Effect Of SMEEDS Formulation Of Glimepiride In Combination With Boswellic Acid Extract In Diabetic Induced Rats To Mimic Diabetic Complications

Rachappa Dhondiba Mahale¹*, Dr. Vipul P Patel²

Abstract
The current study's objective was to examine the impact of Boswellic acid when combined with a novel glimepiride formulation. The impact on fasting blood glucose levels of the commercially available glimepiride formulation, Boswellic acid SMEDDS, and Glimepiride SMEEDS alone and in combination was examined for up to 120 minutes. Control and streptozotocin-induced diabetic rats were measured for body weight, fasting blood glucose level, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum urea nitrogen, uric acid, serum cholesterol, serum triglyceride, and serum total proteins. At end of study, the activity of catalase (CAT), superoxide dismutase (SOD), and malondialdehyde (MDA) levels were assessed in kidney homogenate. By lowering blood glucose, safeguarding renal functions, and maintaining normal morphology, glimepiride and BSE SMEDDS therapy greatly decreased the pathogenic features of T2DN. The management of glycemic control, lipid metabolism, and anti-oxidative and anti-inflammatory capabilities may be related to the mechanism of action for this impact. This suggests that the unique combination being suggested will have a considerable effect on blood glucose levels and help to imitate long-term consequences of diabetes including nephropathy.

Keywords: Antidiabetic, Streptozotocin, Boswellic acid, Glimepiride, SGOT, SGPT, MDA

Introduction
The T1IDM oral hypoglycemic agents include Sulfonylureas, Biguanides, Thiazolidinediones, Meglitinides, and Alpha-glucosidase inhibitors. The effective ‘Glimepiride (GMP)’ is an oral blood-glucose-lowering drug of the sulfonylurea class. The mechanism of action of Glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells and increasing the sensitivity of peripheral tissues to insulin [1]. Boswellia serrata Triana & Planch (B.S) is a moderate-to-large branching tree were found in India, North Africa and the Middle East. Strips of B.S bark are peeled away yielding a gummy oleo-resin [2]. B.S contains

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of pharmacological effects particularly anti-hyperglycemia effect [4], antioxidant effects may have beneficial effects in peptic ulcer [5] and also anti-inflammatory effects in asthma [6], inflammatory bowel disease [7], cancer [8], and osteoarthritis [9].The hexane and alcoholic extracts of B.S protect liver against toxicity and damage induced by carbon tetrachloride, paracetamol or thioacetamide [10]. Preparations that contain B.S oleo gum resin reduce blood sugar in STZ-induced diabetic rats. In another study the root and leaf extracts of Boswellia glabra also reduced blood glucose levels in
Alloherbal combination of a synthetic drug Glimepiride and a Phytochemical Boswellic acid (BSE) by self-micro emulsifying drug delivery system concept. Therefore, the aim of the present investigation was to study the effect of Boswellic acid when given in combination with a novel glimepiride formulation.

Materials and Methods
Drugs and chemicals
Glimepiride was obtained as gift samples from Zydus life sciences (Ahmedabad, India), Micro Labs Limited (Mumbai, India) and Dr. Reddy's Laboratories Limited, Hyderabad, India. Boswellic acid extract were supplied by Gurjar Phytochem Pvt. Ltd. Indore. Aeroperl 300 was obtained as a gift sample from Evonic Pharma, Mumbai, India. Syloid XDP 3150 was obtained as a gift sample by Grace GmbH & Co. KG, Germany, Trancutol P by Gattefossé. The uric acid Kit is purchased from Beacon Diagnostic Pvt. Ltd, Navsari, India. Creatinine Kit, Blood urea nitrogen kit, and Total protein kit is obtained from Span Diagnostic Pvt. Ltd, Surat, India. Histopathology study has been performed in Gujarat Veterinary Research and Diagnostic Center, Ahmedabad.

Animals
Maintenance of animals
The project was approved by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and the Institutional Animal Ethics Committee K. B. Institute of Pharmaceutical Education & Research, Gandhinagar; Project no KBIPER /2021/638. Healthy female wistar rats weighing 180 to 250gm were selected and divided into 6 groups of 6 animals in each. This study has been carried out in, KB Institute of Pharmaceutical Education and Research Gandhinagar. The animals were housed in standard polypropylene cages and maintained under standard laboratory conditions (12:12 hr alternate light and dark cycle; at an ambient temperature of 22 ± 1°C; NMT 60% relative humidity). The animals were fed with a standard rat pellet diet and water ad libitum.

