Extracts of *Guiera senegalensis* J.F. Gmel (Combretaceae) galls ameliorates streptozotocin-induced diabetes mellitus rats status

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ABSTRACT

Background: A good number of medicinal and dietary plants are used for diabetes treatment in Burkina Faso.

Aim of the Study: The present study aimed to investigate the antidiabetic activity of *Guiera senegalensis* galls extracts and its potential mechanisms in streptozotocin-induced diabetic rats.

Methodology: The methanol extract was administered by gavage to healthy Wistar rats for the determination of toxicity, to normal and diabetic Wistar rats for the determination of glucose reduction level, lipid profile, insulin level and glycaemic parameters in serum. The histology and immunohistochemistry of the pancreas were also determined.

Results: The acute toxicity results showed that the medium lethal dose (LD_{50}) of the methanol galls extract of *Guiera senegalensis* is greater than 2000 mg/kg body weight in rats. *Guiera senegalensis* methanolic extract (250 mg/kg) and the tolbutamide (100 mg/kg) recorded a significantly ($p < 0.05$) lower level of triglyceride compared to the diabetic group. The methanol extract (250 and 500 mg/kg pc) significantly ($p < 0.05$) decreased the blood glucose level and increased the serum insulin level in diabetic rats. Interestingly, improved ß-cell function and antioxidant status were also observed in *G. senegalensis*-treated diabetic rats when compared to tolbutamide-treated diabetic rats.

Conclusion: These data showed direct evidence that *G. senegalensis* has antidiabetic activity by decreasing blood glucose level, improving insulin secretion and β-cell functions and modulating antioxidant status.

Keywords: Guiera senegalensis, Antidiabetic, Antioxidant, Insulin, ß-cell function

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1. INTRODUCTION

Diabetes mellitus is characterized by high blood glucose levels resulting from defects in insulin secretion, insulin action or both [1] [2]. The number of people suffering from diabetes mellitus is currently approximately 422 million in 2014 and this population is projected to increase up to 642 million by 2040 [3]. Diabetes caused about 1.5 million deaths worldwide in 2012 [4]. WHO predicts that in 20 years, diabetes mellitus will become the 7th leading cause of death, one of the most costly chronic diseases worldwide [5, 6]. Diabetes mellitus is divided into two main groups, namely type 1 diabetes and type 2 [7]. Type 2 diabetes mellitus is the most common form of diabetes characterized mainly by the resistance of insulin and pancreatic β-cell dysfunction [8, 9]. 85-90% of diabetes patients are affected by type 2 diabetes mellitus. Synthetic antidiabetic agents used for the treatment of this disease cause some side effects [10] [11]. Therefore, it is attractive and urgent to search for more effective and with low side effects antidiabetic drugs.

Variety of medicinal plants have been used in the cure and management of chronic diseases like cancer, diabetes, hypertension. The bioactive compounds of medicinal plants are largely used as an alternative treatment for diabetes with fewer side effects [8]. Metformin, a hypoglycemic agent is isolated from a medicinal plant, namely *Galega officinalis*

Guiera senegalensis galls are commonly used as a folk remedy to treat a variety of diseases in Burkina Faso. Flavonoids which are one of the major compounds in the galls of *G. senegalensis* [12] have been reported by many authors to possess remarkable antidiabetic activity by acting as insulin secretagogues, insulin sensitizers, incretin potentiators, modulators of carbohydrate absorption [13, 14]. The flavonoids could also act through many more targets regulating glucose metabolism, by reducing long-term complications of diabetes and as antihyperlipidemic agents [14]. Previous studies showed that the extracts and fractions from the galls of *G. senegalensis* have *in vitro* hypoglycaemic effects by inhibiting highly α-glucosidase and the protein glycation [15]. The objective of the present study was to examine the *in vivo* antidiabetic effects of the galls from *Guiera senegalensis* and its potential mechanisms in streptozotocin-induced diabetic rats.

2. MATERIAL AND METHODS

2.1. Extraction and VLC fractionation

The galls of *Guiera senegalensis* were collected in Ouagadougou, Burkina Faso. Voucher specimen was already deposited in the Herbarium of the University of Ouaga I Pr JKZ under the voucher specimen number Lamien 01. Fifty (50) g of galls powder were extracted using 500 mL of acetone/water (80/20) during 48 h under mechanical agitation at room temperature. The filtrate obtained using Whatman filter paper were concentrated and lyophilized using a freeze-drying system to give the hydroacetonic extract (HAE). Two kg of galls powder was extracted twice with methanol during 72h at room temperature. The concentrated extract was dried under the hood to get the methanol extract.

