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A Comparative Assessment on the Protective Effect of Boswellia Serrata, Arabic Gum Extracts, and their Combination in Streptozotocin-Induced Diabetic Rats

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Abstract: Background: Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels and pancreatic β-cell dysfunction. Natural compounds such as Arabic gum and *Boswellia serrata* have been discovered for their antidiabetic potential, and only a few investigations have been published on the combined impact of Arabic gum with BS. **Aim:** This study evaluates the anti-diabetic effects of *Boswellia serrata* and Arabic gum, individually and in combination, in streptozotocin-induced diabetic rats, to identify the most effective treatment. **Materials and Methods**: Thirty male albino rats (200–300 g) were divided into five groups (n=6). Diabetes was induced using a single intraperitoneal dose of streptozotocin (40 mg/kg), except in the negative control, which received citrate buffer and oral distilled water with 0.5 mL Tween 80. Treatments were given orally for 28 days: diabetic untreated, AG (25 mg/kg), BS (400 mg/kg), and combination (AG + BS). Measured parameters included fasting blood glucose, body weight, serum insulin, insulin resistance, and pancreatic histology with H&E and immunohistochemistry. **Results:** AG showed total antioxidant activity of 26 mg AAE/g, while BS showed 22 mg AAE/g. Significant differences were observed in IR, serum insulin, body weight, and FBG among groups. Histology revealed partial islet recovery with BS alone, whereas the combination group showed the greatest improvement, with preserved islet structure, reduced inflammation, and strong insulin immunoreactivity (>75%), suggesting enhanced therapeutic effect. **Conclusion:** The combination of Arabic gum and *Boswellia serrata* showed superior pancreatic protection compared to individual treatments, suggesting potential complementary use in diabetes. Further studies are needed to confirm efficacy and mechanisms. **Recommendations:** Future studies should investigate the long-term effects, underlying mechanisms, and optimal dosing of Arabic gum and *Boswellia serrata*, while clinical trials are required to confirm their safety and efficacy in diabetic patients. **Recommendations:** Future studies with larger sample sizes and longer intervention durations are needed to determine whether the observed glycation changes persist and to better evaluate long-term safety. Investigating potential synergistic effects between *P. harmala* and *Punica granatum* components may also provide further insight into their metabolic impact.

Keywords: Diabetes mellitus, Oxidative stress, Inflammation, blood glucose, insulin resistance, Pancreatic beta-cells.

Introduction

Diabetes is a kind of metabolic illness characterized by hyperglycemia (elevated blood sugar levels) and develops because of deficiencies in the action of insulin, its secretion, or both. Multiple pathologies contribute to the development of diabetes. These extend from what is Autoimmune destruction of the pancreatic cells, so insulin is not produced, through to disorders that are like a block, perhaps associated with carbs going down, which are resistance to insulin action [1]. Diabetes results from insufficient insulin action, caused by reduced insulin secretion and/or peripheral insulin resistance. These two defects often coexist, making it difficult to identify the primary cause of hyperglycemia [2].T1DM (type 1 diabetes mellitus) is a rare chronic autoimmune disease characterized by progressive β-cell destruction, leading to insufficient insulin secretion. Its etiology is not fully understood but likely involves interactions between genetic susceptibility and environmental factors [3]. Type 2 diabetes mellitus (T2DM) is the most common metabolic and endocrine disorder, characterized by hyperglycemia due to insulin resistance or relative insulin deficiency. Its long-term complications include retinopathy, neuropathy, nephropathy, and peripheral vascular disease, with additional risks in uncontrolled cases. Natural products remain essential in drug discovery, with nearly 80% of the global population relying on plant-based traditional medicine due to its affordability and safety [4].Around 12,000 medicinal plant species may help lower blood glucose and enhance insulin secretion. They are rich in bioactive compounds such as flavonoids, alkaloids, carotenoids, glycosides, phenolic acids, tannins, terpenoids, and saponins. Their antidiabetic effects mainly result from improving pancreatic β-cell function, leading to increased insulin release, reduced intestinal glucose absorption, and enhanced metabolism [5]. *Boswellia serrata*, native to India and found in arid regions of North Africa and the Middle East, is a deciduous tree whose bark produces a gummy oleoresin [6]. It has pharmacological effects including antihyperglycemic, anti-ulcer, and anti-inflammatory actions in conditions like cancer, osteoarthritis, inflammatory bowel disease, and asthma [7]. The dried, delicious sticky substance known as Arabic gum is derived from the stems and branches of *A. seyal* or *A. senegal* [8]. They are rich in non-viscous soluble fibers and are widely used in traditional medicine to treat bleeding disorders, prolapse, leukorrhea, gastrointestinal issues (diarrhea and constipation), and diabetes [9]**.** This study evaluates the dual administration of Arabic gum and *Boswellia serrata* in the management of diabetes mellitus, as no previous research has explored their combined effect. It assesses

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whether their concomitant use offers synergistic or enhanced therapeutic benefits in diabetic models.

Materials and Methods

Materials: A pure, standardized extract of *Boswellia serrata* was obtained from Hunan Naturalin Bio Resources, China, and used in this study; Raw Arabic gum (*Acacia senegal*) from MERYER (Shanghai, China) Chemical Technology; streptozotocin from TCI (Tokyo Chemical Industry), Japan; Tween 80 from Titan Biotech Ltd, India; chloroform from THOMAS Baker, India; sodium citrate buffer. Biochemical analysis: Rat Insulin (INS) ELISA Kit (Sun Long Biotech Co., Ltd., China); Ultrasonic probe sonicator, refrigerated centrifuge (Hettich Universal 320R, Germany), a digital glucometer On Call Plus glucometer (ACON Biotech, Hangzhou, China), and an electronic compact scale (SF-400A, China).

Methods

Extraction

Preparation of Boswellia serrata extract: a pure, standardized extract was purchased and used as received, without further processing.