Grouping of normal and diabetic rats and pre-treatment
Rats were divided into 6 groups, each group containing six animals. The details of treatment for each group are mentioned in the below Table 1.

Table 1: Grouping of normal and diabetic rats and pre-treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control (normal saline)</td>
</tr>
<tr>
<td>II</td>
<td>STZ induced diabetic control with high fructose diet</td>
</tr>
<tr>
<td>III</td>
<td>STZ induced treated with standard glimepiride (1 mg/kg, b.w., p.o) and normal saline</td>
</tr>
<tr>
<td>IV</td>
<td>STZ induced treated with SMEEDS glimepiride formulation (1 mg/kg, b.w., p.o) and normal saline</td>
</tr>
<tr>
<td>V</td>
<td>STZ induced treated with SMEEDS Boswellic acid formulation (100 mg/kg and 200 mg/kg, b.w., p.o) in normal saline</td>
</tr>
</tbody>
</table>

Induction of diabetes in rats
Diabetes was induced by using Streptozotocin (35 mg/kg, b.w., i.p.) in 0.1M citrate buffer (pH 4.5). Citrate buffer was prepared by taking 0.5 g citric acid and 0.4 g dibasic sodium phosphate in 1000 ml water and pH adjusted using 0.1 N HCl/NaOH. After 72 hr, blood samples were collected from rats by retro-orbital puncture and the serum was analyzed for glucose levels. Animals with blood glucose levels >250mg/dL were considered diabetic and were used for the study. The marking of rats was carried out for better identification. Blood samples were collected from retro-orbital vein puncture using heparinised capillary tube sat 0, 15, 30, 60, 90 and 120 minutes. The serum was separated after centrifugation at 8000 rpm for 15 min and stored at-20°C until analysis [12].

Evaluation of various biochemical parameters in STZ-induced diabetic rats
Overnight fasted STZ-induced diabetic rats were divided into 6 groups (I-VI) same as mentioned above and they were treated once a day for 28days and their body weight, fasting blood glucose level, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum urea nitrogen, uric acid, serum cholesterol, serum triglyceride, serum total proteins were estimated. During the study period, the body weight of the animals and blood glucose levels were recorded after 0, 14 and 28 days of the treatment. SGOT, SGPT, serum cholesterol, serum triglyceride, serum total protein levels were estimated initial and 28 days of the treatment. Serum urea nitrogen and uric acid were recorded at end of study [13]. Levels of malondialdehyde (MDA), superoxide dismutase (SOD) and catalase (CAT) activity were measured in kidney homogenate at end of study [14].

Preparation of tissue homogenate
Rachappa Dhondiba Mahale, Dr. Vipul P Patel, Effect Of SMEEDS Formulation Of Glimepiride In Combination With Boswellic Acid Extract In Diabetic Induced Rats To Mimic Diabetic Complications

Reagents: Tris hydrochloride buffer (10mM, pH 7.4)
1.21 g Tris was dissolved in 900 mL of distilled water and the pH was adjusted to 7.4 with 1 M HCl and diluted to 1000 mL with distilled water.

Kidney was kept in cold Tris-HCl buffer (pH 7.4) and was cross-chopped with surgical scalpel into fine slices; the tissue was minced and homogenized in 10 mM Tris-HCl buffer at concentration of 10 % w/v with glass homogenizer at a speed of 2500 rpm. This homogenate was then placed in cooling centrifuge at 6000 rpm at -5 to -1°C for 20-25 minutes and are expressed with respective units. The clear supernatant was used for estimation of different antioxidant enzymes.

Lipid peroxidation assay (MDA)
Principle
Reactive oxygen species (ROS) attack on proteins, DNA and polyunsaturated fatty acids (PUFAs). Polyunsaturated fatty acids (PUFAs) are belonging to the class of lipid biomolecules. ROS Peroxidize PUFAs to finally generate malondialdehyde (MDA) and 4-hydroxy-2-nonenal (HNE). Lipid peroxidation may be enzymatic and non-enzymatic in nature.

