Ethanolic Leaf Extract of Gymnema sylvestre Ameliorates Hyperglycemia and Pancreatic Oxidative Stress in Alloxan induced Diabetic Rats

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Abstract

Diabetes mellitus (DM) is a serious metabolic disorder with altered carbohydrate, fat, and protein metabolism. In the last four decades, India has emerged as an epicenter of the global diabetes mellitus pandemic. Rapid changes in the developmental scenario, demographic changes, and living style in the Indian subcontinent have led to the explosive increase in diabetes. Present research probes with ethanolic extract of Gymnema sylvestre (500 mg/kg.b.w) for treatment of hyperglycemia and related oxidative stress caused by Alloxan (100 mg/kg.b.wt), as a diabetogenic agent. 25 rats were included in the research divided into 5 groups, each containing 5 rats. Group 1 (normal rats), Group II (Diabetic rats (DM), Group III (DM+ treated for 10 days), Group IV (DM+20 days treated), Group V (DM+30 days treated). Blood samples and pancreatic tissues were collected at each interval of time. The blood sample was used for biochemical parameter and tissues were used for the anti-oxidant assay. Gymnema sylvestre extract (GSE) showed glucose-lowering property meanwhile, insulin secretion also increased as compared to Diabetic rats. Other tests like amylase, lipase, ALT, and AST also showed significant recovery after the extract administration. Oxidative stress was found in the Diabetic group, but after extract treatment concentration of superoxide dismutase, Glutathione-S-transferase, catalase, Glutathione peroxidase, Glutathione, and Total thiol was regained. Imbalance in serum electrolyte recovered and dysregulated hematological parameters due to stress and hyperglycemia showed convincing results. The finding suggests Gymnema sylvestre could be used as a hypoglycemic as well as an anti-oxidant agent in diabetes.

Key Words: Diabetes, Gymnema sylvestre, Anti-oxidant, Hyperglycemia, Acute pancreatitis, Alloxan.

Introduction

Diabetes mellitus is a serious metabolic disorder with altered carbohydrate, fat, and protein metabolism. There are currently 425 million people with diabetes worldwide, and this number is expected to reach 629 million by 2045, with type 2 diabetes (T2DM) being the most expressive form of the disease (1, 2).

India ranks second after China with highest number of people suffering from this epidemic globally with another serious prevalent shifting from urban to rural and from older to younger age group (3).

High glucose concentration also promotes advanced glycosylated end products (AGEs). These AGEs in association with persistent hyperglycemia stimulates free radical, and reactive oxygen species (ROS) formation. Oxidative stress has a significant role in further complications of type 2 Diabetes Mellitus. An increase in ROS level leads to elevated or dysregulated production of antioxidants like catalase, superoxide dismutase, glutathione peroxidase, glutathione, and Total thiol was regained. Imbalance in serum electrolyte recovered and dysregulated hematological parameters due to stress and hyperglycemia showed convincing results. The finding suggests Gymnema sylvestre could be used as a hypoglycemic as well as an anti-oxidant agent in diabetes.

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deregulated amylase and lipase concentration is prevalent due to this inflammatory response (7, 8).

Treatment with the synthetic drug is confined to mono target site and the market is flooded with such synthetic drugs. In such condition herbal remedy for the diabetes has been a consistent, less expensive and alternative method over existing synthetic drugs (9). The positive outcome of the phytomedicines with low cost and negligible side effect has revolutionized the drug discovery concept and diabetes management strategies (10).

Gymnema sylvestre is one such herb which shows tremendous hypoglycemic properties with remarkable antioxidant potential. It belongs to Asclepiadaceae family predominantly found in India, China, Australia, and Africa. Its popular name is “gurmar” due to its glucose lowering property. Gymnema sylvestre is considered as a prominent botanical for diabetes management since Ayurvedic era (11).