Arabic gum (Acacia). The Arabic gum was ground, and 40 g was soaked in 200 mL tap water, gently heated to 30 °C for 30 min, then left for 24 h with shaking every 3–4 h. Sonication for 30 min enhanced compound release. The viscous extract was centrifuged at 6000 rpm for 12 min, and the supernatant dried in Petri dishes at room temperature for 4 days, yielding 53.54 g of dried extract. A selective separation isolated AG, which was rehydrated, dried, and weighed 10.74 g, representing 20.05% of the total mixture [10].

Phytochemical Analysis of Bioactive Constituents: Assessing the therapeutic potential of medicinal plants involves identifying and quantifying bioactive phytochemicals responsible for antioxidant, anti-inflammatory, and pharmacological effects [11].

1. **TAC of the Boswellia serrata resin extract**: Approximately 5 mg of resin powder (or Arabic gum) was dissolved in 1 mL distilled water, then mixed with 1 mL TAC reagent containing 0.6 M H_2SO_4, 28 mM sodium phosphate, and 4 mM ammonium molybdate (final volume = 2 mL). The mixture was vortexed, incubated at 100 ± 2 °C for 90 min (1.5 h) in a Binder oven, then cooled to ~25 °C. Absorbance was measured at 695 nm using a UV–V is spectrophotometer against a reagent blank. The recorded absorbance was 0.344.
2. **Molisch's Test for Detection of Polysaccharides in Boswellia serrata and Arabic Gum Extracts:** Polysaccharides in BS and AG were tested using Molisch's test. Equal amounts (3 mg each) were dissolved in 1 mL water, and Molisch reagent (α-naphthol in sulfuric acid) was added to detect carbohydrates.
3. **Detection of Terpenes in Boswellia serrata and Arabic Gum Extracts:** (+)-Boswellic acid and Arabic gum were tested for terpenes using an acid-catalyzed colorimetric method. Both samples (0.2 g) were dissolved, treated with acetic acid, and layered with concentrated H_2SO_4, producing a bluish interface that confirmed terpene presence.
4. **Shinoda Test for Detecting Flavonoids in Boswellia serrata and Arabic Gum:** The Shinoda test was used to detect flavonoids in *Boswellia serrata* and Arabic gum. For each sample, 0.2 g of extract was dissolved in 1 mL of distilled water. Small pieces of magnesium ribbon were added, followed by concentrated hydrochloric acid. The color changed from red to pink after a few minutes, showing the presence of flavonoids.
5. **Detection of alkaloids by Dragendorff's reagent (potassium bismuth iodide) in Boswellia Serrata and Arabic Gum:** Dragendorff's reagent was employed as a qualitative test to identify alkaloids in extracts from *Boswellia serrata* and Arabic gum. For each sample, the same amount of 0.2 g used in earlier phytochemical tests was employed, dissolved in 1 mL of distilled water. A few drops of Dragendorff's reagent were added to the acid layer.

Study Design: This experimental study used male Wistar rats to evaluate the potential anti-diabetic effect of Arabic gum, *Boswellia serrata,* and their combination. The study adhered to standard ethical protocols for animal experimentation. thirty healthy adult male rats weighing 200 and 300 g were housed under standard laboratory conditions for two weeks of acclimatization. The animals were maintained at 30°C with and libitum access to standard chow (NC), a carbohydrate (CHO) diet, and tap water throughout the experimental period.

Induction of diabetes in rats and measurement of blood glucose levels. Diabetes was induced in the overnight fasted rats by a single intraperitoneal injection (i.p.) of STZ at a dose of 40mg/kg body weight, dissolved in freshly prepared cold citrate buffer pH 4.5 [12].

Following acclimatization, the rats were randomly divided into five groups (n = 6)

Group 1: (Negative Control Group): Rats in which received a single intraperitoneal dose of 0.5 ml citrate buffer on the same day that diabetes was induced in the other experimental groups by streptozotocin administration. Thereafter, each rat was orally administered 0.5 mL distilled water containing 0.2 mL Tween 80 by oral gavage once daily for 28 consecutive days.

Group 2: (Diabetic Control Group): Diabetes mellitus was induced by a single intraperitoneal injection of 40mg/kg of STZ in 0.5 ml of citrate Buffer. Thereafter, (0.5 ml of distilled water containing 0.2 ml of Tween 80) by oral gavage once daily for 28 consecutive days.

Group 3: (Arabic Gum Treated Group): The diabetes was induced through a single IP injection of 40mg/kg of STZ dissolved in 0.5 ml of citrate buffer for each rat. The treatment was administered to the rats through oral administration of 25 mg/kg of Arabic gum dissolved in (0.5 ml of water +0.2 ml of Tween 80) from the 1st to the 28th day [13]**.**

Group 4: (Boswellia serrata-Treated Group): Diabetes was induced in the form of a single intraperitoneal injection, 40mg/kg of STZ dissolved in 0.5 ml of citrate buffer, and BS 400mg/kg dissolved in(0.5 ml of water+0.2ml of Tween 80) was orally administered to each rat for a period of 28 days [14].

Group: 5 (Combined(AG+BS) Treated Group): Diabetes was induced using 40mg/kg of STZ dissolved in 0.5 mL citrate buffer, followed by oral administration of 25mg/kg/kg AG and 400mg/kg BS, both dissolved in (0.5 mL of water plus 0.2 mL of Tween 80) for each rat. The treatments were administered with a one-hour interval between AG and BS.

Parameters Measured: Throughout the study, various physiological and biochemical parameters were evaluated. The effects of the treatments are assessed.

Body weight: The Body weight of each rat was recorded on the first day of the study, before the induction of diabetes on the final day of the experiment, immediately before sacrifice.

Fasting Blood Glucose (FBG): Blood glucose levels were assessed at the specified time point using an On Call Plus glucometer after a 12- to 14-hour overnight fast [15].

Before the onset of diabetes (baseline) on day zero.

- Three days after streptozotocin (STZ) injection to confirm diabetes induction.
- Treatment day 10
- Treatment Day 20
- Day 28.

Fasting Serum Insulin: on day 28 of the experiment, which was also the last day of treatment, the animals were fasted overnight before blood collection, and fasting serum insulin levels were measured using an appropriate ELISA kit.

