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ANTIDIABETIC EFFECT OF GUAIACUM OFFICINALE;

ON EXOCRINE FUNCTION AND HISTOPATHOLOGY OF PANCREAS IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT… Introduction: Diabetes is the most genetically transmitted disease all over the world. It badly affects the vital organs and manifest the reduction of pancreatic amylase and lipase. **Objectives:** This study has been designed to investigate the role of *Guaiacum officinale* extract in controlling of diabetes in streptozotocin (STZ) induced type 2 diabetes male albino (Wistar) rats. **Study Design:** Experimental. **Setting:** Baqai Medical University. **Period:** January 2017- June 2017. **Method:** Bark extract of *Guaiacum officinale* **(**500mg/kg) was administered to STZ induced rat. Glibenclamide (GLB) was used as standard drug. The approach of the study was to observe the effect of *Guaiacum officinale* on pancreatic amylase and lipase and its tissue architecture by histopathology. Rats were divided in four groups i-e control, STZ treated, STZ + GLB treated and STZ +extract treated group. **Results:** *Guaiacum officinale* significantly improve the level of pancreatic amylase and lipase as compared to the STZ induced group. Similarly the pancreatic architecture was significantly affected by STZ alone. These changes were considerably reversed by *Guaiacum officinale* and GLB. **Conclusion:** It was concluded that *Guaiacum officinale* herb useful to cure the diabetes and it is effective in protecting pancreas from diabetes induced damages.

Key words: Diabetes, Streptozotocin, Glibenclamide, Lipase, Amylase.

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INTRODUCTION

Diabetes mellitus is a chronic disease that is increasing worldwide day by day. The rapid increase of diabetes may become a serious threat for mankind to all over the world. The morbidity and mortality due to diabetes are associated with a variety of micro-vascular and macro-vascular complications. In 2004 according to World Health Organization more than 150 million people were ill with diabetes and there was no solution to resolve the problem. The number of diabetic patient rise from 135 million in 1995 to 300 million in 2025 and the most common effected countries probably will beIndia, China and United states.[1,2]

The pathogenesis of type 1 diabetes is an autoimmune destruction of pancreatic cell. while type 2 diabetes mellitus caused due to defective glucose induced insulin secretion, increased hepatic glucose uptake, inability of insulin to stimulate glucose uptake in peripheral targeted tissues. These alterations causes changes in transport of glucose in cells, liver, adipose tissue skeletal muscles and GLUTS. Yarborough in 2001 reported that more than 85% of cases of worldwide suffering from type 2 diabetes are either due to insulin resistance or insulin deficiency.[3]

Numerous data is available to demonstrate the antidiabetic activity of various chemicals and herbal drugs.[4,5] Several phytopharmacological activities were reported related to antidiabetic activity of plants. The plant belongs to family zygophyllacea and its used for the treatment of piles, urinary disorders, dysentery, stomach ache, cancer, blood purifier and typhoid.[6,7] Wazir and his co-researchers reported that zygophyllacea plants are useful for the relief of constipation and is used as laxative.[8] Sonarian ethenic group used extract of Guaiacum coultri for the treatment of tuberculosis.[9]

Hypogycemic action is most commonly reported in plants of zygophyllacae. The plants include Guaiacum coultri, and Guaiacum scantum.[10] *Guaiacum officinale* is well reported plant of the same family for its versatile pharmacological activities like antiferility[11,12], anti rheumatic and anti oxidant.[13] Perceval et al. (2014) reported that preparation of leaves extract of Tillandsia recurvata with *Guaiacum officinale* have wound healing potential for treatment of diabetic ulcer in streptozotocin induced type-1 diabetic rat.[14] In this study an attempt has been made to describe the effect of *Guaiacum officinale* in streptozotocin induced model of type 2 diabetes mellitus in male albino (wistar) rats on histology and exocrine functions of pancreas.