**Materials and methods**

For the present research work healthy wistar rats (Rattus norvegicus) of weight ranging from 180-200 gm were selected and provided ambient physical and physiological condition as per the standard protocol and all the experimental protocol was carried based on the guideline adopted by Mahavir Cancer Sansthan ethical comittee, Phulwarisariff Patna.

**Plant materials**

Dried leaves of Gymnema sylvestre.

**Preparation of ethanolic extract**

The dried plant materials i.e., leaf of Gymnema sylvestre blended to fine powder and then soaked with absolute ethanol and kept in dark to avoid from light for 48 hours in order to get the secondary metabolites dissolved in to the solvent. After 48 hours extract was filtered till the clear material appeared. The solvent containing secondary metabolite of both the plant was mounted on the vaccuma rotary evaporator at 40°C. The extract was kept on the vaccuma rotary till the thick paste was not appeared devoid of any solvent material. The colloidal paste was lyophillysed in lyophyliser (Labconco, USA) and was stored in deep freezer at -80°C until further use.

**Experimental Design**

Male healthy rats were utilized for the experimental work divided into five groups namely Normal control, Diabetic control, extract fed for 10 days, extract fed for 20 days, and extract fed for 30 days respectively. Each groups contained five rats. Normal rats were retained on the normal diet without extract. Except normal, all the rats were made diabetic and only those rats were considered for the experimental group which persisted diabetic condition after 10-12 days of Alloxan induction. After subsequent interval of the time different types of sample were collected for various tests.

**Induction of diabetes**

Diabetes was induced by repeated dose of Alloxan monohydrate 100 mg/kg. b.wt in cold citrate buffer bearing pH 4.5.

**Sample collection**

After the treatment of the extract for 10, 20, and 30 days respectively the tissues collected were for anti-oxidant quantification. For anti-oxidant analysis the tissue sample were subjected to preparation of post mitochondrial supernatant (PMS).

**Biochemical estimation**

Biochemical estimation includes plasma glucose (Glucose oxidase/peroxidase method by using systronic UV, Visible Spectrophotometer 119, India) (12), Serum insulin by ELISA (Robonik, Readwell Touch™, Automatic ELISA plate analyser, India), serum amylase (Direct Substrate Method) (13), serum lipase ( Turbidometric U.V. Method) (14), serum electrolyte by flame photometry (systronic 128, Ahmedabad, India), Alanine aminotransferase (ALT) Reitman and Frankel method and Aspartate aminotransferases (AST) Modified IFCC method.

**Hematology estimation**

Hematology estimation include Total RBC by using hayem’s fluid, Total WBC, Hemoglobin (Cyanmethemoglobin method) (15), and differential count using polychromic solution containing Gention violet and Eosin manually by smear preparation.

**Antioxidant enzyme estimation**

Antioxidant parameters were carried out by the published standard literature like Estimation of Catalase was done by (16), estimation of total reduced Glutathione (GSH) (17), estimation of Glutathione Peroxiase (18), estimation of Glutathione-s-transferase by (19), and quantification of Superoxide dismutase (SOD) (20).

**Statistical Analysis**

Statistical analysis was done using Prism graph pad 3.0 software. Data are represented as mean ± SD. Differences between groups were assessed using one way analysis of variance (ANOVA) followed by Tukey multiple range test, compared with entire column. Level of significance were expressed as, *indicates P < 0.001, †P< 0.01, ‡P <0.05, and §P >0.05 non-significant.
Results

Table I. Effect of Gymnema sylvestre (GSE) 500mg/kg.b.wt on fasting plasma glucose and serum insulin

<table>
<thead>
<tr>
<th></th>
<th>Glucose (mg/dl)</th>
<th>Insulin (µIU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>97.80±5.63 a</td>
<td>8.22±0.58 a</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>328±18.23 a</td>
<td>2.37±0.48 a</td>
</tr>
<tr>
<td>Diabetic + 10 Days GSE</td>
<td>276±20.74 b</td>
<td>3.74±0.2 b</td>
</tr>
<tr>
<td>Diabetic + 20 Days GSE</td>
<td>203±24.39 a</td>
<td>4.98±0.81 a</td>
</tr>
<tr>
<td>Diabetic + 30 Days GSE</td>
<td>153±15.25 a</td>
<td>6.79±0.85 a</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P < 0.01, c P < 0.05, and d P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table II. Effect of Gymnema sylvestre (GSE) 500mg/kg.b.wt on pancreatic enzymes Serum amylase and lipase