Insulin Resistance: Insulin resistance was estimated using the HOMA-IR index, calculated as the product of fasting blood glucose and fasting insulin levels divided by 405, using the following equation: HOMA-IR = [fasting serum insulin (µIU/mL) × fasting blood glucose (mg/dL)] / 405 [16].

Statistical Analysis: Data was analyzed using SPSS and presented as mean ± SE. One-way ANOVA with post hoc (Tukey) tests was used for between-group comparisons of biochemical parameters, including fasting serum insulin and HOMA-IR. Paired Student's t-test assessed within-group differences, including changes in body weight.

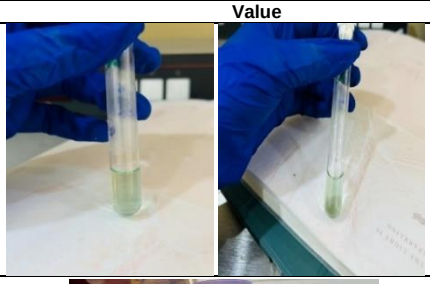
Histopathological Examination

Histopathological Analysis. Pancreatic tissues were collected, fixed in 10% neutral buffered formalin for ≥48 h, and processed via standard paraffin embedding. Five µm sections were cut, mounted on slides, and stained with Hematoxylin and Eosin (H&E). Histopathological evaluation under a light microscope assessed islet morphology, cellular infiltration, necrosis, and vascular changes, with representative photomicrographs captured [17].

Immunohistochemistry (IHC): Five-micrometer paraffin-embedded pancreatic sections were deparaffinized, rehydrated, and heated in pH 6.0 citrate buffer using a microwave for 10–15 min. Endogenous peroxidase was blocked with 3% hydrogen peroxide for 10 min. Sections were incubated overnight at 4 °C with primary antibodies, followed by a biotinylated secondary antibody and streptavidin–horseradish peroxidase. Chromogenic detection was done with DAB, counterstained with hematoxylin, and examined under a light microscope to assess antigen-positive immunoreactivity and distribution, Immunohistochemical analysis was performed following standard protocols as described in previous studies [18].

Result

1-Phytochemical Analysis of Bioactive Constituents

Assay Name	Value	Observation
Total Antioxidant Capacity (TAC) for AG and BS.		The B. serrata resin extract has an antioxidant capacity. The total antioxidant capacity of B. serrata resin extract, confirming the presence of antioxidant compounds in B.S., was 22 mg AAE/g. The total antioxidant activity of Arabica gum, 26 mg AAE/g, developed a green color, indicating the presence of antioxidant compounds in the Arabica gum extract.
Molisch's Test for Detection of Polysaccharides in both AG and BS.		The formation of a purple ring at the interface of the two layers indicated that carbohydrates were present, which are polysaccharides found in both Boswellia serrata and Arabic gum.
Detection of Terpenes in *Boswellia serrata* and Arabic Gum Extracts.		A clear bluish color appeared at the interface, confirming the presence of terpenoid compounds in both *Boswellia serrata* and AG.
Shinoda Test for Detecting Flavonoids in *Boswellia serrata* and Arabic Gum.	There is no red to pink color.	No color change was observed in either sample, suggesting a negative result for flavonoid content in both *Boswellia serrata* and Arabic gum.
-Detection of Alkaloids Using Dragendorff's Reagent (Potassium Bismuth Iodide) in Boswellia Serrata and Arabic Gum.	There is no reddish-brown precipitation.	Neither sample showed this characteristic precipitate, indicating a negative result for alkaloid content in both *Boswellia serrata* and Arabic gum.

2- Body Weight Changes

This study explains the change in the body weight for the experimental groups over the 28 days of the experiment. According to the resulting data there are no significant changes in body weight observed in the negative control group throughout the experimental period (p-value > 0.05). In the diabetic control group (DM), a significant reduction was observed on days 19 and 28 compared with day 0 ($p < 0.05$), whereas no significant difference was detected on day 10 ($p > 0.05$). In AG treated group, a significant increase was observed on day 28 compared with days 0 and 10 ($p < 0.05$), while no significant differences were detected involving day 19 ($p > 0.05$). In BS treated group the observed changes were not statistically significant ($p > 0.05$). In the Combination treated group no statistically significant differences were found among the study time points ($p > 0.05$), as shown in figure1.

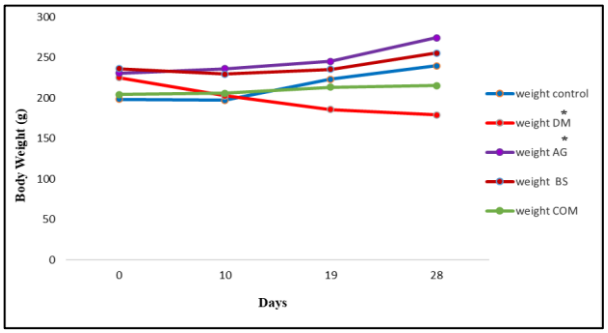


Figure (1): Changes in rat body weights over the 28 days of experiment. (*) On the diabetic control group Indicates a significant difference p-value < 0.05, there is a considerable change in the body weight of diabetic control group during the 28 days of experiment, (*) On the AG treated group Indicates a significant difference p-value < 0.05, there is a considerable change in the body weight of AG treated group during the 28 days of experiment.