Materials and Methods

Animals

In the present study 144 male rats of weight 180 grams (±20 gms) were recruited from the animal house of Baqai Medical University, Karachi, Pakistan. All the animals were acclimatized for housing condition before starting the experiment. Each animal was kept in separate cage under controlled climatic condition during entire study in an alternating 12 hour light and dark cycle. All the animals had full access for water and food adlibitum.

Preparation of Guaiaum Officinale Extract

The bark of *Guaiacum officinale* was collected from trees grow in university of Karachi, department of Botany (University of Karachi) identified as voucher specimen (No.33 KU). The bark was dried in open air then chopped. The 10 kg of air dried chopped bark was grounded and then extracted thrice a time with methyl alcohol at room temperature. By freezed drying process under reduced pressure, methanol was removed from plant extract to produce a gummy residue of brownish appearance.

Experimental Design

All the animals were divided into four groups and each group comprised of 12 animals. Drugs were administered according to following schedule.

Group A: Control group received distilled water orally for 28 day.

Group B: The animals of group B received streptozotocin (30 mg/Kg) as single dose through IP route.

Group C: The animals of group C (STZ induced diabetic rat) received GLB 0.5 mg/ kg for 28 days orally.[15]

Group D: The animals of group D (STZ induced diabetic rats) received bark extract of *Guaiacum officinale* (500mg/Kg) orally.

Collection of Blood Sample for Estimation of Pancreatic Enzyme

The blood samples were collected in vacutainer containing gel tubes through cardiac puncture technique.[16] The serum was separated by centrifugation at 4000 rpm for 10 minutes. Pancreatic lipase was determined by LIP, Lipase calorimetric assay, Cobas®, according to enzymatic colorimetric assay and pancreatic amylase was determined by AMYL-α- amylase liquid according to IFCC Cobas®.

Sacrifice of Animals

After collection of blood for assay of pancreatic enzymes, animals were sacrificed by cervical decaptation after 1 month of treatment rats were dissected.[15,17] Pancreas were isolated, preserved and preceding section and staining.[18]

Preparation of Pancreas Tissue for Histological Examination

The tissues of animals were flushed with saline and put into 10 % normal buffered formalin for histopatholgical evaluation. After 24 hours, tissues were embedded in paraffin wax as standard protocol. Five micrometer thick section were prepared from these block and put into poly-1-lysine coated glass slide and stained with haemotoxylin and eosin as standard procedure. The slides of all groups were observed under light microscope for histological changes.

Statistical Analysis

All the quantitative results of enzymes were analyzed statistically using SPSS software version 21.Values were compared with control using ANOVA, considered $p<0.05$ was significant.

RESULTS

Pancreatic Enzymes

Amylase

The pancreatic enzymes (amylase) level in treated group, (*Guaiacum officinale*) was 353.80±1.083*** (Mean ±SEM) shown in table 1graph 1, while the value of Glibenclamide group (standard group) was 384.50±16.132*** (Mean ±SEM) with comparison of control group 272.50±1.491 (Mean ±SEM) presented in Table-I and Figure-1 and 2, demonstrated that both treated and standard group showed highly significant results.

The level of amylase in streptozotocin group 30 mg/kg (positive control) was 199.30±14.463*** (Mean±SEM) showed in table no. 1 graph no.1, indicated highly significant result.

Lipase

The lipase level of Guaicum officinale in treated group was 115.50±2.282*** (Mean± SEM) shown in table no1 graph no.1, and the level of lipase in standard group (Glibenclamide group) was 69.40± 2.495*** (Mean±SEM) with comparison of control group was 118.40±4.025 (Mean±SEM). The results of treated group was found significant.

The level of lipase of albino rats in diabetic group induced by streptozotocin was 78.50±1.293*** (Mean±SEM) showed in Table-I Figure-1, was found highly significant.

HISTOPATHOLOGICAL OBSERVATIONS OF PANCREAS

Control Group

During microscopical examination, the general architecture of pancreas was normal. Normal islets of langerhens and pancreatic ducts were seen in Fig (A)(1).

