Hypoglycemic and Biochemical Effects of some Medicinal Plant Extracts on Alloxan Induced Diabetic Rats

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Abstract: Hypoglycemic and biochemical effects of some mixed medicinal plant extracts were tested on alloxan diabetic rats. The studied extracts were a mixture of Ambrosia maritima, Trigonella-foenum Graecum, and Centaurium - Spicatum, (extract 1), Lupinus albus, Nigella sativa and Gum arrabia (extract II) and Aloe-Ferox and Peganum-harmala (extract III). The hypoglycemic activity of the plant extracts was compared with the hypoglycemic effect of the synthetic drug substance repaglinide [NovoNorm tablets 2 mg repaglinide (Novo Nordisk)]. Male albino rats of the Sprague-Dowely strain weighing about 100 gram were used in the present study and blood samples were collected at zero time (before treatment) and then after 6, 12 and 24 hours from treatment. Blood samples were subjected to biochemical analyses such as blood glucose, liver function, kidney function and lipid profile. Extract 1 exhibited the higher hypoglycemic activity, while extracts II and III induced the lower hypoglycemic activity. The abnormal increase in the mean values of creatinine, urea, aspartate-aminotransferase (AST), alanine-aminotransferase (ALT), triglycerides (TG) and total cholesterol in the induced diabetic rats was greatly improved by each of the three plant extracts.

Keywords: Medicinal plant, Hypoglycemic, Transaminase, Repaglinide

1. Introduction

Diabetes has been well known as a wasting disease due to insulin deficiency in human. The ancient Indian literature of the prechristian era have distinctly recorded the most important symptoms of this disease. Some of the earlier workers mentioned the use of herbal and mineral preparations for treatment of this disease. It was found of 42 plants which are considered to be useful in treatment of diabetes (1).

Thus medicinal plants continue to provide valuable therapeutic agents, both in modern and traditional medicine (2 – 5). Noteworthy most of the plants and herbs are rich in the fiber content which is responsible for their hypoglycemic effect, therefore, the addition of certain forms of dietary fibers to the diet of diabetic subjects significantly decreased post-prandial hyperglycemia and is expected to improve and control the blood glucose concentration (6).

It is indicated that, the lactuavirosal (lebbin), Aloe (sabir), Ambrosia maritima (Damsisa), Geranum robertinanum L, (requemoya) and Myrrh exerted an obvious hypoglycemic effect after treatment of the alloxan diabetic rats (7, 8).

They are found that, Trigonella-foenium graecum prevented glucosurea in mild diabetes and improved sever diabetes in human. Despite of the hypoglycemic effect of fenugreek seeds and their major alkaloid trigonilinone, there has been a renewed interest in these seeds (9, 10). A considerable medical interest exists in the use of volatile oil extracted from Nigella sativa producing a significant consistent decrease of blood glucose level in alloxan-diabetic rats (11, 12).

Our study is planned to examine the new hypoglycemic agents from natural products, hopefully to minimize the side effects and improve the diabetic condition.

2. Material and methods

1) Experimental animal

In the present study 112 of albino male rats weighing about 100 gm were obtained from the animal house of the Assuit university. The rats were housed in cages with eight animals each at random. They were given the regular laboratory stock diet and evaluated after overnight fasting for the pre-dose blood analysis of glucose, total proteins, urea, creatinine, aspartate-aminotransferase (AST), alanine-aminotransferase (ALT), triglycerides and total cholesterol using standard analytical methods. The analysis of these compounds was also performed in all rats at the end of seven days from the treatment. The rats received a single subcutaneous injection of 40, 80, 120 and 140 mg alloxan per kg body weight separately, each in 0.2 ml saline solution respectively. The blood glucose level of each rat was estimated at intervals of 1, 2 and 3 days. Another four groups received a single intragastric intubation dose of 1.5 ml from plant extract I, extract II, extract III and NovoNorm tablets (2 mg Repaglinide). The blood glucose levels were measured both prior to the introduction of the dose and after 6, 12 and 24 hours.