3- Fasting Blood Glucose Levels

FBG levels were assessed on days (0, 3, 10, 20, and 28) of the study. On day 0, no significant differences were observed among the negative control, diabetic control, AG, and combination groups (P > 0.05). However, the BS group showed a significant difference compared with the diabetic control (DM) group (P < 0.05). At day 3, all diabetic groups (DM, AG, BS, and COM) showed significantly higher FBG levels than the negative control group (P < 0.05). In addition, the AG group differed significantly from the diabetic group (P < 0.05).At day 10, the diabetic control group exhibited significantly higher fasting blood glucose levels than all other groups (P < 0.05). The BS group showed significantly lower FBG level than the combination group (P < 0.05), while no significant difference was observed between the AG and combination groups (P > 0.05). At day 20, the diabetic group remained significantly different from all other groups (P < 0.05). Moreover, the BS group showed a significant difference compared with the AG group (P < 0.05). At day 28, the diabetic group showed significantly higher fasting blood glucose levels than all other groups (P < 0.05), whereas no significant differences were observed among the AG, BS, and combination groups (P > 0.05), as shown in **Figure 2.**

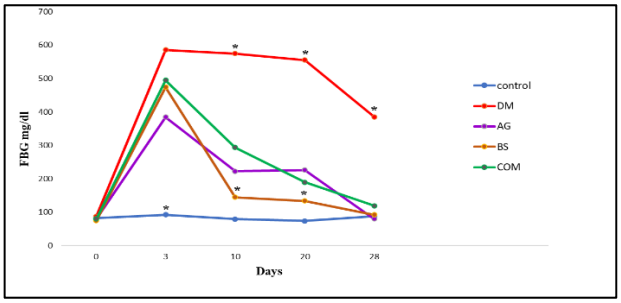


Figure (2): Changes FBG levels of rats, For all groups from 0 day to 28th days ,* On the negative control group at day 3 indicated a significant differences (P < 0.05) in the FBG of (Neg C) compared with the other experimental groups,* On DM group on days (10,20 and 28) indicated a significant differences in the FBG of DM group compared with the other experimental groups,* On BS treated group at day (10,20) indicated a significant difference (P < 0.05) in FBG compared with the COM and AG treated group respectively.

4- Insulin Resistance (IR)

In this study results showed that; the IR values were significantly different among the experimental groups. The diabetic control group (DM) showed an exponentially marked (significant) increase in IR compared to the negative control group (p < 0.001), Treatment with the (AG, BS, COM) significantly reduced IR levels compared with the diabetic control group (p < 0.001), The combination treatment (COM) also produced a significant difference in IR compared with the AG treated group (p < 0.05), as shown in **Figure 3.**

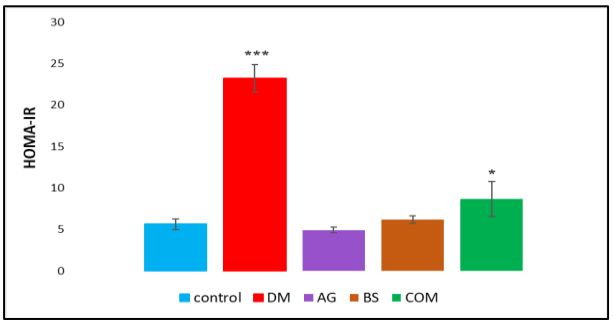


Figure (3): Insulin resistance levels in all groups following 28 days of treatment with (AG), (BS), and their combination (AG+BS).

5- Serum Insulin

The results of this study showed a significant variation in serum insulin levels among the experimental groups. The diabetic control group (DM) showed a significant reduction in serum insulin levels compared with the negative control group (p < 0.05). Treatment with AG, BS, and their combination (COM) significantly increased serum insulin levels compared with the untreated diabetic control group (p < 0.05). The combination-treated group demonstrated significant difference (in increased) in serum insulin levels when compared with AG treated group (p < 0.05), as shown in **Figure 4.**

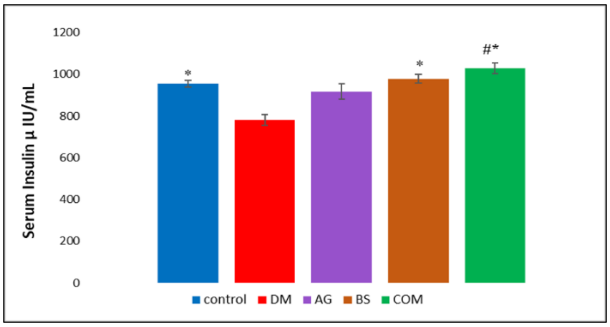


Figure (4): Changes in serum insulin levels among all groups following 28 days of treatment with AG, BS and their combination, (*) On (negative control, AG, BS, COM) groups indicate a significant increase in serum insulin compared with the diabetic control group (p< 0.05), while (#) on COM group indicate a significant increase in serum insulin of the combination (AG+BS) group compared with the AG treated group (p < 0.05).

Histopathological examination: The pancreas has both exocrine and endocrine roles. The exocrine part secretes digestive enzymes, while the endocrine part (islets of Langerhans) releases insulin and glucagon to control blood glucose. Damage to the islets reduces insulin secretion, leading to diabetes. Therefore, histopathological examination helps assess pancreatic cellular changes and treatment effects [15].Microscopic analysis revealed normal pancreatic structure in controls, while diabetic rats showed damaged, shrunken islets with inflammation. Treatments (Arabic gum, Boswellia serrata, and their combination) improved islet structure, cell integrity, and reduced inflammation compared to diabetics.