<table>
<thead>
<tr>
<th></th>
<th>Amylase (U/L)</th>
<th>Lipase (U/L)</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>80.80±10.33 a</td>
<td>37.01±9.62 a</td>
<td>33.0±3.31 a</td>
<td>35.80±5.65 a</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>350.0±23.02 a</td>
<td>170.0±11.51 a</td>
<td>125.4±10.74 a</td>
<td>115.4±10.74 a</td>
</tr>
<tr>
<td>Diabetic + 10 Days GSE</td>
<td>318.0±14.83 b</td>
<td>146.0±17.10 c</td>
<td>98.20±12.81 b</td>
<td>108.8±10.66 a</td>
</tr>
<tr>
<td>Diabetic + 20 Days GSE</td>
<td>268.0±11.51 a</td>
<td>118.0±16.81 a</td>
<td>75.80±65.3 a</td>
<td>90.50±9.68 b</td>
</tr>
<tr>
<td>Diabetic + 30 Days GSE</td>
<td>184.0±9.61 a</td>
<td>91.0±9.61 a</td>
<td>61.0±6.51 a</td>
<td>75.00±5.7 c</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P < 0.01, c P < 0.05, and d P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table III. Effect of Gymnema sylvestre (GSE) 500mg/kg.b.wt on Superoxide, Glutathione, and Catalase

<table>
<thead>
<tr>
<th></th>
<th>Superoxide Dismutase (SOD) (U/ml)</th>
<th>Glutathione (GSH) (mg/mL)</th>
<th>Catalase (CAT) (mU/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>9.51±0.90 a</td>
<td>17.30±1.85 a</td>
<td>9.27±1.21 a</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>4.25±0.45 a</td>
<td>7.67±0.66 a</td>
<td>2.42±0.43 a</td>
</tr>
<tr>
<td>Diabetic + 10 Days GSE</td>
<td>4.88±0.39 a</td>
<td>9.38±1.40 d</td>
<td>3.26±0.37 d</td>
</tr>
<tr>
<td>Diabetic + 20 Days GSE</td>
<td>5.84±0.38 a</td>
<td>12.44±1.07 a</td>
<td>4.73±0.29 a</td>
</tr>
<tr>
<td>Diabetic + 30 Days GSE</td>
<td>7.54±0.19 b</td>
<td>14.89±1.40 a</td>
<td>6.89±0.49 b</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P < 0.01, c P < 0.05, and d P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table IV. Effect of Gymnema sylvestre (GSE) 500 mg/kg.b.wt on Glutathione peroxidase, Glutathione-S-transferase, and Total thiol.

<table>
<thead>
<tr>
<th></th>
<th>Glutathione (GPx) (nmol/NADPH oxidized/min)</th>
<th>Peroxidase (µmol of GSH consumed/mg protein/min)</th>
<th>Total Thiol (nmol/NADPH oxidized/ min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>5.63±0.52 a</td>
<td>1.90±0.15 a</td>
<td>5.16±0.69 a</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>1.78±0.39 a</td>
<td>0.79±0.07 a</td>
<td>1.31±0.21 a</td>
</tr>
<tr>
<td>Diabetic + 10 Days GSE</td>
<td>2.67±0.46 c</td>
<td>0.94±0.04 d</td>
<td>2.33±0.19 b</td>
</tr>
<tr>
<td>Diabetic + 20 Days GSE</td>
<td>3.61±0.33 a</td>
<td>1.28±0.12 a</td>
<td>3.45±0.22 a</td>
</tr>
<tr>
<td>Diabetic + 30 Days GSE</td>
<td>4.22±0.37 a</td>
<td>1.68±0.11 c</td>
<td>4.22±0.48 a</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P < 0.01, c P < 0.05, and d P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table V. Effect of Gymnema sylvestre on the status of serum electrolyte in treated and non treated groups.

