Abstract—The hypoglycemic activity of Olive leaf extract was investigated in fasting healthy rats and alloxan–diabetic rats. Olive leaf extracts are traditionally used to lower blood pressure and reduce the sugar in diabetes. Blood samples were collected from the tail of rats and serum glucose measured on the 1st, 7th, 14th days of the experiment. A significant reduction in blood glucose of diabetic animal’s 350.5±17 mg/dl in case of administration of Olive leaves in comparison with diabetic control 373.5±14 mg/dl, while Glibenclamide drug produced a reduction in blood glucose 235.5±12 mg/dl. The results indicate a prolonged action in reduction of blood glucose by Olive leaves and the mode of action of the active compounds of Olive leaves is probably mediated through enhance secretion of insulin from the β-cells of Langerhans or through extrapancreatic mechanism. The present study clearly indicated a significant antidiabetic activity with the Olive leaves and supports the traditional usage for the control of diabetes.

Keywords—Alloxan, Diabetes Mellitus, hypoglycemic plant, Olive leaves.

I. INTRODUCTION

DIABETES mellitus is the most challenging metabolic disorder as it cannot be cured but needs only to be managed. In 2010, diabetes mellitus was estimated to affect approximately 6.4% of the world’s adult population, or 285 million people. It is estimated that by 2030, the population affected by diabetes will increase to 7.7% of all adults, or 439 million people [11].

On the other hand, impaired glucose-induced insulin secretion with a decrease in pancreatic β cell mass will eventually lead to chronic hyperglycemia [8]. In spite of the hypoglycemic agents, diabetes and the related complications continue to be a major medical problem [9].

Many traditional plant treatments for diabetes exist, and their drugs are frequently considered to be less toxic and free from side effects than synthetic ones.

Antihyperglycemic herbs increase insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver [5].

Olive leaf extracts are traditionally used to lower blood pressure and reduce the sugar in diabetes. These are just some of the many uses of olive leaf extracts as a supplement [13]. As an antiviral and an antimicrobial agent, it holds a lot of promise in the field of nutraceuticals as a natural and effective way to boost the immune system in infections. Olive leaf and diabetes is now something that has been looked into through many different studies [14].

II. MATERIALS AND METHODS

A. Samples and Chemicals

Preparation of decoction: first, cleaning 100 g of olive leaves with water to clear the dust and sand that it may have then, boiling the leaves in one liter and a half of water. The water boils for three minutes and takes the mixture off and let it drain. Then, collect the fluid and save the mixture in a glass container for the usage.

Glibenclamide was provided by Diamond Pharmaceutical company, Amman, Jordan, while alloxan (Sigma Chemical Company, USA). All other reagents used were of analytical grade.

B. Animal Experiments

Rats of original Wistar strain bred in the Central Animal House, Department of Biological sciences, College of Science, Yarmouk University were used in this study. Experiments were carried out in male rats weighing between 180 and 220 g. Rats provided with a standard diet and water ad libitum. All they kept in cages with Wide Square mesh at the bottom and maintained in a well-ventilated animal house with 12 h light and dark cycle.

C. Induction of experimental diabetes

Diabetes was induced in the rats by a single intraperitoneal injection of alloxan (150 mg /kg body weight). Since alloxan is capable of producing fatal hypoglycaemia as a result of massive pancreatic insulin release, rats were treated with 20% glucose solution (15–20 ml) intraperitoneally after 6 h. The rats were then kept for the next 24 h on 5% glucose solution bottles in their cages to prevent hypoglycaemia (Stanely Mainzen Prince et al., 1998a). After 5 days when the
condition of diabetes was stabilized, rats with blood glucose range of 200 - 300 mg/dl were selected for the study.

D. Experimental procedures

Plasma glucose was estimated by the use of an Ames One Touch Glucometer (LifeScan; Johnson and Johnson, New Brunswick, NJ). Blood glucose values were measured on the 1st, 7th, 14th days of the experiment. Rats were divided into five experimental groups of six rats each: Group 1. Served as control, Group 2 Received Olive leaf extract orally through intragastric intubation at doses of 2 ml/kg body weight and served as control, Group 3. Diabetic rats received alloxan (150 ml/kg body weight), Group 4. Diabetic rats received orally olive leaf extract 2 ml/kg, Group 5 Diabetic rats were given glibenclamide 600 μg/kg body weight [7].

E. Data and Statistical Analysis

Data was expressed as mean ± standard deviation of means. Statistical analysis was made by using Student's unpaired t-test.

III. RESULTS

Table 1. Shows mean values of changes in body weight in the treatment and control groups. Administration of olive leaves extract had increasing body weight by 22.7%.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Initial body weight</th>
<th>Final Body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>221.4±14.92</td>
<td>277.6±12.85</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>205.8±8.34</td>
<td>231.2±11.42</td>
</tr>
<tr>
<td>Normal+Olive leaves</td>
<td>207.2±6.37</td>
<td>254.6±10.01</td>
</tr>
<tr>
<td>Diabetic+ Olive leaves</td>
<td>183.6±6.05</td>
<td>172.3±2.52</td>
</tr>
<tr>
<td>Diabetic+Glibenclamide</td>
<td>182.2±3.76</td>
<td>207.8±36.91</td>
</tr>
</tbody>
</table>

Table 2. BLOOD GLUCOSE CONCENTRATION (mg/dl) OF NORMAL AND EXPERIMENTAL ANIMALS.