Procedure
0.2 mL of tissue homogenate, 1.5mL of 20 % acetic acid, 0.2mL of sodium lauryl sulfate and 1.5mL of thiobarbituric acid were added. The volume of the mixture was made up to 4mL with distilled water and then heated at 95°C in a water bath for 60 min. After centrifugation at 3000 rpm for 10 min, the organic upper layer was taken and its optical density is recorded at 532 nm against an appropriate blank without the sample [14].

Calculation
The amount of malondialdehyde (MDA) was calculated using the following formula and expressed as nmol MDA/ mg protein using a nano molar extinction coefficient of 1.56 x 10⁵ M⁻¹.Cm⁻¹.

\[ \text{MDA (nmol/mg protein)} = \frac{(O.D.)_{\text{Test} \times \text{Total volume of reaction mixture}}}{1.56 \times 10^5 \times 10^{-8} \times \text{sample volume}} \times \frac{1}{\text{mg protein/ml}} \]

Statistical analysis
All values of pharmacokinetic and pharmacodynamic studies were expressed as mean ± SD. The data were statistically evaluated using one-way analysis of variance (ANOVA) followed by post hoc Dunnet’s t-multiple comparison tests using Graph Pad Prism software. Values corresponding to P≤0.05 were considered significant.

Result and Discussion
Oral glucose tolerance test (OGTT) in STZ-induced diabetic rats
STZ-induced diabetic rats were fasted overnight and divided into 6 groups (n=6). The effect of the marketed glimepiride formulation, Boswellic acid SMEDDS, Glimepiride SMEEDS alone and their combinations on fasting blood glucose level was studied up to 120 minutes. Blood samples were drawn from the retro-orbital plexus of the rats after overnight fasting at '0'(Initial fasting blood sample) followed by 50% glucose loading 2 ml/kg and blood sugar level measured for 15, 30, 60, 90 and 120 minutes after the treatment(Table 2).

Table 2: Effect of different formulations on blood glucose levels (mg/dl) at different time intervals

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Dose(mg/kg)</th>
<th>0 min</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
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<tbody>
<tr>
<td>Control</td>
<td></td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td></td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Marketed Glimepiride Formulation</td>
<td>1mg/kg</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
</tr>
<tr>
<td>Glimepiride SMEEDS</td>
<td>200mg/kg</td>
<td>139</td>
<td>144</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
<td>149</td>
</tr>
<tr>
<td>Boswellic acid SMEEDS</td>
<td>1mg/kg</td>
<td>135</td>
<td>146</td>
<td>147</td>
<td>147</td>
<td>147</td>
<td>147</td>
<td>147</td>
</tr>
<tr>
<td>Boswellic acid SMEDDS + Glimepiride SMEEDS</td>
<td>200 mg/kg + 1 mg/kg</td>
<td>129</td>
<td>146</td>
<td>146</td>
<td>146</td>
<td>146</td>
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<td>146</td>
</tr>
</tbody>
</table>

M ±SE = Mean ±Standard Error. N=6; *P<0.05; **P<0.01; ***P<0.001 when compared with control

In pharmacodynamic study, the mean serum glucose level and percentage glucose change at 60 minutes time interval found significant increase as compared to other time points for all groups. The data reveals that there is a maximum control on serum glucose level with respect to initial value, in combination of glimepiride SMEDDS and Boswellic acid SMEDDS, pre-treated groups (26%) increase, when compared to marketed glimepiride formulation (76%), control group (38 % increase) and diabetic group (85 % increase) respectively. The increase in hypoglycaemic action with concomitant administration of glimepiride SMEDDS and Boswellic acid SMEDDS was more in diabetic rats compared to alone treated drugs and with control group, which suggests that, there is an enhanced
impact on glucose reduction capacity of glimepiride SMEDDS in diabetic rats when given in combination with Boswellic acid SMEDDS (Figure 1).