Streptozotocin Group (Positive Control Group)

During microscopic studies, general architecture of pancreas was normal. In STZ treated group at 200X Shrinkage of islets cells of pancreas were seen while no change was observed in exocrine cells in Figure-A(2). Size reduction in iselet cell of pancreas were observed in different fields. Pancreatic duct appeared normal in Figure-A(4) and moderate lymphocyte infiltrations were also seen in Figure-A(3). Parenchymal fibrosis and acinar cell injury were almost absent.

Glibenclamide Group (Standard Group)

The pancreatic section of standard group (GLB treated diabetic rats) showed normal general architecture of pancreas but the number and size of islets cells of pancreas were decreased in Figure-B(5). Structure of islets cells of pancreas were not well defined along with damaged and vaculized islet cells. Moderate lymphocyte infiltration were also seen in Figure-B(6) while pancreatic duct was almost normal in Figure-B(7).

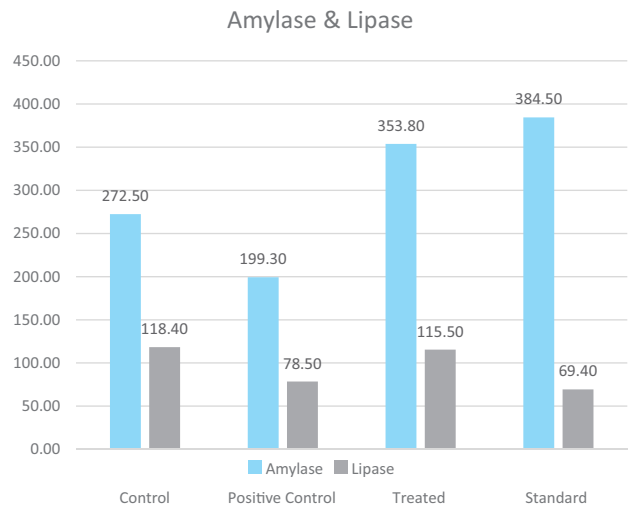
Guaiacum Officinale (Treated Group)

The pancreatic section of treated group (G. officinale treated diabetic rats) showed normal pancreatic architecture with normal number and size of islets cells in Figure-B(8). Pancreatic duct was in normal in diameter and not obstructed in Figure-B(10). Fibrosis and congestion were absent in almost all the fields. Islets cells secretions and exocrine cell of pancreas were regular showed in Figure-B(9).

DISCUSSION

Diabetes and its complications are the main leading problems for health care professionals to treat as it mostly leads to vital organ damage. According to International Diabetes Federation in 2012, people living with diabetes globally and that value project up to 565 million by 2030. Eddouks et al. (2004) reported the current survey and proved that more than 800 plants have antidiabetic properties.[5] Andrade-cettoet al. (2005) reported that more than 500 species are used as a medicine for diabetes in Mexico.[19] Guaiacum couteri, Guaiacum sanctum are used as a anti diabetic agent. Kanetoet al. (2005) reported that herbal medicines may work by preventing the oxidative stress that were involved in dysfunctioning of β-cell in diabetes.[20] Edwin et al. (2006) and Andrew (2000)reported that the pancreas is a vital exocrine gland for secretion of insulin.[21,22] Insulin is responsible for transport of glucose from blood to the cells.

In the present study the purpose was to evaluate



Graph-1. Effect of Guaiacium officinale extract on pancreaticenzymes in albino rats at a dose of 500mg/kg.