2.2. Animals

Sixty (60) Wistar rats of both sexes weighing about 180-200 g obtained from the animal house of the ICCBS, University of Karachi, Pakistan were used in the study. They were maintained under standard laboratory conditions of natural photo period of 12-hour light - dark cycle. The rats were kept in clean cages with ad libitum access to water and food. The experimental design was conducted in accordance with the guidelines approved by the institutional animal ethical committee of ICCBS, University of Karachi, Pakistan.

2.3. Acute toxicity test

The acute toxicity of the *Guiera senegalensis* methanolic extract was determined in Wistar rats. A single oral administration of four different doses of the extract (500, 1000, 1500 and 2000 mg/kg of body weight) was given to different groups (3 rats /group).

Mortality and general behaviour of all rats were observed during the initial 4-h and intermittently for the next 6-, 24-, 48-, and 72-h following the administration of the extract.

2.4. Induction of type 2 diabetes

Wistar rat received intraperitoneally a solution of streptozotocin (30 mg/kg) in 1.0 ml citrate buffer (0.5 M, pH 4.5) freshly prepared followed by 5% glucose solution administration. The procedure was repeated the second week. The seven days

after the second administration of streptozotocin solution, the blood glucose was measured. Rats with fasting blood glucose higher than 200 mg/dL were considered to be diabetic and used for this study.

2.5. Experimental design

2.5.1. Acute extract treatment

The diabetic rats were randomly divided into four (4) groups (I-IV) (n = 5)

Group I-II: diabetic rats treated with tolbutamide and glibenclamide, respectively at the dose of 5 mg/kg

Group III- IV: diabetic rats treated with hydroacetonic and methanolic extracts, respectively at the dose of 500 mg/kg.

The extracts and control drugs were fed to diabetic rats overnight and blood glucose levels were measured at 0, 30, 60, 120 and 180 min using a glucometer (Accu-Chek Go; Roche Diagnostics).

2.5.2. Chronic extract treatment

The experimental rats were divided into five groups of five animals each:

Group I: Non-diabetic control that did not receive STZ

Group II: diabetic rats without any treatment

Group III: diabetic rats treated with tolbutamide at a dose of 100 mg/kg

Group IV: diabetic rats treated with methanol extract of *G. senegalensis* at a dose of 250 mg/kg

Group V: diabetic rats treated with methanol extract of *G. senegalensis* at a dose of 500 mg/kg

The extracts and tolbutamide were administered orally once daily via syringe to the diabetic rats. The control rats were given an equivalent volume of water. Animal weights were measured every week throughout the experiment, and the dose was adjusted accordingly.

2.5.3 Collection of biological samples and estimation of biochemical parameters

The diabetic rats were randomly divided into four (4) groups (I-IV) (n = 5):

Group I-II: diabetic rats treated with tolbutamide and glibenclamide, respectively at the dose of 5 mg/kg

Group III- IV: diabetic rats treated with hydroacetonic and methanolic extracts, respectively at the dose of 500 mg/kg.

The extracts and control drugs were fed to diabetic rats overnight and blood glucose levels were measured at 0, 30, 60, 120 and 180 min using a glucometer (Accu-Chek Go; Roche Diagnostics).

2.5.4. Haematoxylin and eosin staining

Tissues sections were deparaffinised in xylene, rehydrated in graded 2-propanol series, washed in water and then stained with H & E. Nikon 90i microscope (Nikon) and Nikon DXM 1200C camera using NIS-Elements image analysis software AR 3.0 (Nikon) were respectively used to visualise pancreatic sections and obtain images.

2.5.5. Immunohistochemical staining

Immunohistochemical staining was done according to the method described by Hafizur *et al.* [16]. Two sections from each rat were triple stained for insulin, glucagon and nuclei. For this purpose, each section was deparaffinised, rehydrated, washed in water, subjected to antigen retrieval, cooled to room temperature and incubated with a blocking solution for 10 min at room temperature. Then, each section was incubated with a mixture of guinea-pig anti-insulin (1:100) and mouse anti-glucagon (1:1500) for 1 h. The sections were incubated with a mixture of Texas Red-conjugated donkey anti-guinea-pig IgG (1:100) and Cy2-conjugated donkey anti-mouse IgG (1:100) for 30 min after washing with PBS. DAPI was used to stain the nuclei. The sections were after washed with PBS and mounted in Fluoromount solution (Sigma). The immune-reaction was visualized using Nikon TE2000E fluorescent microscope equipped with a Nikon DS-2MBWc camera in DAPI, fluorescein isothiocyanate and Texas Red channels. NIS-Elements image analysis software AR 3.0 (Nikon) was used to get the images and Adobe Photoshop CS2 to perform the image processing.