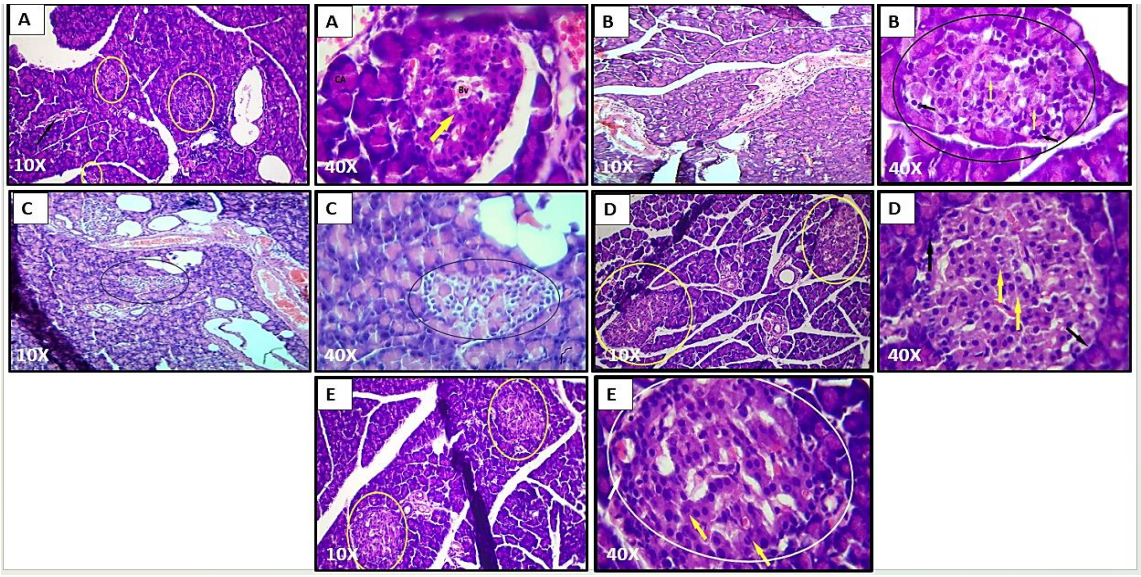


Figure (5): sections of the pancreatic tissue that explain the control and treated rats. **(A)** Section shows standard pancreatic tissue architecture with normal looking pale islet of Langerhans (yellow circles) embedded within the Centro acinar cells (white arrow), with well-defined borders, contain beta cells in the center, delicate blood vessels show no congestion (black arrow), High power section shows standard pancreatic tissue architecture with normal looking size and shape of the islet of Langerhans embedded within Centro acinar cells (CA), with well-defined borders, containing well intact pale oval beta cells in the center (yellow arrow) next to delicate blood vessels (Bv). **(B)** Section shows pancreatic tissue with degenerative changes seen mainly in the islets of Langerhans (black circle) with shrunken size, ill-defined boundaries, partial loss of its cellular integrity, and beta cells revealed degenerative changes. Centroacinar cells also reveal degenerative changes (black arrows), blood vessel congestion (white arrow), and mononuclear inflammatory cells infiltration (yellow arrows). **(C)** High power tissue section shows improvement and restoration of pancreatic islet of Langerhans size and shape (black circle), with well-demarcated boundaries (white arrow), preserved cellular integrity, preserved beta cells mainly in the center (black arrows), with no degenerative changes. Very mild inflammatory reaction. No blood vessel congestion (double white arrows). **(D)** Section shows intact pancreatic tissue architecture with preserved exocrine pancreatic lobes with centroacinar cells, and restoration of the islet of Langerhans number, size, and shape (yellow circles), with preserved cellular integrity containing intact beta cells mainly in the center, with no degenerative changes: very mild inflammatory reaction and reduced blood vessel congestion. **(E)** Section shows preserved pancreatic tissue architecture with a prominent rise in the number of the islets of Langerhans (yellow circles), restoration of their size and shape with well-defined borders, intact cellular integrity, with beta cells mainly in the center with no degenerative signs, few inflammatory reactions, and no blood vessel congestion.

Immunohistochemistry, Immunohistochemistry (IHC), developed in the early 1980s, is a key technique in surgical pathology for cell classification and diagnosis. It uses antibodies to detect specific antigens in tissues and cells, helping identify cell type and organ origin. Today, IHC is mainly done on formalin-fixed paraffin-embedded tissue but can also be applied to frozen or plastic-embedded sections [16]. Immunostaining of pancreatic tissues showed strong insulin expression in control rats, weak or absent staining in diabetic rats, and restored β-cell insulin expression—with larger, more numerous islets and stronger cytoplasmic staining—after treatment with Arabic gum, *Boswellia serrata,* or their combination.

