid the final product of ATP degradation (Nukatsuka *et al.,* 1990). Then the xanthine oxidase catalyses` reaction in which the superoxide anion is formed (Nukatsuka *et al.,* 1988). As a result of superoxide anion generation of hydrogen peroxide and hydroxyl radicals are formed (Nukatsuka *et al.,* 1990; Takasu *et al.,* 1991). The inhibition of xanthine oxidase by allopurinol restricts the cytotoxic effect of STZ *in vitro*. It can be stated that potent alkylating properties of STZ are the main reason of its toxicity (Nukatsuka *et al.,* 1990). However, the synergistic action of both NO and ROS may also contribute to DNA fragmentation and other deleterious changes caused by STZ. Therefore, inhibition of intracellular ROS or NO production can substantially restrict STZ toxicity and reverse STZ induced pancreatic $\beta$-cell destruction.

*Hunteria umbellata* (HU) *K. Kchum* (*Apocynaceae*) is a small tree of about 15–22 m in height with a dense evergreen crown (Oliver, 1986). It is found in rain forest zone of the southern part of Nigeria where it bears such local names as Osu (Edo), Erin (Yoruba) and Nkpokiri (Ibo) (Boone, 2006). It is also found in Ubongi-Shari in Ghana and the rain forest regions of Cameroon and Gabon. The leaves have been described as broad, abruptly acuminate and broadly lineate (Kaey and Onochie, 1964; Boone, 2006). The fruit is about 5–25 cm in diameter and consists of two separate globose mericaps 3–6 cm long, yellow, smooth. 8–25 seeds embedded in a gelatinous pulp (Kaey and Onochie, 1964).

*Hunteria umbellata* have been widely employed in traditional herbal medicine in the treatment of peptic ulcers, piles yaws, dysmenorrhea, fever, infertility (Eluojoba, 1995), helminthic infection (Oluwemimo and Usifoh, 2001), bacterial infection (Anibijuwon *et al.,* 2011) and Diabetes (Igbe *et al.,* 2009). Recent research on the use of extracts of HU focuses on its use as a potent antidiabetic agent (Igbe *et al.,* 2009; Adeneye *et al*., 2010). In spite of its use as a potent antidiabetic agent little is known of the possible mechanism behind its antidiabetic potentials. This present research focusses on investigation of the possible mechanism behind the use of HU in the treatment of diabetes.

## MATERIALS AND METHODS

### Plant Material

The seeds and leaves HU were collected from a farmland in Efon, a town near Benin City. The plant was identified by Mr. Nweke Sunny, a Curator at the Department of Pharmacognosy, Faculty of Pharmacy, University of Benin, Benin City.

### Preparation and Phytochemistry of Extract

The seeds as well as leaves of HU *(K Schum)* plants were sun dried for 8 weeks. The air-dried specimens were pounded using a wooden mortar and pestle and milled into fine powder in an electric blender A quaintly of 500 g of the powdered specimens was extruded in distilled water by percolation for 48 h. The mixture was filtered, and the filtrate evaporated at 60°C using a vacuum Rotary evaporator. A pasty residue was freeze-dried using a vacuum freeze drier and stored in a desiccator. An aliquot portion of the crude extract residue was dissolved in distilled water for use on each day of the experiment.

### Animals and Treatment Regimen

Twenty-four Adult Wistar rats were used for the experiment. The rats were selected into two control group (negative control Group A and positive control Group B) and two treatment Groups C and D each containing six animals each ($n = 6$ per Group). The rats in each group were giving 300 g/day Growers' mash and water *ad libitum*. Rats in the positive (STZ-injected rats) control Group B were injected with 50 mg/kg body weight of STZ intraperitoneally prepared with 0.05 M citrate buffer solution (Akbarzadeh *et al.,* 2007) while the negative (non-STZinjected) control Group A rats were injected with a corresponding volume of Citrate buffer without STZ. Rats in the treatment groups were injected with 50 mg/kg body weight of STZ and

treated with 250 mg/kg body weight aqueous extract of seeds of HU (Group C) and 250 mg/kg body weight aqueous extract of leaves of HU (Group D) respectively. The extracts were administered orally using an Orogastric tube.