2.6. Statistical analysis

The results are presented as mean ± Standard Deviation for triplicate analysis. The data were subjected to one-way analysis of variation ANOVA with Turkey's Least Significant Difference test. $P < 0.05$ was considered significant. The Pearson Correlation test for correlation analysis was used. The statistical analysis was performed using XLSTAT version 7.5.2 (Addinsoft, Paris, FRANCE).

3. RESULTS AND DISCUSSION

3.1. Acute toxicity test

The administration of methanol extract from galls of *Guiera senegalensis* up to a dose of 2.0 g/kg body weight did not cause any mortality of rats and they were physically active. Any significant changes in behaviors were observed. The acute toxicity result proves that the methanol galls extract had no observable adverse effect at the doses tested; implying that the medium lethal dose (LD_{50}) is greater than 2000 mg/kg body weight in rats.

3.2. Acute antidiabetic effect of *G. senegalensis*

Acute effects of *G. senegalensis* extracts on blood glucose levels of control and diabetic rats are shown in Fig.1.

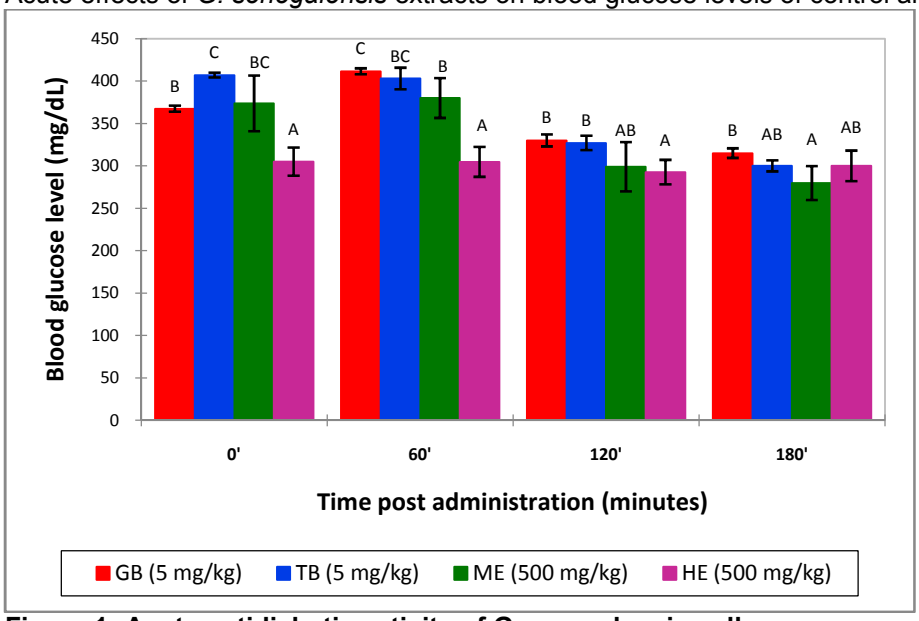

Figure 1: Acute antidiabetic activity of G senegalensis galls

Means followed by the same letter do not differ statistically between the different groups ($p < 0.05$).

The blood glucose of rats was followed during 3 h for the different extracts (HAE, ME) and for antidiabetic references drugs (tolbutamide and glibenclamide). The extracts and fractions were used at the dose of 500 mg/kg and antidiabetic reference drug at the dose of 5 mg/kg. After feeding the tolbutamide to the fasting rats, the blood glucose decreased significantly at 60 min and 120 min respectively of 0.98 % and 19.66 % compared to its initial value (0 min). The glibenclamide showed a reduction in blood glucose level at 120 min post administration of 10.2 %. The tolbutamide was used as positive control for chronic antidiabetic activity of *G senegalensis* methanol extract study. The level of blood

glucose was significantly lower in diabetic rats treated with methanolic extract at 120 min (19.98 %) and 180 min (25.16 %), respectively. The hydroacetonic extract reduced the blood glucose of diabetic rat of 0.11 %, 4.04 % and 1.64 % respectively at 60, 120 and 180 min after administration compared to the initial value. The methanolic extract showed a good reduction of the diabetic blood glucose level compared to hydroacetonic extract.