<table>
<thead>
<tr>
<th>Groups</th>
<th>0 Day</th>
<th>7 days</th>
<th>14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>119.0±3.0</td>
<td>121.8±5.0</td>
<td>109.8±2.0</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>116.2±22.0</td>
<td>413±17.0</td>
<td>373.5±14.0</td>
</tr>
<tr>
<td>Normal+Olive leaves</td>
<td>108.2±13.0</td>
<td>98±6.0</td>
<td>102.7±8.0</td>
</tr>
<tr>
<td>Diabetic+Olive leaves</td>
<td>104.0±4.0</td>
<td>369±18.0</td>
<td>350.5±17.0</td>
</tr>
<tr>
<td>Diabetic+Glibenclamide</td>
<td>110.4±8.0</td>
<td>328.3±21.0</td>
<td>235.5±12.0</td>
</tr>
</tbody>
</table>

Values are given as mean ± S.D. for six rats in each group.

Olive leave produced a dose-dependent hypoglycemia in normal rat’s 102.7±8.0 mg/dl. It produced maximum reduction in blood glucose at the 14th day of experiment in comparison with normal control 109.8 ± 2.0 mg/dl (Table 2).

Dose-dependent reduction in blood glucose was also observed in alloxan-induced diabetic rats treated with Olive leaf extract. The percent reduction in blood glucose tended to be higher in the diabetic condition compared to the normal state. A significant reduction in blood glucose of diabetic rats 350.5±17 mg/dl in case of administration of olive leaf extract in comparison with diabetic control 373.5±14 mg/dl (Table 2). Glibenclamide drug (600μg/kg) produced a significant reduction in blood glucose 235.5±12 mg/dl compared to control value 109±2 mg/dl.

IV. DISCUSSION

Patients with diabetes mellitus are likely to develop certain complications such as retinopathy, nephropathy and neuropathy as a result of oxidative stress and overwhelming free radicals. Treatment of diabetic patients with medicinal plant extract may be of advantage in attenuating these complications. Our results indicates a significant, rising in plasma blood glucose after induction of diabetes. During 14 days of treatment of diabetic rats with 2 ml/kg body weight of Olive leaf extract, the levels of blood glucose were significantly restored to establish values that were not different from normal control rats. Untreated diabetic rats on the other hand demonstrated persistent alterations in the blood glucose. These results demonstrate that olive leaf extract may be of advantage in inhibiting hyperglycemia and oxidative stress induced by diabetes and suggest that its administration may be helpful in the prevention of diabetic complications associated with oxidative stress.

Olive leaf extract contains concentrated amounts of the compounds hydroxytyrosol and oleuropein. Many studies indicate that substances are responsible for many of the health benefits of extra virgin olive oil. However, olive leaf extract has proved more potent than these substances administered alone. The extracting methods used vary for different products, and concentrations can vary greatly, too, so purchase olive leaf extract that is standardized to either hydroxytyrosol or oleuropein [13].

Alloxan induces diabetes by damaging the insulin secreting cells of the pancreas leading to hyperglycemia [10]. The cytotoxic action of this diabetogenic agent is mediated by reactive oxygen species, Alloxan and the product of its reduction, dial uric acid; establish a redox cycle with the formation of super oxide radicals. These radicals undergo dismutation to hydrogen peroxide [2]. Therefore, highly reactive hydroxyl radicals are formed by the Fenton reaction. The action of reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration causes rapid destruction of β-cells [4].

It is well established that sulphonylureas produce hypoglycemia by increasing the secretion of insulin from pancreas and these compounds are active in mild alloxan-induced diabetes whereas they are inactive in intense alloxan diabetes nearly all β-cells have been destroyed [3].

Since our results showed that the administration of Olive leaf decoction and glibenclamide to diabetic rats restored the level of blood glucose. Alloxan-treated rats receiving the Olive leaf decoction showed rapid normalization of blood glucose levels in comparison to control and this could be due to the possibility that some β-cells are still surviving to act upon by the decoction to exert its insulin releasing effect also glibenclamide reduced blood glucose levels in hyperglycemic animals, the state of diabetes is not severe. Moreover, oral
administration of decoction produced hypoglycemia in normal animals. This suggests that the mode of action of the active ingredients of olive leaves is probably mediated by an enhanced secretion of insulin, like sulphonylureas [1].

V. CONCLUSIONS

Our results demonstrate that Olive Leaf Extract may be helpful in inhibiting hyperglycemia and oxidative stress caused by diabetes, and that it may be able to help diminish the complications of diabetes.

Finally, our study clearly indicated a significant antidiabetic activity with the Olive leaf decoction and supports the traditional usage to control of diabetes.

REFERENCES