**Procedure for Pancreatic islet-cell Destruction**

Islet Cell destruction was induced by a single intraperitoneal injection of 50 mg/kg body weight STZ dissolved in 0.05 M sodium citrate buffer (pH - 4.6). Rats in Group A were given corresponding volume of citrate buffer used in dissolving STZ intraperitoneally. The extent of Islet cell damage and recovery was assessed during the experimental period by determination of fasting blood glucose (FBG) concentration from blood samples obtained by repeated needle puncture of their tail tip vein after every 72 h following a 12 h fasting. Fasting glucose concentration in the blood samples was determined using a fine test glucometer and compatible glucose test strips. All animals were kept and maintained under laboratory conditions of light, humidity and temperature.

**Sacrifice of the Animals**

Animals received treatment for 14 days. FBG concentration was taken on the $15^{th}$ day, and animals were sacrificed by cervical dislocation. A midline incision was made through the anterior abdominal wall of the rats. 5 ml blood samples were collected, from the descending abdominal aorta, in heparin coated tubes for serum antioxidant estimation and the pancreas were excised and a part washed in normal saline for tissue antioxidant estimation, and the other part was fixed in 10% buffered formal saline for routine histological examination.

**Antioxidants Estimation**

Blood samples were collected in heparin coated tubes and pancreas was place in 5 ml of normal saline. Centrifugation was done using a Denley BS400 Euslaw centrifuge at 4°C and 5000 rpm for 5 min. Superoxide dismutase (SOD) determination, using Randox Assay Kits manufactured by Randox Laboratories ltd, Ireland, Uk as described (Fridovich, 1974), which were based on the production of O anions by the 2-xanthine/xanthine oxidase system. The activity of catalase (CAT) was measured in the homogenates by measuring the CAT degradation of hydrogen peroxide using a redox dye according to methods of Cohen *et al.,* 1970. The assay was carried out in a visible spectrum microplate reader (DNM-9602 Perlong Beijing) which measures the change in color intensity of degradation at 570 nm. The change in color intensity is directly proportional to the CAT activity in the sample. Plasma concentrations of thiobarbituric acid reactive species (TBARS) were determined using the Malondialdehyde Assay Kits according to the method of Buege and Aust, 1978.

**Histological Procedure**

Procedure for hematoxylin and eosine was carried out according to the method of Drury and Wallington (1980).

**Photomicrography**

The sections were examined under Leica DM750 research microscope with a digital camera (Leica ICC50) attached. Digital photomicrographs of the tissue sections were taken at ×400 magnifications. Pancreatic islet cells in the photomicrographs were cropped at 369 × 348 pixels in Microsoft Office Picture manager manufactured by Microsoft corporation, Redmond, Washington and counted using the counter window of IMAGE J software with RGB color developed by the National Institute of Health, Maryland, USA.

**Statistical Analysis**

The data were analyzed using descriptive and inferential statistics. All values were presented as mean ± standard error of the mean for six rats each of four groups. The significance of the difference in the means of all parameters was determined using one-way analysis of variance (95% confidence interval). Least Square difference, *post-hoc* tests was carried out for all groups with control and comparison of all pairs of groups respectively. All statistical analysis was carried out using Statistical package for Social Sciences (SPSS) (version 16) manufactured by international Business Machine Corporation (IBM) in Armonk, New York.

**Ethical Approval**

The animals were housed, fed and cared for in accordance with the guidelines of the School of Basic Medical sciences ethical committee. The research was approved by the research ethics committee of the School of Basic Medical sciences , University of Benin, Benin city.