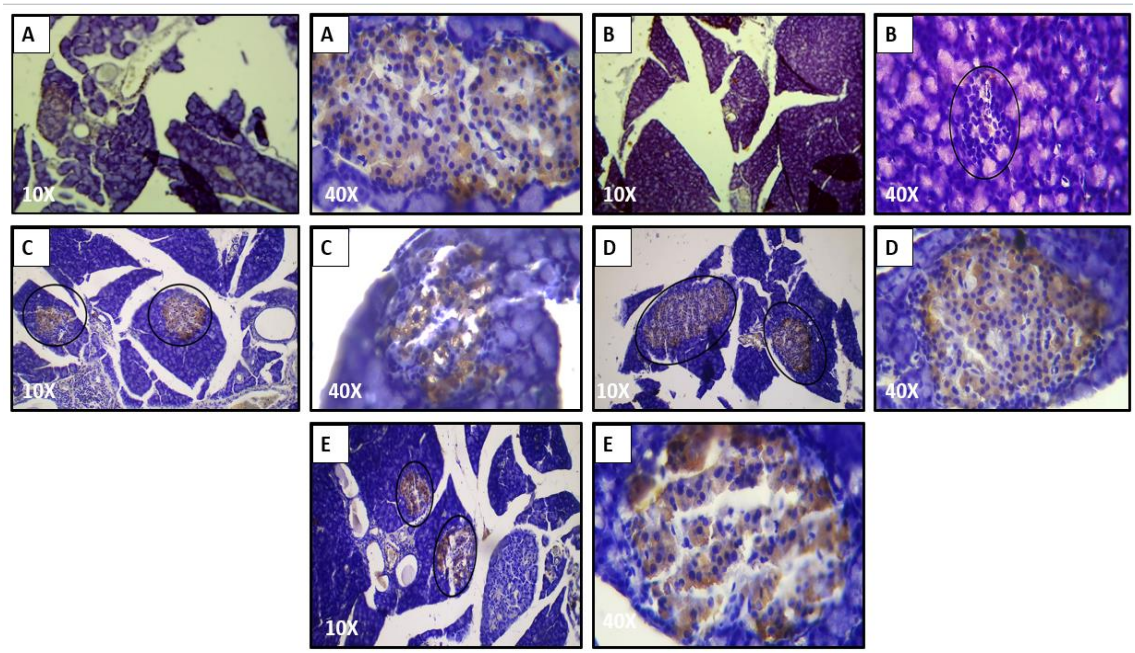


Figure (6): Determination of insulin in the pancreatic cells of control and diabetic treated rats. **(A)** The section shows a positive expression of the insulin marker, characterized by a diffuse, strongly brownish cytoplasmic stain in more than 90% of the pancreatic islets of Langerhans, predominantly in the central epithelial cells. **(B)** The section shows a shrunken islet of Langerhans, with an ill-defined border, embedded in centroacinar cells that are negative for the insulin marker. **(C)** The section shows multiple islets of Langerhans with improved size and shape, as well as the restoration of B-cells, which exhibit positive expression for the insulin marker, characterized by a diffuse, strongly brownish cytoplasmic stain in approximately 50% of the pancreatic islets of Langerhans, predominantly in the central epithelial cells. **(D)** The section shows multiple islets of Langerhans (Black circles) with improved size and shape, as well as the restoration of B-cells with positive expression for the insulin marker, characterized by a diffuse, strong, brownish cytoplasmic stain in more than 60% of the pancreatic islets of Langerhans. **(E)** The section shows multiple islets of Langerhans (Black circles) with improved size and shape, as well as the restoration of B-cells with positive expression for the insulin marker, characterized by a diffuse, strong, brownish cytoplasmic stain in more than 75% of the pancreatic islets of Langerhans.

Discussion

The phytochemical analysis showed that both *Boswellia serrata* and Arabic gum extracts have notable antioxidant properties [19]. The total antioxidant capacity (TAC) measured 22 mg AAE/g for BS resin, while Arabic gum slightly exceeded this at 26 mg AAE/g. These findings suggest both extracts hold significant antioxidant activity, likely due to bioactive compounds such as polyphenols, flavonoids, and terpenoids [20]. Additionally, the development of a green color in the TAC assay confirmed the presence of antioxidants. These findings align with previous research indicating that *Boswellia serrata* resin contains boswellic acids and other phytochemicals with potent radical scavenging activity [21]. Meanwhile, Arabic gum is rich in various compounds, including polysaccharides and phenolic compounds, which possess characteristic antioxidant properties [22]. The higher total antioxidant capacity (TAC) observed in Arabic gum may be attributed to its greater concentration of water-soluble antioxidant molecules compared with *Boswellia serrata*. Molisch's test confirmed polysaccharides in both extracts by a purple ring, supporting their antioxidant roles in free radical scavenging and metal chelation, consistent with TAC results. Terpenoids were also detected (bluish interface), known for anti-inflammatory, antioxidant, and antimicrobial activities, underscoring the extracts' therapeutic potential against oxidative stress and inflammation [23]. The Shinoda test was negative in both extracts, this observed in the current study may be attributed to the use of aqueous extraction, which could be less efficient than methanol in extracting flavonoids and alkaloids from BS oleo-gum-resin, as previous studies reported positive findings for these compounds in methanolic extracts, the high TAC values suggest terpenoids and polysaccharides are the main contributors. Dragendorff's test was also negative, confirming the absence of alkaloids. These results align with the composition of Arabic gum (mostly polysaccharides and glycoproteins) and *Boswellia serrata* (rich in terpenoids and boswellic acids), highlighting the role of non-alkaloid compounds in their bioactivity.

Body Weight Changes

The significant reduction in body weight observed in the diabetic control (DM) group is most likely associated with the severe metabolic alterations induced by streptozotocin (STZ)-mediated β-cell destruction, leading to insulin deficiency and impaired cellular glucose uptake [24].Treatment with AG significantly increased body weight during the treatment period, suggesting a protective effect against diabetes-associated metabolic deterioration, this improvement may be related to the hypoglycemic activity of Arabic gum, which could enhance glucose metabolism and reduce excessive catabolic activity, antioxidants and anti-inflammatory properties that may attenuate oxidative damage and inflammatory responses associated with diabetes, thereby improving nutrient utilization and preserving body tissue integrity, dietary fiber intake, particularly AG, associated with beneficial effects on lipid metabolism and body weight regulation [25]. BS group demonstrated increases in body weight, these changes did not reach statistical significance, Nevertheless, the observed upward trend may still reflect partial amelioration of diabetic metabolic dysfunction, BS is known to possess potent anti-inflammatory and antioxidant activities, which may contribute to reducing oxidative stress-mediated tissue damage and improving overall metabolic status [26].The decrease in body weight gain observed in the high dose of BS group may be associated with the presence of guggulsterone-like constituents reported in BS, these compounds may stimulate thyroid activity, leading to an increase in metabolic rate and energy expenditure, enhanced metabolism can result in greater caloric utilization and subsequent weight reduction [27]. Interestingly, the combination group showed only moderate non-significant improvement in the body weight despite receiving both AG and BS. This finding may suggest that the combined treatment exerted a stabilizing rather than fully restorative metabolic effect during the study period. This finding may reflect the beneficial effect of AG in improving the metabolic status of diabetic rats and preventing diabetes-associated body weight loss, while the presence of high dose of BS in the combination may have moderated excessive weight gain through its reported effects on food intake, leptin sensitivity and adiponectin levels. Therefore, the combination may have helped to stabilize body weight rather than producing a marked or significant weight gain.

Fasting Blood Glucose: The current results show a considerable decrease in fasting basal blood glucose (FBG) levels across all treatment groups Arabic gum (AG), Boswellia serrata (BS), and the combination therapy (COM) compared with the untreated diabetic group. This suggests a potential hypoglycemic effect from both AG and BS and their combination. On Day 3 after STZ induction, diabetic rats showed clear hyperglycemia, confirming the successful development of the diabetic model [28]. From Day 10 onward, all treated groups showed a steady decline in FBG. These findings align with previous studies reporting the antidiabetic potential of Arabic gum, also attributed to its high soluble fiber content, which can delay intestinal glucose absorption and improve glycemic regulation, AG possesses antioxidant and anti-inflammatory properties that may contribute to preservation of pancreatic β-cell integrity and enhancement of insulin sensitivity [29]. The marked reduction in FBG observed in the BS treated group may be attributed to Suppression of inflammatory mediators and reactive oxygen species, decreasing the resistance to insulin, restoring pancreatic beta cells ,modulation of hepatic glucose metabolism, reduce gluconeogenesis, partial restoration of pancreatic function and improved peripheral glucose metabolism [30]. The combination-treated group demonstrated a reduction in blood glucose levels. Although the combination included both agents, it did not produce a superior glucose lowering effect compared with each treatment alone this could be attributed to the relatively short treatment duration, the selected dose ratio, and the possibility that the combined treatment did not produce an additive effect on fasting blood glucose under the current experimental conditions.