**Figure 1**: Effect of different formulations on blood glucose levels (mg/dl) at different time intervals

**Body weight**

There was a gradual curtail in the bodyweight of animals in diabetic control group from initial to 28 days. The diabetic rats of marketed glimepiride formulation, GMP, BSE alone and GMP+BSE formulation combination with treated groups showed a gradual and significant increase in the body weight from 14 days onwards. The increase in the body weight was observed till the end of the study (28 days). The significant effect of the combination and alone pre-treated drugs on body weight of the animals was comparable to that of all formulations at each time interval of the study except diabetic control group (Figure 2). This significant improvement in body weight indicates the ability of combination of drugs and individual drugs to prevent loss of body weight in diabetic rats. It reveals that these drugs do not have any effect on degradation of depot fat to maintain the body weight as the effect is comparable with control and other groups [15].

**Serum SGOT & SGPT levels**

There is a significant effect of the combination of GMP and BSE SMEDDS in reducing serum glutamic-oxaloacetic transaminase (SGOT) and Serum glutamic pyruvic transaminase (SGPT) levels in diabetic pre-treated rats. There was 106.4% increase in SGOT levels in Diabetic control rat as compared to normal control rats where as in GMP+BSE SMEDDS combination shown only 21.9% and 35.5% in alone GMP SMEDDS formulation and 46.5% in marketed glimepiride alone formulation after 28 days respectively (Figure 3). There was a 98.0% increase in SGPT levels in Diabetic control rat as compared to normal control rats where as in GMP+BSE SMEDDS combination shown only 14.1% and 17.3% in alone GMP SMEDDS formulation and 51.7% in marketed glimepiride alone formulation after 28 days respectively(Figure 4). This indicates that there is very well control on SGOT and SGPT levels when in diabetic pre-treated rats in combination with GMP and BSE SMEDDS. This significant reduction in SGOT and SGPT levels further strengthens the antidiabetogenic effect of these drugs because increased gluconeogenesis and ketogenesis occur in diabetes, which may be due to high levels of SGOT and SGPT [16].

**Figure 2**: Effect of BSE, GMP formulation and marketed glimepiride formulation on body weights of STZ-induced diabetic rat

**Figure 3**: Effect of BSE, GMP formulation and marketed glimepiride formulation on Serum SGOT levels of STZ-induced diabetic rats
Rachappa Dhondiba Mahale, Dr. Vipul P Patel, Effect Of SMEEDS Formulation Of Glimepiride In Combination With Boswellic Acid Extract In Diabetic Induced Rats To Mimic Diabetic Complications

Figure 4: Effect of BSE, GMP formulation and marketed glimepiride formulation on serum SGPT levels of STZ-induced diabetic rats

Serum total protein
A significant effect found for the combination of GMP and BSE SMEEDDS in controlling serum total protein levels in diabetic pre-treated rats. There was 13.9 % reduction in serum total protein levels in Diabetic control rat as compared to normal control rats whereas in GMP+BSE SMEEDDS combination shown only 2.3 % and 6.5% in alone GMP SMEEDDS formulation and 9.5 % reduction in marketed glimepiride formulation as compared to normal control group after 28 days respectively(Figure 5). The well control in the reduction of serum total protein level brought out by these drugs SMEEDDS formulation reflects its antidiabetogenic effect as the reduction in protein level takes place in diabetes due to deficiency of insulin, which stimulates uptake of amino acids into muscle and increases protein synthesis[17].

Figure 5: Effect of BSE, GMP formulation and marketed glimepiride formulation on total serum protein levels of STZ-induced diabetic rats

Serum triglyceride & serum cholesterol levels
A significant effect found for the combination of GMP and BSE SMEEDDS in controlling serum triglyceride & serum cholesterol levels in diabetic pre-treated rats. There was 197.4 % increase in serum triglyceride levels in Diabetic control rat as compared to normal control rats whereas in GMP+BSE SMEEDDS combination shown only 103.0 % and 142.2 % in alone GMP SMEEDDS formulation and 147.6 % increase in marketed glimepiride formulation as compared to normal control group after 28 days respectively(Figure 6). There was 44.3 % increase in serum cholesterol levels in Diabetic control rat as compared to normal control rats whereas in GMP+BSE SMEEDDS combination shown only 6.2 % and 11.32 % in alone GMP SMEEDDS formulation and 22.1 % increase in marketed glimepiride formulation as compared to normal control group after 28 days respectively (Figure 7). These results of serum triglyceride levels and serum cholesterol levels clearly indicate that, combination of GMP and BSE SMEEDDS have more anti-hypertriglyceridemia and anti-hypercholesterolemic activity than alone pre-treated groups and with control group.