## RESULT

**Effects of *Hunteria unbellata* Seeds and Leaves on Fasting Blood Glucose Concentration**

The FBG concentration is shown in Figure 1. FBG

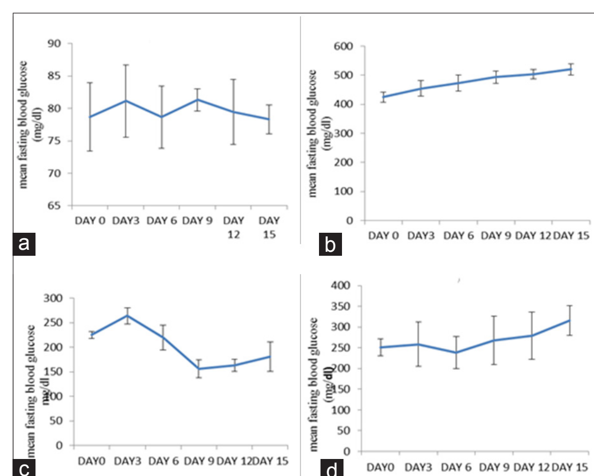


**Figure 1:** Line graph showing sequential (a) changes in fasting blood glucose (FBG) concentration of rats in Group A. (b) Changes in (FBG) concentration of rats in Group B. (c) Changes in (FBG) concentration of rats in Group C. (d) Changes in FBG concentration of rats in Group D

concentration of rats in a negative control Group A fluctuated within normal range (78.67 ± 5.26 mg/dl vs. 78.33 ± 2.33 mg/dl) during the experimental period of 14 days. This fluctuation was insignificant ($P < 0.05$). Rats in the positive control Group B showed significantly ($P < 0.05$) elevated FBG concentration (424.33 ± 16.82 mg/dl vs. 520.33 ± 18.7 mg/dl) during the experimental period. The FBG concentration of the treatment Groups C and D dropped (185.0 ± 4.83 mg/dl vs. 167.06 ± 1.39 mg/dl and 191.67 ± 5.27 mg/dl respectively). Group C showed a significant ($P < 0.05$) drop while Group D showed an insignificant ($P < 0.05$) drop.

**Effects of *Hunteria unbellata* on the Antioxidant Profile**

The Bar Chart below illustrates the activities of SOD, CAT, and malondialdehyde (MDA) in serum and pancreas of STZ-induced diabetic rats treated with aqueous extracts of HU seeds as well as leaves. The activity of SOD in serum and pancreas of Group B rats was significantly ($P < 0.05$) low (70.24 ± 4.05 μ/ml and 49.27 ± 5.29 U/ml respectively) when compared with control Group A, non-induced, negative induced, control rats, (103.60 ± 5.4 U/ml and 108.97 ± 4.32 U/ml respectively). There was increased SOD activity in Serum and pancreas Group C (STZ-induced diabetic rats treated with aqueous extract of HU seeds) rats (102.41 ± 4.83 U/ml and 86.31 ± 7.3 U/ml) and Group D (STZ-induced diabetic rats treated with aqueous extract of HU leaves) rats (104.83 ± 3.11 U/ml and 103.17 ± 5.54 U/ml).These increases were significant ($P < 0.05$) when compared with the control B (STZ-induced diabetic, positive induced, control rats) but not significant when compared with the control A.