<table>
<thead>
<tr>
<th></th>
<th>Sodium (mmol/L)</th>
<th>Potassium (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>142.2±3.19 a</td>
<td>4.08±0.3 a</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>131.0±2.23 a</td>
<td>5.28±0.19 a</td>
</tr>
<tr>
<td>Diabetic + 10 Days GSE</td>
<td>134.04±3.20 a</td>
<td>4.97±0.12 a</td>
</tr>
<tr>
<td>Diabetic + 20 Days GSE</td>
<td>137. 0±2.7 a</td>
<td>4.7±0.15 a</td>
</tr>
<tr>
<td>Diabetic + 30 Days GSE</td>
<td>140.4±2.19 a</td>
<td>4.35±0.17 a</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P < 0.01, c P < 0.05, and d P >0.05 non- significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.
Table VI. Effect of Gymnema sylvestre on the status of RBC, Hb, and WBC in treated and non treated groups.

<table>
<thead>
<tr>
<th></th>
<th>Normal Control</th>
<th>Diabetic Control</th>
<th>Diabetic + 10 Days GSE</th>
<th>Diabetic + 20 Days GSE</th>
<th>Diabetic + 30 Days GSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Erythrocyte (million/mm3)</td>
<td>5.9±0.20 a</td>
<td>4.35±0.28 a</td>
<td>4.64±0.29 d</td>
<td>4.93±0.20 c</td>
<td>5.28±0.22 a</td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>14.95±0.28 a</td>
<td>12.38±0.24 a</td>
<td>13.30±0.33 a</td>
<td>13.69±0.27 a</td>
<td>14.16±0.21 a</td>
</tr>
<tr>
<td>Total Leucocyte (thousand/mm³)</td>
<td>6.48±0.16 a</td>
<td>8.24±0.23 b</td>
<td>7.80±0.35 d</td>
<td>7.46±0.30 a</td>
<td>7.03±0.16 a</td>
</tr>
<tr>
<td>Lymphocyte (%)</td>
<td>45.0±4.12 a</td>
<td>58.0±2.55 a</td>
<td>54.60±2.79 d</td>
<td>51.40±2.70 c</td>
<td>49.00±3.08 b</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P< 0.01, c P <0.05, and d P >0.05 non-significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Table VII. Effect of Gymnema sylvestre on the status of differential leukocyte count in treated and non treated groups.

<table>
<thead>
<tr>
<th></th>
<th>Normal Control</th>
<th>Diabetic Control</th>
<th>Diabetic + 10 Days GSE</th>
<th>Diabetic + 20 Days GSE</th>
<th>Diabetic + 30 Days GSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil (%)</td>
<td>51.40±2.40</td>
<td>42.20±1.92</td>
<td>43.80±1.48</td>
<td>47.0±1.58</td>
<td>50.0±1.58</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>1.0±0.70</td>
<td>1.80±0.83</td>
<td>2.80±0.83</td>
<td>3.40±0.54</td>
<td>2.40±0.89</td>
</tr>
<tr>
<td>Basophil (%)</td>
<td>0.50±0.54</td>
<td>0.50±0.54</td>
<td>1.0±0.63</td>
<td>1.0±0.63</td>
<td>0.66±0.51</td>
</tr>
<tr>
<td>Monocyte (%)</td>
<td>0.83±0.40</td>
<td>0.50±0.54</td>
<td>0.66±0.51</td>
<td>1.0±0.63</td>
<td>1.0±0.89</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (Standard Deviation); *indicates P < 0.001, b P< 0.01, c P <0.05, and d P >0.05 non-significant. One-way ANOVA was performed followed by Tukey multiple range test, compared with entire column.