Figure 6: Effect of BSE, GMP formulation and marketed glimepiride formulation on serum triglycerides levels of STZ-induced diabetic rats

Lipid peroxidation and MDA absorbance
Reactive oxygen species (ROS) attacks on proteins, DNA and polyunsaturated fatty acids...
The polyunsaturated fatty acids (PUFAs) are belonging to the class of lipid biomolecules. ROS peroxidise PUFAs to finally generate malondialdehyde (MDA) and 4-hydroxy-2-nonenal (HNE). Lipid peroxidation may be enzymatic and non-enzymatic in nature. The combination of BSE, BA with glimepiride groups found gradually increased (p<0.01) in total antioxidant status when compared with BSE, BA, glimepiride alone pre-treated groups and with control group at all time intervals of the study. A significant effect found for the combination of GMP and BSE SMEDDS in controlling MDA absorbance in diabetic pre-treated rats. There was 120.5 % increase in MDA absorbance in Diabetic control rat as compared to normal control rats whereas in GMP+BSE SMEDDS combination shown only 52.3% and 62.3% in alone GMP SMEDDS formulation and 73.4 % increase in MDA absorbance marketed glimepiride formulation as compared to normal control group after 28 days respectively (Figure 8). This reflects that the combination of these drugs may stimulate the antioxidant mechanisms and interfere with PK and PD.

Figure 8: Effect of BSE, GMP formulation and marketed glimepiride formulation on MDA absorbance of STZ-induced diabetic rats

Uric acid
Serum uric acid level has been studied to evaluate impact of proposed unique formulation in diabetic pre-treated rats. There is a significant effect of the combination of GMP and BSE SMEDDS in reducing serum uric acid in levels diabetic pre-treated rats. There was 5.67 % increase in serum uric acid levels in diabetic control rat as compared to normal control rats whereas in GMP+BSE SMEDDS combination shown decrease of 9.8 % and increase of 0.7 % in alone GMP SMEDDS formulation and 1.5% in marketed glimepiride alone formulation after 28 days respectively (Figure 9).

Figure 9: Effect of BSE, GMP formulation and marketed glimepiride formulation on Serum uric acid levels of STZ-induced diabetic rats

Serum urea
A strong positive correlation between the serum urea levels in diabetic and non-diabetic rats. The mean (± S.D.) urea level in control group was found to be 48±11.6 whereas in for the formulations diabetics it was found to be 65.3±12.6, for GMP SMEDDS formulation 72.0±20.3, for marketed glimepiride alone 83.0±13.1 and for diabetic control group found as 100.8±22.7. For the diabetic control group there significant increase in serum urea i.e. 110 % as compared to control group and only 36.1 % increase found for proposed combination of GMP and BSE SMEDDS and for BSE SMEDDS found as 28.7%. Good control of blood glucose level helps to prevent progressive renal impairment and diabetic nephropathy is one of major cause of chronic renal failure. In order to prevent the progression of diabetes mellitus to diabetic nephropathy, vigilant monitoring of serum urea and creatinine are simple biomarkers available in patients with proteinuria if microalbuminuria screening test cannot be performed. We would like to conclude that blood urea and serum creatinine levels are simple tests helpful in diabetics who are poorly controlled to assess the renal function. The observed indicates that there is a very good control on serum urea for the proposed combination of GMP and BSE SMEDDS formulation helps to prevent diabetic nephropathy which cannot be controlled by alone glimepiride formulation (Figure 10).
Creatinine
Creatinine is a breakdown product of creatine phosphate in muscle and its clearance rate from blood to urine (CCr) correlates with glomerular filtration rate. A strong positive correlation found between the serum creatinine levels in diabetic and non-diabetic rats. Serum urea and blood urea nitrogen which are kidney function parameters were significantly increased in the diabetic group as compared to non-diabetic group, as compared with the control group. 95 % increase found in the serum creatinine levels in diabetic rats as compared to non-diabetic control rats group whereas only 68.5 % increase found in diabetic rats treated with combination of GMP and BSE SMEDDS (Figure 11).