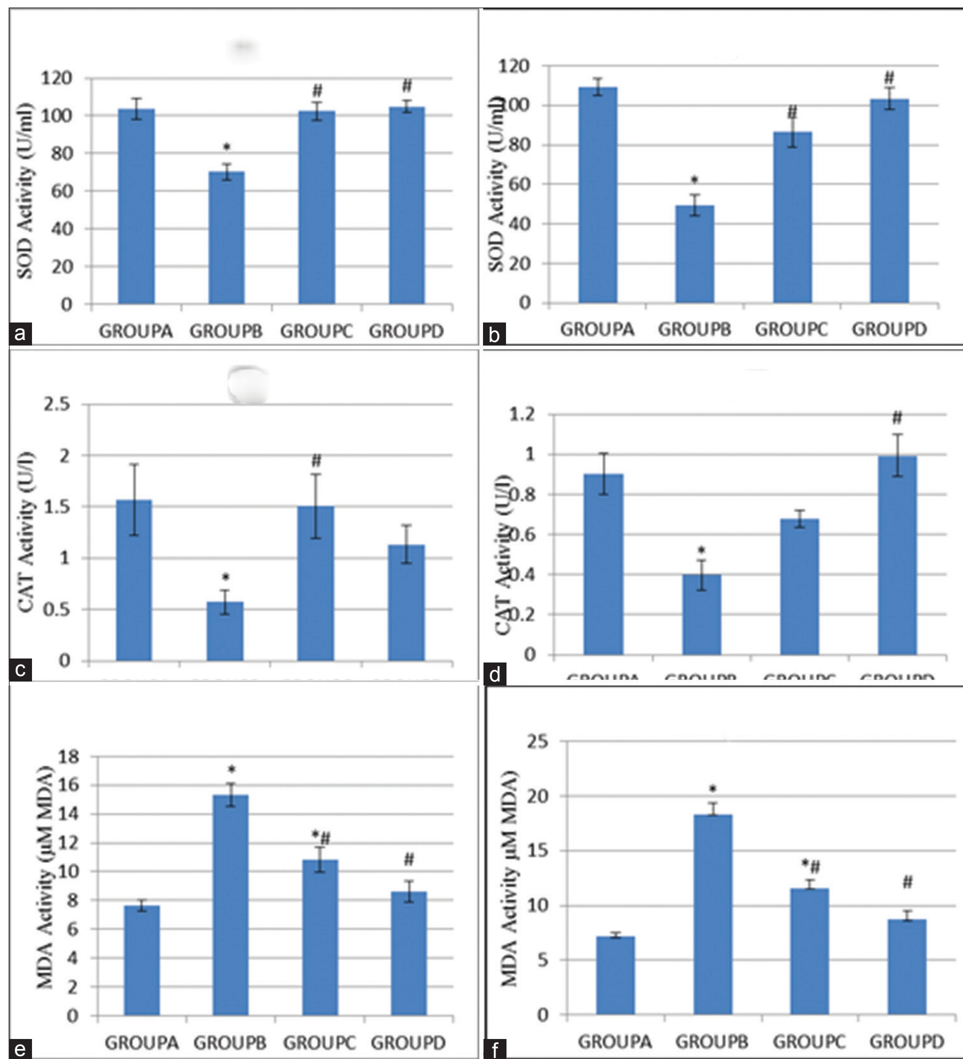


**Figure 2:** Bar Charts showing (a) serum superoxide dismutase (SOD) activity of streptozotocin (STZ)-induced diabetic rats treated with extract of *Hunteria umbellata*. (b) SOD activity in pancreas of STZ-induced diabetic rats treated with extracts of *Hunteria umbellata*. (c) Serum catalase (CAT) activity of STZ-induced diabetic rats treated with extracts *Hunteria umbellata*. (d) CAT activity in pancreas of STZ-induced diabetic rats treated with extracts of *Hunteria umbellata*. (e) Serum thiobarbituric acid reactive species (TBARS) activity of STZ-induced diabetic rats treated with extracts of *Hunteria umbellata*. (f) TBARS activity in pancreas of STZ-induced diabetic rats treated with extracts of *Hunteria umbellata*.*' and '#'represents significance of mean values when compared with control A and B respectively using Bonferroni multiple comparison test

The Bar Chart in Figure 2c and d shows CAT activities in the serum and pancreas. The CAT activity of positive control Group B was significantly ($P < 0.05$) lowered in serum and pancreas (0.57 ± 0.12 U/L and 0.40 ± 0.08 U/L respectively) when compared with negative control Group A (1.57 ± 0.35 U/L and 0.90 ± 0.10 U/L respectively). On treatment with aqueous extract of HU leaves (treatment Group D), there was an insignificant ($P < 0.05$) increase (1.13 ± 0.18 U/L) in serum CAT activity when compared with both positive control Group B (0.57 ± 0.12 U/L) and negative control Group A (1.57 ± 0.35 U/L) but increased significantly ($P < 0.05$) in pancreas (0.99 ± 0.11 U/L) when compared with control Group B. The CAT activity of treatment Group C (STZ-induced rats treated with aqueous extract of HU seeds) significantly ($P < 0.05$) increased (1.51 ± 0.31 U/L) in serum when compared with positive control Group B and insignificantly ($P < 0.05$) increased with negative control Group A. Although CAT activity increased (0.68 ± 0.04 U/L) in pancreas of Group C but the increase was not significant ($P < 0.05$) when compared with negative control Group A and positive control Group B.