2) Plant extracts

Three plant mixture were prepared; (5 gm seeds dry weight) from each examined plant in the mixture of Ambrosia maritima (Damsisa), Trigonella-foenum Graecum (Hulba), and Centaurium – Spicatum (Hashishet el acrab), (extract 1), Lupinus albus (Termis), Nigella sativa (Habet elbara) and Paswella carterii (Gum arrabbia) (extract II) and Aloe-Ferox (Sabir) and Peganum-harmala (Harmal) (extract III). Each plant was finely ground then the prepared mixtures were separately boiled with distilled water (100 ml) for 10 minutes.
3) Blood samples
They were collected at zero time (before treatment) and then 6, 12 and 24 hours after the treatment. Blood samples were subjected to biochemical analysis concerning blood glucose, liver function, kidney function and lipid profile.

4) Biochemical examinations

A two way analysis variance (ANOVA) was calculated according to Mason (1976) (20) for testing the significance of difference between various treated groups.

5) Statistics
Results are represented as mean ± standard deviation (S. D). A two way analysis variance (ANOVA) was calculated according to Mason (1976) (20) for testing the significance between various treated groups.

3. Result and Discussion

The present data demonstrate that, the subcutaneous injection of rats with 40 or 80 mg alloxan /kg body-weight was not enough to induce diabetes in these rats and their blood glucose levels were within normal range (92±6.1 mg/dl) and (110±4.2 mg/dl) respectively, while the injection of rats with 120 mg alloxan/kg body-weight lead to a moderate diabetic rats (240±6.1 mg/dl) (Table 1). These results are in agreement with those reported data before who used 120 mg/kg body weight to produce moderate diabetic rats (268 mg/dl, 238 mg/dl and 270 mg/dl, respectively). Injection with 140 mg alloxan /kg body weight led to a severe diabetic rats (410 mg/dl) and the rats were died within four days (21, 22, 23).

Extract 1 induced the higher hypoglycemic activity after 24 hours (167±4.5 mg/dl). While Extracts II and III exhibited lower hypoglycemic activity Table (2).

There was a significant increase in the mean value of serum creatinine (3.6±0.5 mg/dl), urea (98.6±4 mg/dl), AST (82.6±7 U/ml), ALT (76.4±5 U/ml), triglycerides (236.1±11 mg/dl) and total cholesterol (280.3±11 mg/dl) of the diabetic rats as compared with the normal rats (Table 3). These results were compatible with those who found that the liver was necrotized in alloxan diabetic rats. This supports the view that the hypoglycemic phase of alloxan poisoning may be the result of liver damage. Therefore the high levels of transaminase enzymes found in this study may be due to hepatotoxic effect of alloxan (8, 24).

On the other hand, serum from rats treated by extracts I; II and III showed significant decrease in the mean values of creatinine (1.06±0.08, 1.11±0.1, 1.13±0.2 mg/dl), urea (55.4±6, 58.1±6, 61.3±5 mg/dl), AST (43.2±4, 54.1±4, 56.2±5 U/ml), and ALT (48.4±2, 53.4±4, 52.2±8 U/ml). After treatment with herbal extracts and repaglinide (synthetic drug), a clear improvement in the triglycerides and total cholesterol levels was recorded (Table 3).

Many natural products are promoted to improve the health status of patients with diabetes. The results concerning the effect of extracts of the plants under study on blood glucose of alloxan induced diabetic rats are in agreement with those of found that the presence of sesquiterpene lactones in damsisa act as a hypoglycemic agents (7, 25). Also it was reported that Ambrosia maritima extracts produced significant hypoglycemic effect on the diabetic rats due to the presence of the sesquiterpene lactones, damsin, ambrosin, hymenin as well as umbelliferone and flavonoids (27). Furthermore, they found that damsisa increased the level of serum insulin in the diabetic rats (8).

They are found that the Aloe forex significantly reduce blood sugar levels in diabetic rats and increased the levels of serum insulin in the same rats due to the major constituents of alkaloids, nicotinic acid, coumarine and scopletin (7, 8).

Trigonella-foenum graecum seeds exert mild and transient hypoglycemic effect. Also it was noticed that, Trigonella prevents glucosuria in mild diabetes and improves sever diabetes in human (28). It described the hypoglycemic effect of Trigonella seeds which may be due to their major alkaloid trigonillin, and suggested the, antidiabetic effect of Trigonella may be due to, at least in part, to intestinal glucosidase inhibition. Also, it proved that the addition of 4-hydroxyisoleucine extracted from Trigonella seeds on isolated rat pancreas in the presence of 8.3 mM glucose increased the secretion of insulin (29, 30, 31).