3.3. Effects of the extracts on fasting serum glucose levels after 10 and 28 days of treatment

Fasting blood glucose levels in STZ-induced diabetic rats were increased significantly. Fasting blood glucose concentrations of diabetic rats, after being treated with extracts and positive drugs were reduced significantly at the 10^{th} and 28^{th} days comparatively with diabetic control group ($P < 0.05$). As shown in Table 1, the administration of the methanolic extract (250 mg/kg and 500 mg/kg) reduced significantly the fasting blood glucose levels of diabetic rats respectively of 70.94 % and 55.31 % at the 10^{th} day ($P < 0.05$).

Table 1: Hypoglycemic activity of *G senegalensis* galls

Group	Day 1 (mg/dL)	Day 10 (mg/dL)	Day 28 (mg/dL)
Diabetic group	380.2 ± 38.66	403.6 ± 56.36	305.91 ± 15.60**
Tolbutamide treated group (100 mg/kg)	444.6 ± 80.03	136 ± 43.17**	193.93 ± 12.99**
ME treated group (250 mg/kg)	241.6 ± 87.98*	70.2 ± 8.52**	151.75 ± 13.37**
ME treated group (500 mg/kg)	311 ± 77.23	139 ± 86.71**	236.05 ± 10.77**

**P < 0.05 and **P < 0.001 when compared with diabetic non-treated group*

The tolbutamide, positive control at the dose of 100 mg/kg remarkably reduced the blood glucose level. Tolbutamide reduction capacity of blood glucose did not significantly show difference from those of methanolic extract (250 mg/kg). The fasting blood glucose concentrations increased significantly in control diabetic rats comparatively to its initial value (day 0). The galls of *G senegalensis* at the dose of 250 mg/kg and 500 mg/kg also exhibited a significant hypoglycaemic activity at 28^{th} day of treatment when compared to tolbutamide hypoglycaemic activity. The methanolic extract at the dose of 250 mg/kg highly reduced the blood glucose level than those of 500 mg/kg. These results imply that methanol extract of galls from *G senegalensis* possess hypoglycaemic activity in STZ-induced diabetic rats.

3.4. Effect of methanol extract on serum lipids level in diabetic rats after 28 days of treatment

The concentrations of the serum lipids are presented in Table 2.

Table 2: Effect of Methanol extract on lipids level

	Total cholesterol (mg/dL)	HDL-Cholesterol (mg/dL)	Triglycerides (mg/dL)
Diabetic non-treated group	50.05 ± 3.17 ^{b}	20.58 ± 2.85 ^{b}	85.22 ± 8.42 ^{a}
Tolbutamide treated group	51.55 ± 2.55 ^{b}	28.89 ± 5.39 ^{a}	70.39 ± 8.76 ^{b}
Methanol treated group (250 mg/kg)	59.91± 5.14 ^{a}	27.20 ± 2.51 ^{ab}	66.50 ± 3.50 ^{b}
Methanol treated group (500 mg/kg)	61.07 ± 2.53 ^{a}	26.33 ± 3.51 ^{ab}	77.67 ± 9.33 ^{ab}

Means followed by the same letter do not differ statistically between the different groups ($p < 0.05$).

Some significative differences were observed in lipids profiles of treated diabetic rats comparatively to the untreated diabetic group. Serum level of HDL-cholesterol was not significantly increased in the methanol extract treated groups (250 and 500 mg/kg) compared with the diabetic group (P <0.05). The tolbutamide treated group showed an increase of HDL-cholesterol level comparatively to the untreated diabetic group. Although the concentration of total cholesterol was increased significantly in the methanol extract treated groups (250 and 500 mg/kg). The tolbutamide did not significantly reduce the level of total cholesterol in diabetic rat. The methanol extract at the dose of 250 mg/kg and the tolbutamide also recorded a significantly lower level of triglyceride compared to the diabetic group.

3.5 Serum insulin levels in diabetic rats after 28 days of treatment

Table 3 shows plasma insulin concentrations in the experimental rats.