The concentration of TBARS in serum and Pancreas is evaluated and shown in Figure 2e and f. TBARS concentration in Serum and pancreas was significantly ($P < 0.05$) higher (15.32 ± 0.79 μM MDA and 18.33 ± 1.01 μM MDA respectively) in Group B than negative control Group A (7.63 ± 0.39 μM MDA and 7.14 ± 0.38 μM MDA respectively). TBARS concentration in serum and pancreas of treatment Groups C (10.82 ± 0.78 μM MDA and 11.55 ± 0.81 μM MDA respectively) and D (8.62 ± 0.76 μM MDA and 8.72 ± 0.78 μM MDA respectively) was higher than Group A. The comparison with treatment Group C was significantly ($P < 0.05$) higher, comparison with treatment Group D was not significant ($P < 0.05$).

**Effect on Histology of Pancreas Islets**

Figures 3 and 4 represents photomicrograph of pancreas section of animals in Group A (control) showing even distribution of the pancreas Islet cells.Group B (diabetic induced) pancreas showing uneven distribution of pancreas islet cells and vacuolation of the central part of the pancreas islets occupied by $\beta$-cells. Group C (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU seeds extract) showing restored islet-cell cytoarchitecture similar to control. Group D (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU leaves) showing restored pancreatic islet-cell cytoarchitecture similar to control. Morphometric analysis is shown in Figure 5. There was significant ($P < 0.05$) reduction in whole nuclei of Pancreas Islet of animals in group B compared with control. Although whole nuclei in diabetic animals treated with Hunteria umbellate extracts (Groups C and D) showed significant ($P < 0.05$) reduction compared with control, there was significant ($P < 0.05$) increased compared with untreated diabetic animals (group B).

## DISCUSSION

Sterptozotocin is an antimicrobial agent originally derived from the soil micro-organism *Streptomyces achromogenes* (White, 1963; Herr *et al.,* 1967; Weiss, 1982). It has been used as a chemotherapeutic alkylating agent in the treatment of metastasizing pancreatic islet cell tumors and in other malignancies (Evans *et al.,* 1965; Schein *et al.,* 1974). In 1963, Rakieten and collaborators reported that STZ is diabetogenic (Rakieten *et al.,* 1963). Since then STZ has been used to induce experimental diabetes mellitus in laboratory animals (Rerup, 1970). This insulinopenia syndrome called "STZ diabetes" (Schein *et al.,* 1967) is due to the ability of this compound to induce a specific necrosis of the pancreatic $\beta$-cells (Arison *et al.,* 1967; Lenzen *et al.,* 1996). The effect of *HU* extracts on the toxic action of STZ on pancreatic Islet-cells was the main focus of this research. The photomicrographs above shows that STZ induce Islet-cell necrosis by distorting cytoarchitectural arrangement of cells and reduce islet cell population [Figure 3] in group B rats and this effect was reversed in the photomicrographs C and D with almost same semblance as the control shown in Figure 4. This result was supported by the evaluated FBG concentration shown in Figure 1. Steptozotocin injected diabetic rats in Group B showed significant ($P < 0.05$) elevation of FBG. This result is indicative of pancreatic $\beta$-cell dysfunction that is accompanied by hypoinsulinemia and