Serum Insulin

The significant reduction in serum insulin levels observed in the diabetic (DM) control group confirms the destructive effect of STZ on pancreatic β-cells. STZ preferentially accumulates within β-cells through GLUT2 glucose transporters, where it induces DNA alkylation, mitochondrial dysfunction, and excessive generation of ROS. These processes ultimately result in β-cell necrosis and marked impairment of insulin biosynthesis and secretion [31].Treatment with AG significantly increased serum insulin levels compared with the untreated diabetic group, suggesting partial preservation or restoration of pancreatic β-cell function. This beneficial effect may be attributed to the antioxidant and anti-inflammatory properties of AG, which could reduce oxidative stress-mediated β-cell injury and improve pancreatic cellular integrity. In addition, AG may enhance insulin secretion indirectly through improvement of glycemic control and reduction of glucotoxicity, thereby decreasing metabolic stress imposed on residual β-cells [32].BS treatment significantly elevated serum insulin levels relative to the diabetic control group, this effect may indicate preservation and partial restoration of pancreatic β-cell function following STZ-induced damage. This effect may be attributed to the antioxidant and anti-

inflammatory properties of BS, particularly its boswellic acid constituents, which can attenuate oxidative stress and inflammatory injury within pancreatic tissues, also be partially attributed to other constituents, including polysaccharides and phenolic compounds [33].The combination treated (COM) group demonstrated the greatest restoration of serum insulin levels with a significant difference compared with the AG alone and showed no significant difference when compared with the negative control group and BS treated group. This finding suggests that the improvement in insulin level may be mainly related to the protective effect of BS on pancreatic beta cells, while AG may have provided an additional supportive effect. The near normalization of insulin levels observed in the combination group suggests that both agents may exert complementary mechanisms involving reduction of oxidative stress, attenuation of inflammatory injury, and improvement of pancreatic cellular recovery. The superior restoration of serum insulin levels observed in the combination group may have contributed to the improvement in glycemic regulation and insulin resistance observed in this study. Restoration of serum insulin levels likely contributed to improved glucose utilization, reduced hepatic glucose output, and enhanced metabolic regulation. Collectively, these findings suggest that AG and BS possess significant pancreatic protective effects and may ameliorate diabetes-associated β-cell dysfunction through antioxidant, anti-inflammatory, and insulin-preserving mechanisms.

Insulin Resistance (IR)

The markedly elevated insulin resistance (IR) observed in the diabetic control group reflects profound impairment in glucose homeostasis following STZ-induced diabetes, inducing pancreatic β-cell destruction and insulin deficiency, persistent hyperglycemia [34]. Treatment with AG significantly reduced IR levels compared with the untreated diabetic control group, this improvement due to ability of AG to inhibit absorption of glucose in the intestine , reduce postprandial hyperglycemia, attenuate oxidative stress-mediated metabolic dysfunction, improved insulin signaling together with the antioxidant and anti-inflammatory activities of AG [35]. BS treatment significantly improved insulin resistance, which may be attributed to the biological activities of boswellic acids and other active phytoconstituents. Restore insulin sensitivity by suppressing inflammatory stress and protecting insulin-responsive tissues from oxidative damage [36].The combination treated group also exhibited a significant reduction in IR compared with the diabetic group. However, its effect appeared less pronounced than that observed with AG or BS alone. This finding may indicate that although the combined therapy exerted beneficial metabolic effects, the interaction between both treatments did not produce greater improvement in insulin sensitivity than either treatment administered individually under the current experimental conditions. The moderate response may reflect differences in the mechanisms of action or the interaction between both agents.

Histopathological Changes

Histopathological examination provides direct evidence of structural changes including β-cell damage, inflammatory cell infiltration, and tissue degeneration induced by STZ. Since oxidative stress, hyperglycemia, and inflammation are major contributors to pancreatic injury in diabetes, histopathological evaluation enables correlation of these structural alterations with the biochemical findings of the present study [37]**.**Histopathological examination of the pancreatic tissue in the normal control group revealed normal pancreatic architecture with intact islets of Langerhans, well-preserved β-cells, and normal acinar organization. No evidence of cellular degeneration, inflammatory infiltration, vascular congestion, or structural abnormalities was observed. While in the diabetic control group revealed marked structural alterations compared with the negative control group. The islets of Langerhans appeared shrunken and irregular in shape with ill-defined boundaries and partial loss of normal cellular organization. Degenerative changes in pancreatic β-cells were evident by cytoplasmic vacuolation, nuclear degeneration, and fragmentation of cellular integrity. In addition, congestion of blood vessels and infiltration of mononuclear inflammatory cells were observed within the pancreatic tissue, indicating severe inflammatory and vascular disturbances associated with STZ-induced diabetes [38].Histopathological examination of the pancreatic tissue in the AG group demonstrated marked improvement compared with the untreated diabetic group, suggesting a protective effect of AG against STZ-induced pancreatic injury. The restoration of pancreatic architecture and preservation of β-cell integrity may be attributed to the antioxidant and anti-inflammatory properties of AG, which likely reduced oxidative stress-mediated cellular damage and inflammatory activation within pancreatic tissue. The observed histological improvement is consistent with the biochemical findings of the present study, reflecting attenuation of oxidative stress and inflammation responses may have contributed to preservation of pancreatic beta-cell viability and restoration of endocrine function. These findings suggest that AG possesses significant cytoprotective effects and may attenuate diabetes-associated pancreatic degeneration through modulation of oxidative and inflammatory pathways [39]. BS group demonstrated noticeable improvement compared with the untreated diabetic group, indicating a protective effect of BS against STZ-induced pancreatic damage. The restoration of islet architecture and preservation of β-cell morphology suggest partial restoration of pancreatic endocrine function and reduction of diabetes-associated tissue injury. The observed histological improvement may be attributed to the potent antioxidant and anti-inflammatory properties of BS particularly its boswellic acids, which likely reduced oxidative stress, inflammatory cell infiltration, and cellular degeneration within pancreatic tissue. The combination-treated group (AG+BS) demonstrated the most prominent improvement among all treated groups, indicating a substantial protective and restorative effect against STZ-induced pancreatic injury. The marked restoration of islet architecture, preservation of β-cell integrity, and absence of obvious degenerative changes suggest near normalization of pancreatic tissue organization and endocrine function. The superior histological improvement observed in the combination group may be attributed to the complementary antioxidant and anti-inflammatory activities of both AG and BS. Simultaneous reduction of oxidative stress and inflammatory responses may have enhanced protection of pancreatic β-cells from ROS-mediated damage and inflammatory degeneration, thereby preserving cellular integrity and improving tissue recovery.