Discussion

Recent reports of chemotherapeutics resistant in treatment of diabetes mellitus have forced the research community to look towards nature for the better remedy and hence the herbal drugs are emerging as a future hope in control of diabetes mellitus. The present study involved Gymnema sylvestre with the same intention. Considering this in view, a comprehensive study involving various anti-oxidative, biochemical, and hematological parameters was probed and validated.

Plasma blood glucose level plays a vital role in complications associated with diabetes like renal, eye, neurological damages. Contributors of the complications in diabetes are glycosylation of biomolecules, increased cellular oxidative tension, serum osmolality etc. In the present study, reduction in blood glucose concentration was achieved (56.4%) (p<0.001) after administration of phytochemical extracts on the 30th days. Decrease in blood glucose level (65%) was associated with enhanced insulin (p<0.001) (Table I) production and alleviation of oxidative stress. Insulin is the primary hormone involved in the regulation of blood glucose level. Alloxan induced diabetic rats showed nearly (71.11%) (p<0.001) (Table I) decrease in insulin level. Significant recovery in insulin level was observed after 30 days of administration of phytochemical extracts. The results corroborate with previous findings (21).

Increased concentration of amylase and lipase in the present investigation in diabetic subjects beyond 3 times (p<0.001) the normal rats indicates the condition of acute pancreatitis as per the Atlanta classification (22-24) after administration of the ethanolic herbal extract (500 mg/kg.b.wt) the normalization of the enzyme concentration to 2.09 times (p<0.001) and 2.21 times (p<0.001) (Table II) of amylase and lipase indicates amelioration of excessive oxidative stress, ischemia, and necrosis (25). Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) are the most commonly used indicators of cell necrosis led ischemia, toxicity, and its elevation is due to leaking from the hepatic cell (26). Diabetic subjects showed mild increase in ALT (3.78 times) and AST (3.22 times) (Table II) the control value. Ethanolic extract of Gymnema sylvestre brought significant recovery in the concentration of transaminases to a significant level. Recovery in ALT and AST indicates ameliorative property of extract in overcoming the necrosis caused by the oxidative stress due to prolonged hyperglycemia (27).

Superoxide dismutase (SOD) enzyme plays a significant role in cellular enzymatic defense system. SOD activity in diabetic rats significantly decreased by 55.3% (p<0.001) when compared with that in normal rats. Ethanolic extract administration rescued the concentration of superoxide dismutase to 48.38% (p<0.01) as compared to the diabetic rats. The results obtained are in agreement with previous studies (28). Hyperglycemia is usually concerned with metabolic disturbances affecting cellular redox potential, particularly, imbalanced NADPH/NADP+ ratio and reduced glutathione levels (29). The present study evidences decreased glutathione level to 55.31% (p<0.001) in diabetic group. Rats fed with the Gymnema sylvestre herbal extract restored the Glutathione level to 43.3% (p<0.001) (Table III) as compared to the diabetic groups (30).

Catalase is essential for scavenging the voluminous and toxic hydrogen peroxide in the biological system (31). Diabetic rats registered 73.89% (p<0.001) decrease in the catalase activity as compared to normal control but upon extract administration it regained concentration to 64.87% (P<0.01) (Table III) as compared to diabetic rats. This restoration of the enzyme suggests ameliorating properties of the extract.
against inflammation, apoptosis, and necrosis caused by hyperglycemia and oxidative stress (32).

Glutathione peroxidase (GPx) plays a remarkable role in the reduction of lipid and hydrogen peroxides (33). Diabetic rats represented 68.38% reduction (P<0.001) in the GPx activity addresses increased hydrogen peroxide and tissue damage by activation inflammation by various molecular pathways (34). Increased peroxide stress was reduced to 57.81% (P<0.001) (Table III) on the 30th days of extract administration as compared to the diabetic control. Glutathione-S-transferase (GST) counteracts with reactive oxygen species (ROS) by enzymatic conjugation with glutathione (GSH) (35). There was 58.42% (P<0.001) decrease in glutathione S transferase enzyme in diabetic controlled rats while after treatment the concentration in context to diabetic group was increased to 52.97% (P<0.05) (Table IV). Thiol/disulfide homeostasis plays important vital roles in detoxification, antioxidant protection, and regulation of enzymatic activity and transcription factors, apoptosis, and cellular signal mechanisms (36). Total thiol registered 68.95% (p<0.01) recovery after 30th day of extract administration against diabetic group with marked 74.1% (p<0.001) (Table IV) decrease in Total thiol concentration. The results were in congruence with (37).