SOD and catalase
Figure 12 considerably (p<0.01) decreased SOD level illustrates the liver's increased oxidative stress. Compared to the diabetic control group (58.55 ±5.01), oral supplementation with the marketed formulation (60.12±3.21) and the BSE formulation (58.55±5.01) significantly (p<0.05) increased SOD levels, indicating a better capacity to scavenge harmful reactive oxygen species. Especially the GMP and BSE combined formulation (65.46 ± 2.05) became closer to the normal control group (70.46 ± 1.02) than GMP formulation (63.25 ± 1.48) in regulating levels of SOD.

As shown in Figure 13, significantly (p < 0.01) decrease of catalase, illustrated the enhanced oxidative stress in liver. Oral supplementation of marketed formulation (24.21±1.30) and BSE formulation (23.25±1.92) resulted in significantly (p < 0.05) increase of catalase compared to the diabetic control (15.10±1.07). Especially the GMP and BSE combined formulation (26.32± 1.20) became closer to the normal control group (28.03±1.02) than GMP formulation (21.22±1.31) in regulating levels of catalase. The enzyme Superoxide dismutase (SOD) and Catalase (CAT) are the well known enzymes present in plasma which act as antioxidants by transforming reactive oxygen species and reactive nitrogen species into the stable compounds [18]. Antioxidants have been shown to prevent the destruction of cells [19] by inhibiting the peroxidation chain reaction.
and thus they may provide protection against the development of diabetes [20].

**Histopathology of kidney and pancreas**

- a. Kidney of normal control group showing intracytoplasmic golden-brown pigmentation
- b. Kidney of Diabetic group showing intracytoplasmic golden-brown pigmentation
- c. GMP Administered Kidney showing basophilic tubules and minimal thickening of bowmen capsules
- d. Kidney medulla of BSE-administrated group showing mineralization
- e. Kidney of GMP MF administered group showing basophilic tubules and minimal infiltration of mononuclear cells
- f. Kidney of animals with GMP and BS administered group showing intracytoplasmic golden brown pigmentation inline to control group.

**Figure 14: Histopathology of kidneys**

- a. Pancreas of normal control rats showing normal architecture
- b. Pancreas of the Diabetic control group showing minimal infiltration of mononuclear cells
- c. Pancreas of GMP administrated group showing normal architecture
- d. Pancreas of BSE administrated group showing mitotic figures
- e. Pancreas of GMP MF administered group showing normal architecture
- f. Pancreas group administered with GMP and BS showing mitotic figures.

The Glomerular hypertrophy occurs in diabetic nephropathy, hyper filtration occurs due to the enlargement of the glomeruli. The dimensions and size of renal glomeruli, glomerular area, mesenchymal matrix cells and glomerular basement membrane increases in diabetes, and a mild decrease occurs in size of parenchymal matrix. Microscopic slides of the kidney tissues demonstrates that the combination of Glimepiride and Boswellic acid novel formulation with good control of pharmacokinetic and Pharmacodynamic parameters have aid in the Protective effects against damage caused by diabetes. Boswellic acid can largely reduce the harmful effects of diabetes, that including lymphocytic inflammation in the port areas as that shown in alone treatment of glimepiride marketed formulations.

**Conclusion**

By lowering blood glucose, safeguarding renal functions and maintaining normal morphology, glimepiride and BSE SMEDDS treatment greatly decreased the pathogenic features of T2DN. The management of glycemic control, lipid metabolism, and anti-oxidative and anti-inflammatory capabilities may be related to the mechanism of action for this impact. This suggests that the unique combination will have a considerable effect on blood glucose level regulation and help to imitate long-term consequences of diabetes such nephropathy. The results of the current investigation suggested that BSE influences glimepiride metabolism, presumably via inhibiting CYP2C9. The effect of glimepiride on decreasing blood sugar is significantly increased when it is combined with BSE or BA. To prevent or manage diabetic long-term complications, glimepiride dosages may therefore need to be administered with additional care if herbal treatments containing BSE are also being used.

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References