Tableau 3: Insulin, TAS and HbA1c levels

	Insulin (IU/mL)	TAS (mmol/L)	HbA1c (%)
Non-diabetic Control group	2 ± 0.17 [a]	0.78 ± 0.13 [bc]	6.26 ± 0.23 [bc]
Diabetic un-treated group	0.08 ± 0.01 [c]	0.57 ± 0.08 [c]	10.49 ±1.17 [a]
Tolbutamide treated group	0.2 ± 0.02 [bc]	0.70 ± 0.04 [c]	8.44 ± 3.44 [ab]
Methanol treated group (250 mg/kg)	0.27 ± 0.05 [b]	0.92 ± 0.08 [ab]	6.72 ± 1.10 [bc]
Methanol treated group (500 mg/kg)	0.16 ± 0.07 [bc]	1.07 ± 0.21 [a]	4.64 ± 0.40 [c]

Means followed by the same letter do not differ statistically between the different groups ($p < 0.05$).

There was a significant increase of plasma insulin in treated diabetic rats compared with untreated diabetic rats. The normal rats have the highest level of insulin (02 ± 0.17 IU/mL). The untreated diabetic rats possess the lower insulin content (0.083 ± 0.01 IU /mL). Oral administration of methanol extract at the concentration of 250 mg/kg to diabetic rats significantly increased the level of serum insulin compared to diabetic control rats (0.273 ± 0.05 IU/mL). This increase is comparable to that of tolbutamide or the same extract at the dose of 500 mg/Kg. The concentration of serum insulin was increased significantly by 69.51% and 47.92% in diabetic rats treated with methanol extract respectively at the dose of 250 and 500 mg/kg.

3.6. Blood/serum glycaemic parameters in diabetic rats

Effect of methanol extracts on the percentage of HbA1c and TAS in streptozotocin induced diabetic rats is shown in Table 3.

The administration of *G senegalensis* methanol extract in diabetic rats exhibited a remarkable glycaemic control by reduction of HbA1c percentage and increase of total antioxidant status.

As shown in Table 3, there was a statistical ($P < 0.05$) decrease in the levels of HbA1c but significant increase of TAS ($P < 0.05$) in methanol treated group (250 and 500 mg/kg) and tolbutamide treated group. There is no significant difference in HbA1c levels between the groups treated with galls methanol extract at the two doses (250 and 500 mg/kg) and normal rats' group. The methanol extract of *G senegalensis* at the dose of 500 mg/kg decrease significantly the haemoglobin glycosylation comparatively to tolbutamide at the dose of 100 mg/kg. The methanol extract at the dose of 500 mg/kg possessed the highly antioxidant activity *in vivo* of 1.066 mmol/L follow of the same extract at the dose of 250 mg/kg. The methanolic extract improves the total antioxidant status of diabetic rats.

3.7. Pancreas histology

The tissue sections of pancreas have been submitted to the staining of H & E to detect the histological alterations induced by the STZ and to know the protection effect of galls methanol extract from *Guiera senegalensis*. Fig 2 shows the micrograph of the β-cells of pancreatic tissues of the experimental groups.