Oxidative stress mediates inflammation and apoptosis in pancreatic tissues which is reflected by altered anti-oxidative enzymes. Alleviation of inflammation and apoptosis in diabetic rat pancreatic tissue was a result of extract, resulted in balanced anti-oxidative enzyme and reduced oxidative stress (38).

Decrease in the sodium ion (7.87%) (p<0.001) concentration was noticed in diabetic group; it was either due to intestinal malabsorption or due to excessive excretion in urine which registered decreased serum sodium concentration however the value was maintained to the normal range after the herbal extract administration. Potassium ion being stable was little increased (29.41%) (p<0.001) (Table V) but it is normal range in diabetic condition however this increase was insignificant and it doesn’t give any reason to reach to any pathological condition but it was restored after extract administration.

RBC in diabetic rats was lying in the normal range but towards the lower extreme. The reason behind decrease in the RBC count may be its membrane modification and reduced Na+K+ATPase activity and high lipid peroxidation of the RBC membrane (39). Herbal extract administration led to the normalization of the same. This recovery was due to availability of ATP to the membrane and thus increased Na+K+ATPase activity to the cell which led to increased cell viability along with reduced peroxide stress and this finding can be correlated with results of (40).

Present research registered elevated WBC (27.16%) (p<0.01) count in diabetes which might be due excess fat storage, and low-grade inflammation [40]. Treatment with Gymnema sylvestre led to normalization of the WBC. Reduced hemoglobin (17.19%) (p<0.001) (Table VI) concentrations are the

common findings in diabetic condition. Study on the Alloxan induced diabetic rats were represented with lower hemoglobin, the present study correlates with (41). Challenged oxidative enzyme (Catalase) pertaining oxidative stress also mediates low hemoglobin in diabetic state (42). Ethanolic herbal extract of Gymnema sylvestre regained the normal level due to restoration of anti-oxidative enzyme.

The Lymphocyte and Neutrophil count was assessed in the all group to investigate the wellness of the rats during diabetic states. Slight increase in the lymphocyte and Neutrophil count was noticed in diabetic as compared to normal control.

Monocytes, Basophil, and Eosinophil are the other differential leukocyte cells. In the present research work neither diabetic rats showed any impact nor the treated group showed any significant result (p>0.05) (Table VII) regarding alteration in these parameters however there are certain evidences which supports connection of the diabetic complication with the mentioned parameters need to be probed and evaluated on a large sample size.

**Conclusion**

Diabetes is a multifactorial disorder which couldn’t be controlled by synthetic drugs which are single target specific. Alternate and complementary medicine in the form of phytochemical has gained attention of the entire research community. Present study showed hypoglycemic properties of Gymnema sylvestre extract (GSE) by decreasing glucose concentration and increased insulin production. This was probably due to histioarchitectural remodeling of pancreatic tissue which can be evidenced by decreased oxidative load in the tissues. Antioxidative properties were more convincing in the pancreatic tissue. Restoration of pancreatic juices like amylase and lipase was little convincing which needs to be validated on a large sample size. Restoration of ALT and AST to an extent indicated hepatoprotective nature of extract. However the hematological study suggests fluctuation of RBC, WBC, Hb, and lymphocyte due to hyperglycemia and oxidative stress. Other differential cells didn’t impacts more because they didn’t show any significant alteration.

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**Conflict of interest**

Authors declare no conflict of interest regarding publication or any other activity related to this article.

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