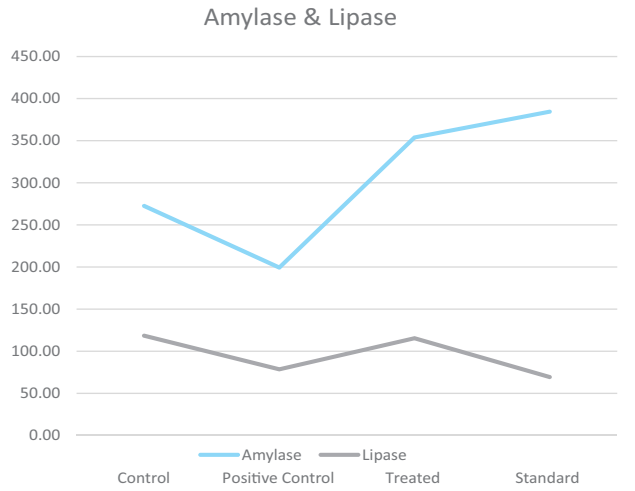


Figure-2. Effect of Guaiacium officinale extract onpancreatic enzymes in albino rats at a dose of 500mg/kg.

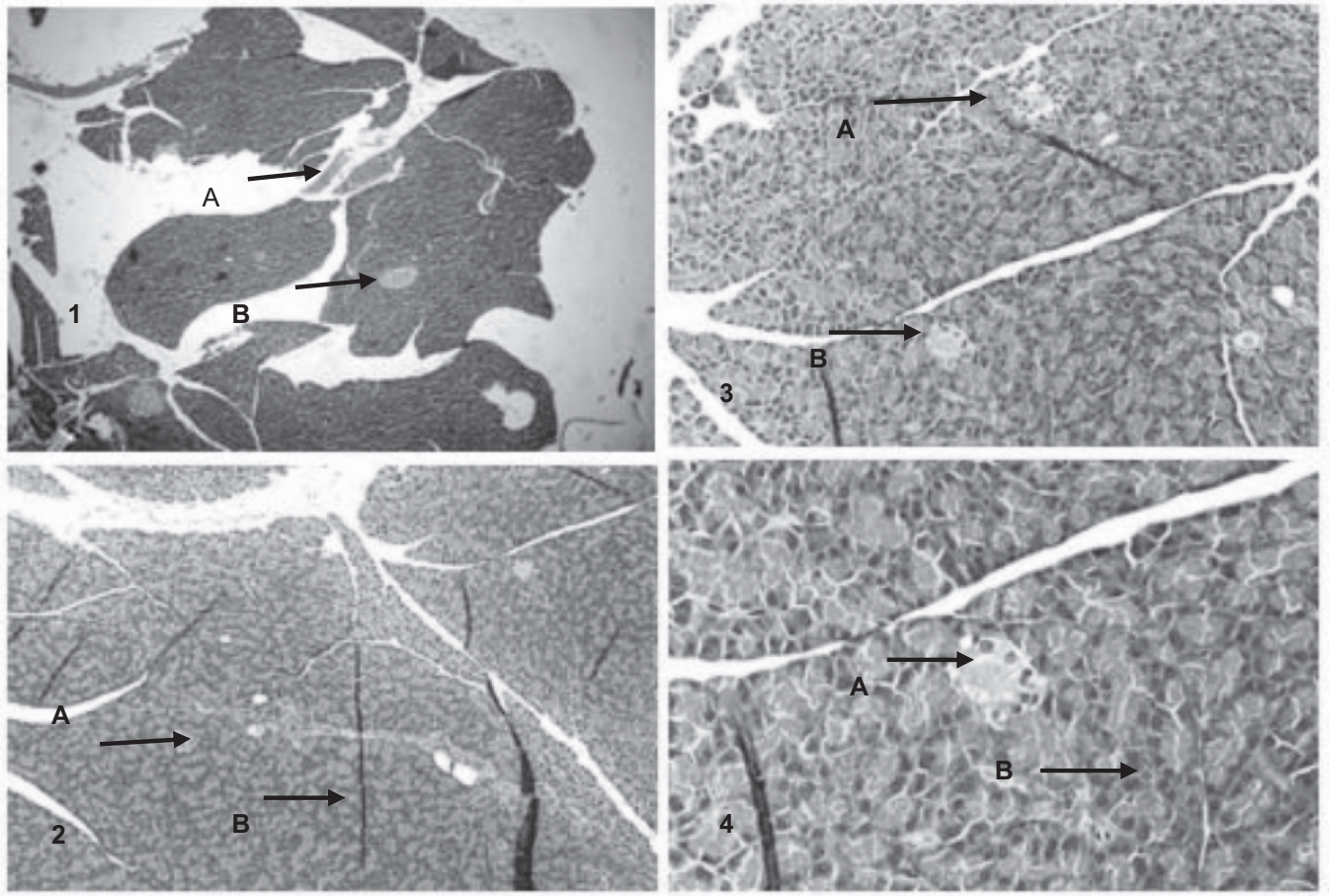


Fig A; (1)Photomicrograph of a 5 micron thick H&E stained paraffin section from the pancreas of control male albino rat showing normal islets of langerhens (A) Pancreatic Ducts(B) X 100. (2)The pancreas of STZ treated group showing shrinkage of islets of langerhens(A) Normal exocrine cells(B) X 200. (3) Lymphocytes infiltration(A) shrinkage of islets of langerhens (B) X200. (4) showing shrinkage of islets of langerhens (A) Normal exocrine cells(B) X400