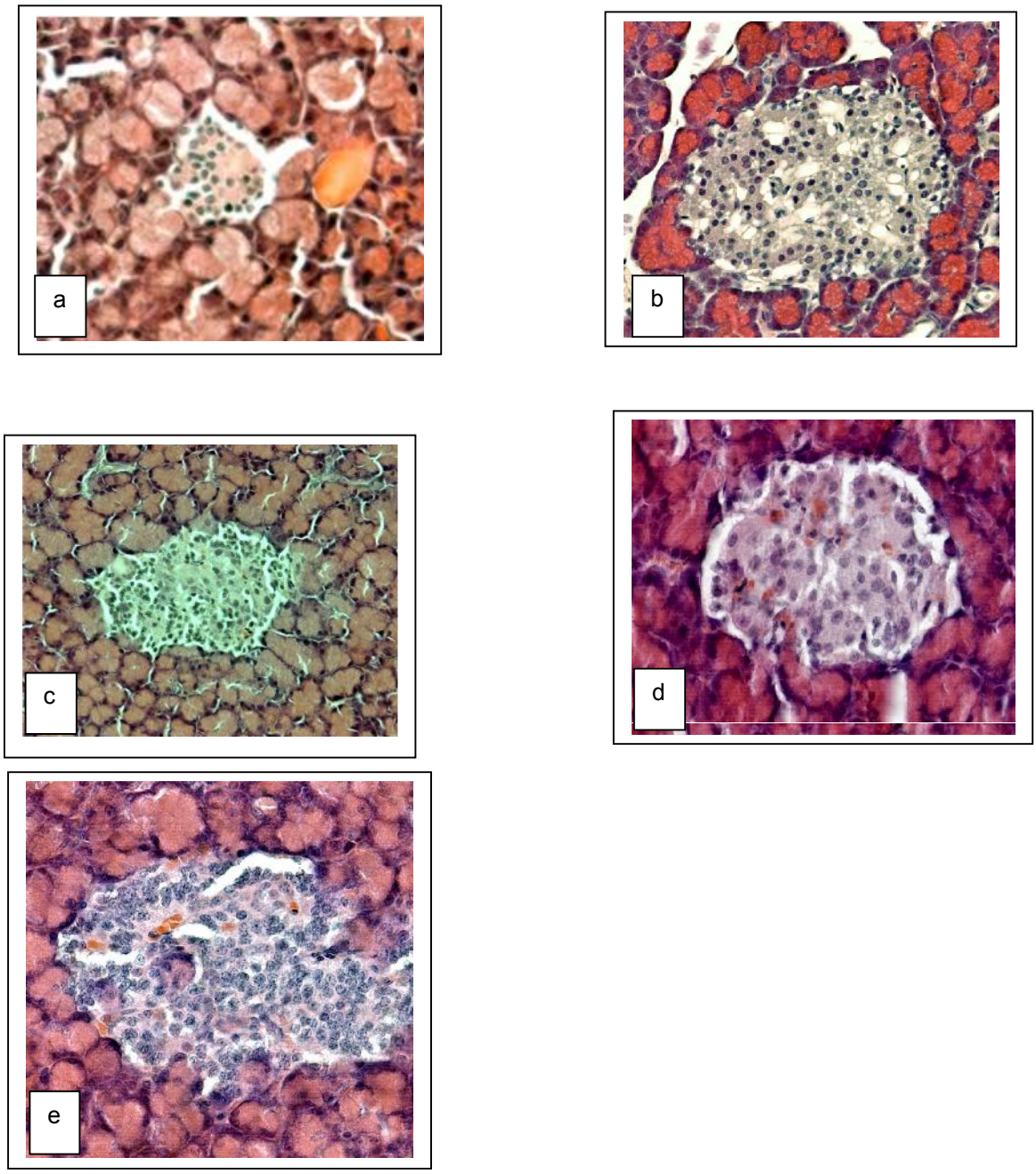

Fig 2: Light microscopic study of the pancreatic islets (10 X) in the different experimental groups: *(a) untreated diabetic; (b) non-diabetic control (c) Tolbutamide-treated 100 mg/kg; (d) G senegalensis 250 mg/kg; (e) G senegalensis 500 mg/kg*

Pancreatic tissues of the control group (a) showed normal architecture of islets. Evaluation of the pancreas histopathology in STZ- induced diabetic rats showed an extensive destruction of islets, atrophy of β-cells and vascular degenerative changes in the islets.

The reduction of islets number in diabetic rats was significantly higher comparatively to the islets number in normal rats. Treatment of *Guiera senegalensis* galls extract (250 and 500 mg/kg) in diabetic rats increased the number of islets (c and d). *Guiera senegalensis* galls extract showed a restoration capacity of pancreatic islet cells in diabetic rats comparable to that observed for tolbutamide (e).

3.8. Immunohistochemistry of the pancreas

Fig 3 shows pancreatic islets stained for insulin, glucagon and DAPI fluorescence.