Immunohistochemistry

Immunohistochemical examination of the pancreatic tissue in the negative control group demonstrated strong positive insulin expression within the islets of Langerhans, particularly in centrally located β-cells. The diffuse brown cytoplasmic staining observed in most pancreatic islet cells reflects normal insulin synthesis, storage, and secretory activity under physiological conditions. The intense insulin immunoreactivity observed in the negative control group indicates preserved β-cell integrity and normal endocrine pancreatic function without evidence of cellular degeneration or impairment [40].In the diabetic control group, immunohistochemical examination revealed a marked reduction in insulin expression within the islets of Langerhans compared with the negative control group. The weak or absent brown

cytoplasmic staining observed in many β-cells reflects severe impairment of insulin synthesis and secretory activity following STZ-induced diabetes, the islets appeared shrunken and disorganized, indicating substantial β-cell damage and loss of normal pancreatic endocrine architecture. These findings may be attributed to the selective cytotoxic effect of STZ on pancreatic β-cells through induction of oxidative stress, DNA alkylation, and inflammatory responses, ultimately leading to β-cell degeneration and depletion of intracellular insulin content [41]. The AG treated group demonstrated a marked improvement in insulin expression within the pancreatic islets compared with the diabetic group. The presence of diffuse strong brown cytoplasmic staining in a considerable proportion of β-cells indicates recovery of insulin-producing beta-cell function within the islets of Langerhans. This may be attributed to the antioxidant and anti-inflammatory properties of AG, preservation β-cell integrity and supporting insulin biosynthesis. In addition, the restoration of insulin immunoreactivity observed in the AG treated group was consistent with our biochemical findings, including improved serum insulin levels and reduced hyperglycemia. The BS treated group demonstrated a considerable restoration of insulin expression within the pancreatic islets compared with the diabetic group. The presence of diffuse, strong brown cytoplasmic staining in a large proportion of β-cells indicates restored insulin expression, suggesting recovery of insulin producing activity and preservation of endocrine pancreatic function. This may be attributed to the potent antioxidant and anti-inflammatory effects of BS, particularly its boswellic acid constituents, which may protect pancreatic β-cells from oxidative and inflammatory damage induced by streptozotocin. BS has been reported to reduce inflammatory mediators and oxidative stress, thereby improving β-cell survival and maintaining insulin synthesis [42]. The combination group (AG+BS) demonstrated the most prominent restoration of insulin expression among all treated groups. The pancreatic islets showed strong diffuse brown cytoplasmic staining in more than 75% of pancreatic β-cells, indicating marked recovery of insulin-producing activity and preservation of pancreatic endocrine function. In addition, the islets of Langerhans appeared larger, more organized, and structurally closer to the normal architecture compared with the diabetic group. These findings suggest that the combined administration of AG and BS exerted an enhanced protective effect on pancreatic β-cells against STZ-induced damage. The enhanced insulin immunoreactivity observed in this group may be attributed to the complementary antioxidant and anti-inflammatory actions of both agents, which collectively reduced oxidative stress, suppressed inflammatory mediators, and preserved β-cell viability and functional integrity. Furthermore, the marked restoration of insulin-positive β-cells in the combination group was strongly supported by the biochemical and histopathological findings of the present study, including increased serum insulin levels, reduction of fasting blood glucose, decreased oxidative stress, and restoration of pancreatic tissue architecture. The stronger insulin expression observed in the combination treated rats compared with the single treatment groups may indicate a more effective preservation of β-cell function and insulin biosynthesis.

Conclusion

This study shows that Arabic gum and *Boswellia serrata* exert protective effects against streptozotocin-induced pancreatic damage in diabetic rats. The combination treatment showed the greatest improvement in pancreatic structure and insulin immunoreactivity, suggesting a combined beneficial effect. These findings support their potential as alternative therapies for diabetes, although further studies and clinical trials are required.

Recommendations

Based on the study findings, Arabic gum and Boswellia serrata, particularly in combination, showed significant improvements in glycemic control, inflammatory markers, antioxidant status, and pancreatic structure. Future studies should investigate long-term effects, underlying molecular mechanisms, and optimal dosing strategies. Clinical trials are needed to assess safety and efficacy in diabetic patients. Additionally, their potential role in preventing diabetes-related complications should be explored.

Disclosure Statement

- **Ethical Approval and Consent to Participate:** Animal handling and experimental procedures were conducted in accordance with the guidelines of the National Institutes of Health for the care and use of laboratory animals. Ethical approval for conducting this study was obtained from the Animal Ethical Committee of the College of Pharmacy, University of Basrah, Iraq (Approval No. EC99; October 26, 2024).
- **Availability of Data and Materials:** All data generated or analyzed during this study were derived from the experimental work conducted by the authors and are available from the corresponding author upon reasonable request.
- **Author Contributions:** Ruaa Abdulwahid Jabbar conducted the experimental work, collected and analyzed the data, and drafted the manuscript. Prof. Dr. Manal Nasser Al-Haydar developed the research concept, designed the study, and supervised the work. Prof. Dr. Manal Abdulkhaliq Ibrahim contributed to the statistical analysis and provided scientific guidance. All authors reviewed and approved the final version of the manuscript.
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