Lupinus albus was found to decrease the blood glucose levels of rats. The hypoglycemic effect of Lupinus albus is due to its content of alkaloids which also significantly impaired the protein utilization (25, 7).

The present study revealed that the effect of (extract 1), (extract II) and (extract III) showed a significant hypoglycemic effect as shown in Table (2), when administered orally to alloxan induced diabetic rats.

<p>| Table 1: Effect of alloxan on the glucose level of the tested normal rats |
|-----------------|-----------------|-----------------|-----------------|
| Mean Glucose levels in normal rats (mg/dl) | Alloxan dose (mg/kg Body Weight) | Mean Blood glucose levels in normal rats (mg/dl) after injection of alloxan |</p>
<table>
<thead>
<tr>
<th></th>
<th>1 day</th>
<th>2 days</th>
<th>3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>85±1 (8)</td>
<td>40</td>
<td>92±6.1</td>
<td>110±6.2</td>
</tr>
<tr>
<td>79±6.7 (8)</td>
<td>80</td>
<td>110±2.3</td>
<td>116±6.2</td>
</tr>
<tr>
<td>84±3.5 (8)</td>
<td>120</td>
<td>240±5.1</td>
<td>255±3.1</td>
</tr>
<tr>
<td>88±4.1 (8)</td>
<td>140</td>
<td>385±7.1</td>
<td>395±6.2</td>
</tr>
</tbody>
</table>

Result Mean ± S.D
*Significant p < 0.05
(8) Number of rats in each group
Table 2: Effect of plant extracts and repaglinide on the blood glucose levels of the alloxan induced diabetic rats

<table>
<thead>
<tr>
<th>Tested Treatment</th>
<th>Glucose levels in normal rats (mg/dl)</th>
<th>Glucose levels in control diabetic rat (mg/dl)</th>
<th>Mean glucose levels of alloxan induced diabetic rats after treatment mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extract I</td>
<td>87±6.2</td>
<td>245±9</td>
<td>195±3 180±7.1 167±4.5</td>
</tr>
<tr>
<td>Extract II</td>
<td>84±3.4</td>
<td>255±8</td>
<td>233±8 202±9.2 175±6.5</td>
</tr>
<tr>
<td>Extract III</td>
<td>78±7.1</td>
<td>248±6</td>
<td>238±3 205±11 185±7.4</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>86±5.2</td>
<td>257±2</td>
<td>199±5 190±8.1 180±6.5</td>
</tr>
</tbody>
</table>

Table 3: Effect of treatment with plant extracts and repaglinide on the concentration of total protein, urea, creatinine, AST, ALT, triglyceride and cholesterol of the alloxan induced diabetic rats

<table>
<thead>
<tr>
<th>Total proteins mg/gm</th>
<th>Urea mg/dl</th>
<th>Creatinine mg/dl</th>
<th>AST U/ml</th>
<th>ALT U/ml</th>
<th>Triglycerides mg/dl</th>
<th>Total Cholesterol mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal rats</td>
<td>125.4±4.5</td>
<td>28.2±1.5</td>
<td>0.52±0.45</td>
<td>23.4±3</td>
<td>28.8±3</td>
<td>116.4±5.7</td>
</tr>
<tr>
<td>Control diabetic rats</td>
<td>75.6±9.1</td>
<td>98.6±3</td>
<td>3.6±0.5</td>
<td>82.6±7</td>
<td>76.4±5</td>
<td>236.1±11</td>
</tr>
<tr>
<td>Extract I</td>
<td>118±8.5</td>
<td>55.4±6</td>
<td>1.06±0.08</td>
<td>43.2±4</td>
<td>48.4±2</td>
<td>195.7±6.1</td>
</tr>
<tr>
<td>Extract II</td>
<td>108.6±4.5</td>
<td>58.1±6</td>
<td>1.11±0.1</td>
<td>54.1±4</td>
<td>45.3±4</td>
<td>190.3±7</td>
</tr>
<tr>
<td>Extract III</td>
<td>120.1±3.5</td>
<td>61.3±5</td>
<td>1.13±0.2</td>
<td>56.2±5</td>
<td>52.2±8</td>
<td>200.2±4.5</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>112.4±9.5</td>
<td>60.2±9</td>
<td>1.8±0.4</td>
<td>57.3±4</td>
<td>40.3±4</td>
<td>196.1±9.6</td>
</tr>
</tbody>
</table>

Result Mean ± S.D
Significant p < 0.05

References