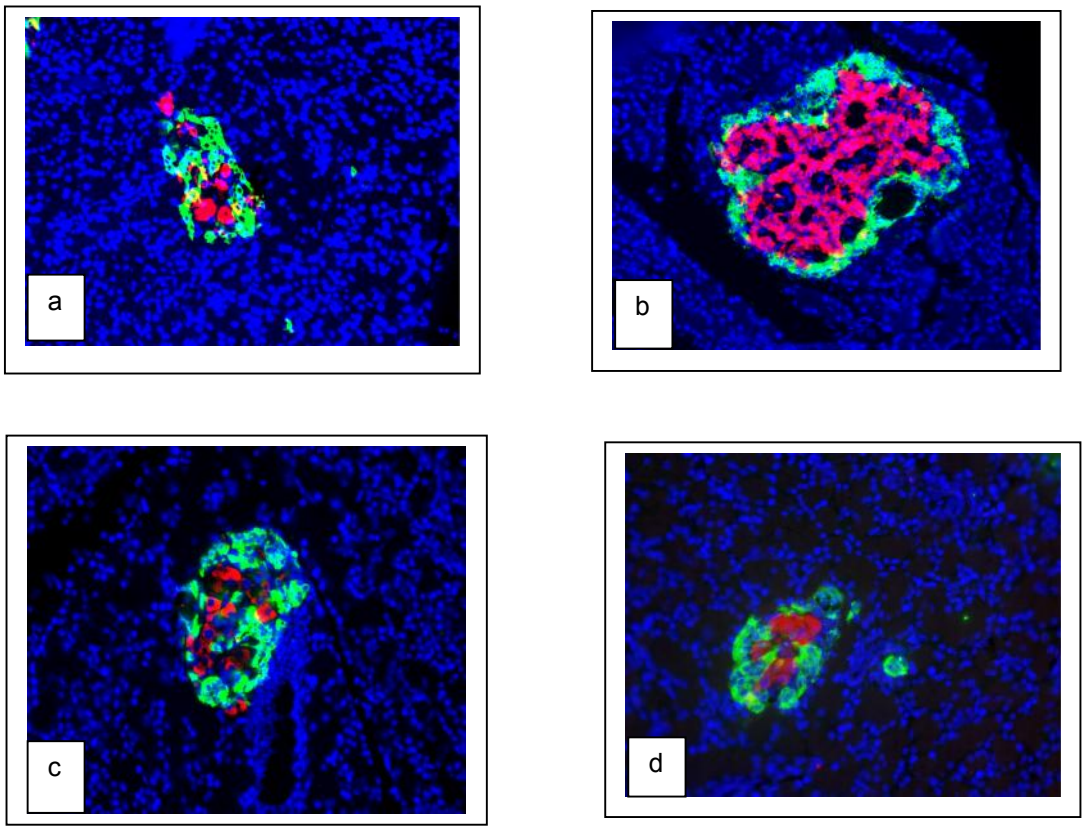

Fig. 3. (a–d) Multichannel fluorescence microscopic study of insulin-positive β-cells (red), glucagon-positive α-cells (green) and nuclei (blue) of the pancreatic islets (20 X) of the different experimental groups: *(a) untreated diabetic; (b) non-diabetic control; (c) Tolbutamide-treated 100 mg/kg, (d) G senegalensis 250 mg/kg*

Insulin-positive cells in the islets of the control rat's pancreas are abundant and are mostly located in the centre of the islet. The total number and the area of the insulin-positive cells were reduced significantly in the untreated diabetic rats. The *G senegalensis* galls extract treated groups (250 and 500 mg/kg) showed an increase of insulin-positive cells number. The total number and the area of the insulin-positive cells were increased in diabetic rats treated with tolbutamide during 28 days. The galls methanol extract of *G senegalensis* showed ability to significant increase the number of cells secreting insulin in the islets compared to tolbutamide. This finding indicates that the galls of *G senegalensis* increase β cells.

The immunohistochemical staining with anti-glucagon antibody did not show a marked change in glucagon secreting cells between diabetic control rats, normal rats and diabetic treated rats. Any significant differences between the nuclei number of the normal rat's pancreas, treated and untreated diabetic pancreas rats are not observed. This observation confirms that our experimental induction model of diabetes is that of type 2 by the relative disturbance and diminution of β-cells.

4. DISCUSSION

Previous studies showed that the galls extract of *G senegalensis* possess *in vitro* antidiabetic activity by strongly inhibiting α-glucosidase, enzyme involved in carbohydrate digestion [15]. However, there is little knowledge about the *G senegalensis in vivo* antidiabetic activity in the literature.

The present study investigated the effect of methanol galls extract of *Guiera senegalensis* on serum/blood glycaemic and lipid parameters and regenerative potential of islet cells in streptozotocin induced diabetic rats. This study showed that the *G senegalensis* galls have anti-hyperglycaemic activity in STZ-induced diabetic rats by reducing the serum glucose level. The treatment of diabetic rats with methanol galls extract of *G senegalensis* showed time dependent antihyperglycemic activity but not dose dependent manner. The antihyperglycemic potential of galls methanol extract of *G senegalensis* could be explained by intestinal enzymes (α-amylase and α-glucosidase) involved in carbohydrates absorption inhibition