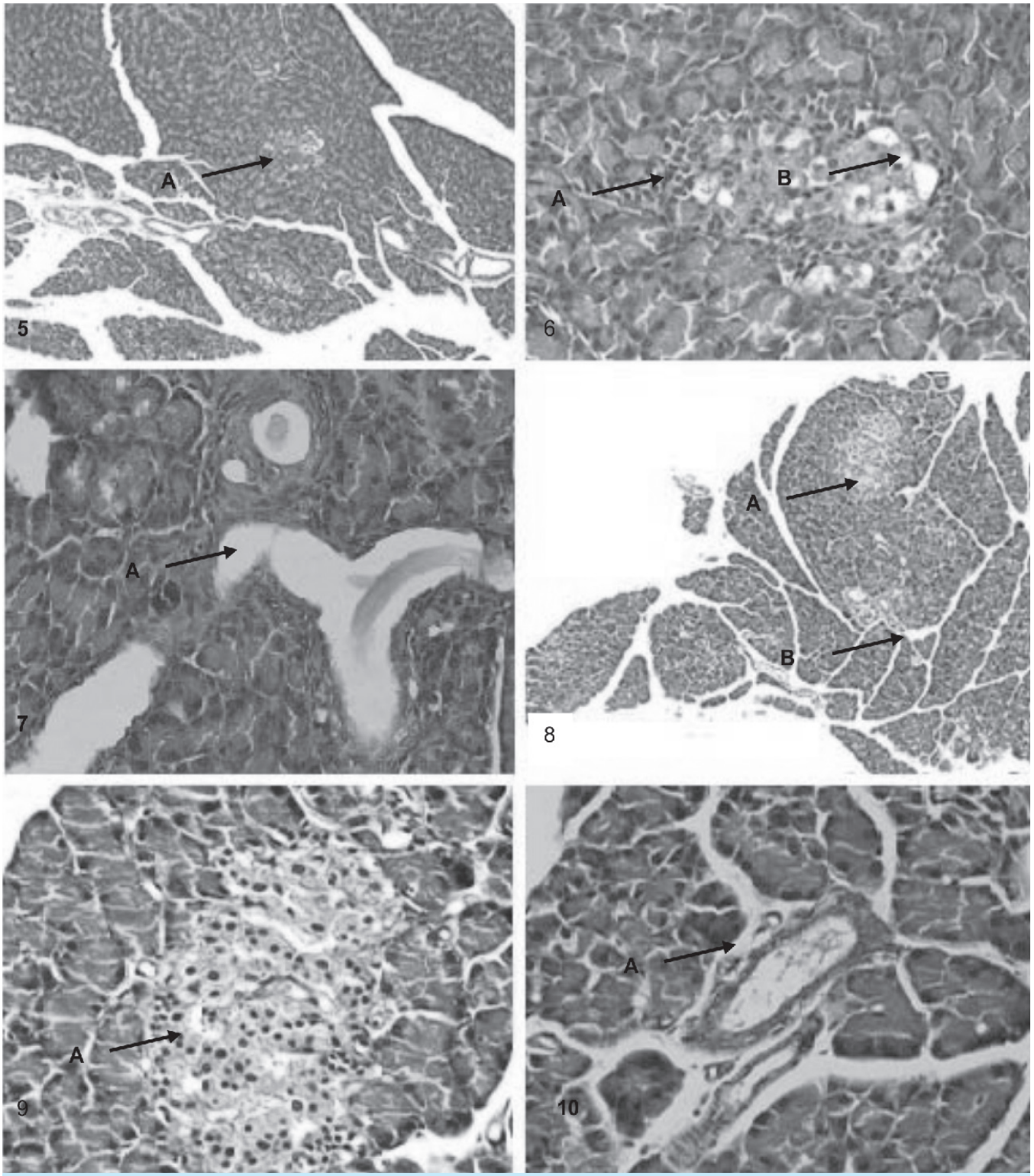


Fig B;(5)Photomicrograph of a 5 micron thick H&E stained paraffin section from the pancreas of Glibenclamide group male albino rat showing shrinkage of islets of langerhens (A) X200. (6) lymphocytes infiltration (A) damage of islets of langerhens/ cytoplasm vacuolization (B) X400.(7)normal duct containing secretions (A) X400 (8) The pancreas of Guaiacum officinale treated male albino rat (Group D)showing normal islets of langerhens (A) Normal secretions in duct (B) Normal exocrine cells (C) X200. (9) Showing normal islets of langerhens(A) X 400. (10) Showing normal pancreatic duct (A) X200.

the effect of G. officinale on pancreatic enzymes and tissues in STZ induced diabetic rats. STZ used globally to induce diabetes in experimental animals.[23] It induce diabetes by destruction of β cell on langerhans by alkylation of DNA.[24,25] Sulfonylureas are worldwide recognized and standard treatment of diabetes mellitus Type 2 by augmenting insulin release from beta cells of pancreas.[26,27] Several herbal remedies have been developed by scientist to prevent and cure the diabetes and its complications. G. officinale is one of the blessing from nature as it is used for the treatment of various inflammatory disorders because of its antioxidant action.[12,28] In this study we have evaluated the antidiabetic activity of bark extract of this plant. The results of the study showed that both pancreatic enzymes amylase (199.30±14.463*** Mean±SEM) and lipase level (78.50±1.293*** Mean±SEM) were reduced significantly in STZ treated group which expressed that diabetes is successfully induced in experimental animals (Table-I). While histological findings of pancreas of the same group also supported the results showed in fig A. Similar changes on pancreatic enzymes were also reported by Skrha, 1987.