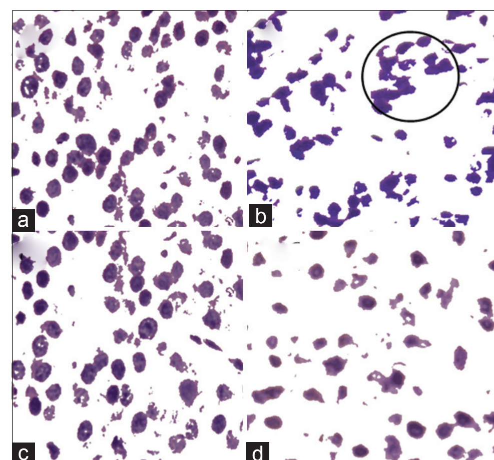


**Figure 3:** Pancreatic Islet (369 × 348 pixels) RGB image on counter window of IMAGE J software showing (a) even distribution of the pancreas Islet cells in negatively induced control Group A (b) uneven distribution of fragmented Islet cells nuclei forming clumps (circle) of pancreatic islet cells of positively (streptozotocin [STZ]) induced control Group B (c) Pancreatic islet-cell in Group C (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU seeds extract) with almost even distribution similar to control group (d) Pancreatic Islet-cell in Group D (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU leaves extract) with sparsely distributed

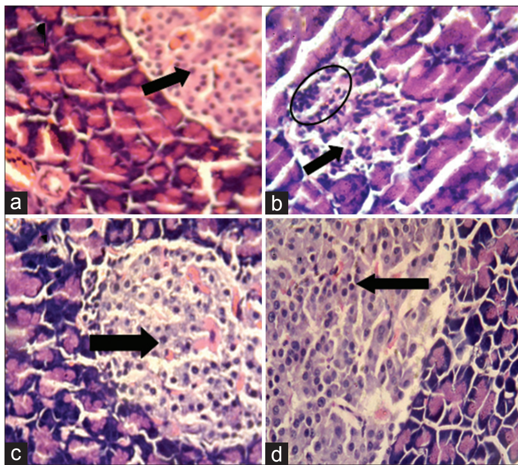


**Figure 4:** Photomicrograph of pancreas section (a) negatively induced control Group A pancreas showing even distribution of the pancreas Islet cells (arrow). (b) positively (streptozotocin [STZ]) induced control Group B pancreas showing uneven distribution (clumps formed in localized areas marked on circle in photomiceograph) of pancreas islet cells (circle) and vacuolation of the central part of the pancreas islets occupied by $\beta$-cells (arrow) (c) Group C (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU seeds extract) showing restored islet-cell cytoarchitecture similar to control (arrow) (d) Group D (STZ-induced islet-cell destruction in rats treated with 250 mg/kg body weight of HU leaves) showing restored pancreatic islet-cell cytoarchitecture similar to control (arrow) (H and E, ×400)

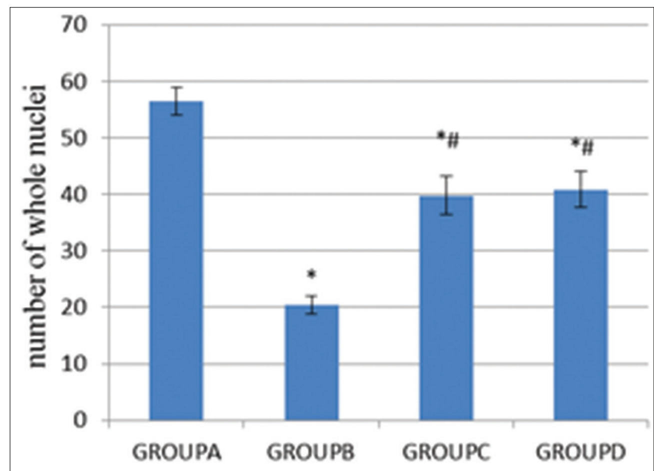


**Figure 5:** Bar chart showing the mean number of whole nuclei in 369 × 348 pixels pancreatic Islet RGB image on counter window of IMAGE J software. '*' and '#'represents significance of mean values when compared with control A and B respectively using Bonferroni multiple comparison test