[15] [10]. The diabetes mellitus is associated by the loss of body weight [8]. The increase of diabetic rat's body weight treated with the methanol extract of *G senegalensis* at the dose of 250 mg/kg (data not shown) indicate that the hypoglycaemic potential of *G senegalensis* may be due by the reversal of gluconeogenesis and glycogenolysis [17]. The galls of *G senegalensis* reduced triglycerides levels and increase HDL-cholesterol level. Ramachandran *et al*. [18] showed an increase of TC, TG, LDL and VLDL levels as well as a decrease of HDL level after administration of STZ compared to normal control rats. The triglycerides reduction potential of galls may be due to its stabilization capacity of glucose level, increase of insulin level or inhibition of lipase activity [18] [19]. The galls of *G senegalensis* showed to significantly increase the serum insulin level compared to tolbutamide. The insulin secretion is associated to the level of peroxide derived from lipoxygenase. Lows levels of peroxides derived from lipoxygenase stimulate the insulin secretion, but the increase endogenous peroxides level could cause oxidative stress and this could lead to cellular dysfunction [20, 21]. *Guiera senegalensis* galls previously showed strong inhibitory activity of lipoxygenase in *vitro* [12]. The galls could be able by lipoxygenase inhibition *in vivo* to reduce the production of peroxides derived from lipoxygenase and to avoid the destruction of β cells. Regeneration of β-cells and increase of insulin production in the β cells could explained the antidiabetic effect of *Guiera senegalensis* galls. Methanol extract of *G. senegalensis* galls enhanced the immunoreactivity of insulin comparatively to that observed with tolbutamide. These results support the histopathological observations where in both the number and structural integrity of pancreatic β-cells were restored. These finding showed that the galls of *G. senegalensis* play an important role in increasing the number of β cells. El-Sawi *et al*. [8] demonstrated that the administration of *I. aquatica* fractions effectively preserved cellular components of the pancreatic islet against the oxidative stress toxicity induced by STZ. Hafizur *et al*. [16] also showed that anti-diabetic activity of *A. officinalis* is due to the enhancement of insulin secretion and the pancreatic β-cell function modulation.

During the diabetes, the excess of glucose in the blood reacts with haemoglobin to form glycosylated hemoglobin (HbA1c) [1]. The amount of HbA1c is directly proportional to the blood glucose content [17]. HbA1c is a marker for long-term glycaemic control evaluation in diabetic patients and predicts risk for the development and/or progression of diabetic complications. Preliminary studies have reported a stable 10% reduction in HbA1c of content determines 35% reduction in the risk of retinopathy, 25% to 44% reduction in risk for kidney disease and 30% reduction in risk for neuropathy [18]. The methanol extract from galls of *G senegalensis* showed a potential of 35.89 and 55.73% reduction of HbA1c level respectively, at a dose of 250 and 500 mg/kg. Several studies have demonstrated an association of diabetes with an increase of free radicals formation and body's defence system a decrease [22]. The oxidative stress is an important condition for diabetic complications development like cardiovascular disease, nephropathy, neuropathy, retinopathy [22]. Many studies showed that flavonoids curb the glucose level, reduce plasma cholesterol and triglycerides significantly, increase hepatic glucokinase activity and stimulate the insulin secretion [1, 8]. Rutin and quercetin are among the major flavonoids of galls from *G senegalensis* [12]. Rutin and quercetin ameliorate hyperglycemia and oxidative stress, by blunting free radical induced toxicity in type 2 diabetes [23] [24]. The presence of these compounds in galls extract could justify the antihyperglycemic and antioxidative activities of *G senegalensis.* The galls of *G. senegalensis* could be used for the treatment or to prevent the development of complications associated with diabetes mellitus. This study shows that one of the antihyperglycemic mechanisms of *G. senegalensis* could be its scavenging capacity to protect the pancreas islets against free radicals induced by streptozotocin.

5. CONCLUSION

In summary, the results of the present study indicated that the methanolic extract of galls from *G senegalensis* has antidiabetic activity. The antidiabetic effect of *G senegalensis* could be attributed to its hypoglycaemic, anti-hyperlipidemic and antioxidative potentials. Insulin content, histology and immunohistochemistry results confirmed that *G senegalensis* induce β-cells regeneration in diabetic rat pancreas. These experimental findings clearly indicate that *G senegalensis* galls may be used as an important source of natural antioxidant with antidiabetic potential.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

PAEDS collected the galls of *G senegalensis* and made the different extractions,

PAEDS and **RH** designed and performed the experiments about the acute toxicity test, the Induction of type 2 diabetes, the extract administration of rats, histology and immunohistochemistry of the pancreas study,

PAEDS wrote this manuscript; **RH, MK, IMC** and **OGN** corrected the manuscript.

All authors read and approved the final manuscript.

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