[29] When STZ induced diabetic rats were treated with GLB, the result revealed that the pancreatic amylase (384.50±16.132*** Mean± SEM) were significantly increased but lipase levels were decreased (69.40±2.495*** Mean± SEM) (Table-I). The levels of amylase (353.80±1.083*** Mean± SEM) and as well as lipase (115.50±2.282*** Mean±SEM) were improved by G. officinale treated diabetic rats (Table-I). In the present study Pancreatic tissue damaged were presented as lymphocyte infiltration and reduction of size and number of islet cells in positive control group (Fig. A). while these changes were considerably reduced in Glibenclamide (standard) and *Guaiacum officinale* (treated group) (Figure-B). Similar improvements were also demonstrated by the plant Merremia emerarginata.[17] These beneficial effects of G. officinale may be due its antioxidant action, previous reported effect of the plant.[12,29,30]

CONCLUSION

In the light of above discussion it was revealed that G. officinale is the useful herbal remedy not only for inflammatory diseases but also beneficial in Type 2 diabetes and its complication. Further mechanistic and clinical studies will require to reveal the molecular mechanism and effects on other organs.

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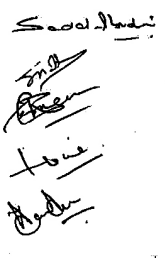
1	Sadaf Ibrahim	Main Author	
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