hence hyperglycemic (type 1-like diabetes mellitus). The FBG concentration of Group C rats (STZ injected rats treated with 250 mg/kg body weight of HU seed extract) was significantly ($P < 0.05$) reduced to considerably hypoglycemic range but 250 mg/kg body weight of HU leave extract given to STZ injected rats did not reduce the FBG concentration, but it was able to maintain it within fluctuating hyperglycemic ranges. This result corresponds with the findings of Adeyemi *et al.,* 2009. Adeyemi *et al.* the hypoglycemic effect of lower doses of HU seed extracts (50–200 mg/kg) in normal and drug-induced hyperglycemia. Their result showed that seed extracts of HU caused progressive and significant ($P < 0.05$, 0.01 and 0.001) dose-related reduction of blood glucose concentration in both normal and drug-induced hyperglycemic rats. In a similar research carried out by Igbe *et al.,* 2009, it was reported that 400 mg/kg body weight of seed extract of HU significantly ($P < 0.05$) reduced blood glucose concentration in diabetic rats.

The effects of STZ on glucose and insulin homeostasis reflect toxin-induced abnormalities in pancreatic $\beta$-cell function. The involvement of ROS in the toxic action of STZ, which may be produced during uric acid generation as the final product of ATP degradation by xanthine oxidase from hypoxanthine, has also been considered (Nukatsuka *et al.,* 1990). And indeed, some evidence for a participation of ROS has been obtained in experiments with scavengers (Sandler and Swenne, 1983; Okamoto, 1996). Some minor generation of ROS including superoxide and hydroxyl radicals originating from hydrogen peroxide dismutation during hypoxanthine metabolism may accompany the effect of STZ and accelerate the process of $\beta$-cell destruction (Sandler and Swenne, 1983; Okamoto, 1996). Following the importance of ROS in pancreatic $\beta$-cell destruction occasioned by STZ, he antioxidant profile in serum and pancreas homogenates was analyzed. Results obtained indicates that SOD and CAT activities in serum and pancreas homogenates were significantly ($P < 0.05$) lower in Stretozotocin injected rats (positive induced control Group B) when compared with the nonstreptozotozin injected control rats (negative induced control A). Animals that were injected with STZ and treated with HU extracts (Groups C and D) showed significantly ($P < 0.05$) elevated SOD and CAT activities when compared with the STZ injected rats. Also, there was significant ($P < 0.05$) difference of lipid peroxidation in serum and pancreas homogenates of STZ injected rats (positive induced control Group B) when compared with negative control Group A rats while difference in lipid peroxidation was significantly lowered in the STZ injected rats treated extracts of HU. This suggests that there was increased levels of serum ROS in the strepotozotocin injected rats than the non-STZ injected rats. Increasing evidence in both experimental and clinical studies suggests that ROS plays a major role in the pathogenesis of diabetes mellitus (Maritim *et al.,* 2003). Free radicals are formed disproportionately in diabetes by glucose oxidation, nonenzymatic glycation of proteins and the subsequent oxidative degradation of glycated proteins. In addition, the increase in oxygen free radicals (ROS) in diabetes could be primarily due to increase in blood glucose levels that upon auto-oxidation generate free radicals (Wolff and Dean, 1987). All these may have accounted for the decrease in serum levels of SOD, and CAT activity of the STZ injected Group B rats that was reversed on treatment with aqueous extracts of HU seeds and leaves. The decrease in the activities of SOD and CAT and an increase in TBARS in pancreas homogenate of STZ injected rats would be due to

increase intracellular ROS, which has been reported to be the major contributor to DNA fragmentation and evoked deleterious changes in the pancreatic $\beta$-cells (Takasu *et al.,* 1991; Bedoya *et al.,* 1996), and hence the degenerative changes observed in the photomicrograph of pancreas of Group B rats [Figure 4b]. This effect on the pancreatic Islet cells was reversed on treatment with aqueous extracts of HU seeds and leaves as shown in Photomicrographs of Group C and D rats [Figure 4]. Thus, extracts of HU reversed the effect of STZ on antioxidant enzymes, FBG and pancreatic islet (β)-cell cytoarchitecture and population.

In conclusion, the extracts of HU possess antidiabetic, antioxidant and Islet cells regenerative potential.

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