Original Article

The Effect of *Olea Europaea* Ethanolic Extract on Glucose Tolerance and Glucose Uptake in Hyperglycemic Rats

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Abstract:

The effect of 200,400 and 800 mg/kg of ethanolic extract of *Olea europaea* leaves was evaluated in both glucose-loaded Wistar albino rats and in glucose uptake by using isolated rats hemidiaphragms. The effect of the three doses was studied 1, 2 and 4 hours after loading the fasting rats with glucose. Their effects were compared to control rats administered with the vehicle and to a standard group administered with the standard drug Glibenclamide. 200 mg/kg of the extract was found to be the most effective dose in both models of experiments.

Key words: *Olea europaea*, ethanol extract, hyperglycemic, rats, hemidiaphragm

Introduction:

Diabetes mellitus is a major endocrine disorder and growing health problem in most countries. It afflicts a large number of people of all social conditions throughout the world, and it is an important cause of prolonged ill health and early death. Also diabetes has become an emerging problem in the developing world. In sub-Saharan Africa, for example, the incidence and prevalence of the disease is unknown, diagnosis is often made on the basis of poor information and a loosely defined set of criteria, and access to oral hypoglycemic agents and insulin is patchy and expensive [1]

Due to their low or no side effects, herbal hypoglycemic agents have become a major component in the treatment of the disease and many have proved their anti-
hyperglycemic efficacy. *Olea europaea* plant is native to the Mediterranean region and, both the oil and the fruit are some of the main components of the Mediterranean diet. Olive (*Olea europaea*) leaves are used as anti-rheumatic, anti-inflammatory, antinociceptive, antipyretic, vasodilatory, hypotensive, antidiuretic and hypoglycemic agents in traditional medicine. Many studies carried out on this plant revealed its biological activities as analgesic [2] and its leaves and fruits have been used externally as an emollient for skin ulcers and for healing of inflammatory wounds [3].

**Material and Methods:**

**Plant collection and extraction:**

A weight of 50 grams of coarsely ground leaves of *Olea europaea* dried in shades were extracted with 80 % ethanol with shaking for 48 hours. Then it was evaporated under pressure. The percentage yield was calculated as 19.9 %.

**Animals:**

Thirty Wistar albino rats were divided into five groups with six rats each. They were fasted from food eighteen hours prior to experimentation and had water *ad libitum*.

Blood samples were drawn out through orbital plexus of rats for determination of plasma glucose levels [4].

**Experimental Model:**

The Fasting plasma glucose levels of the five groups were determined and these levels were considered as zero level. Three groups were treated with the ethanolic extract of *Olea europaea* in three different doses. The first group (A) was administered with 200 mg/kg body weight, while the second group (B) was administered with 400 mg/kg body weight of the extract. The third group (C) was administered with 800 mg/kg body weight. The fourth group (D) of rats was administered with 10 mg/kg body weight of the hypoglycemic drug, Glibenclamide. The last group (E) was administered with 10 ml/kg body weight of distilled water and considered as a control group.
Immediately after administration of extract and the drug and distilled water, all of the
groups were injected intraperitonially with 50 % glucose solution at a dose of 2g/kg
body weight.

The plasma glucose level of the groups was monitored one hour, two hours and four
hours after injection with the glucose load [5].

**In vitro study on glucose utilization by isolated rat hemidiaphragm:**

The selected rats were killed by decapitation and diaphragms were taken out quickly
avoiding trauma and divided in to two halves. The hemidiaphragms were then placed
in culture tubes containing 2 ml tyrode solution with 2 g% glucose and incubated for
30 min at 37 °C in an atmosphere of 95% O₂–5% CO₂ with shaking. Four sets of
experiments were performed. The diaphragms were exposed to (a) tyrode solution
with 2 g% glucose which served as control, (b) tyrode solution with 2 g%
glucose + insulin (0.25 IU/ml), (c) tyrode solution with 2 g% glucose + extract
(200 mg/ml) and (d) tyrode solution with 2 g% glucose + insulin
(0.25 IU/ml + extract (200 mg/ml)). Following incubation, the hemidiaphragms were
taken out and weighed. The glucose content of the incubated medium was measured.
Glucose uptake was calculated as the difference between the initial and final glucose
content in the incubation medium [6].

**Results:**

The ethanolic extract of Olea europaea leaves caused significant changes in the
glucose level of hyperglycemic rats. In the first hour, 200mg/kg of the extract caused
the least increase (1.97%) in the glucose level of the glucose loaded rats. This effect
was found to be statistically significant when compared with the increase in the
control group (69%). While at doses of 400 and 800 mg/kg caused significant increase
(36.3 and 13.1 %) respectively. Those increases were found to be lower than that
carried by the control group. In the fourth hour, 200 mg/kg of the extract caused the
glucose level to return to its normal zero-time level before treatment with the glucose
load. This effect was found to be significant when compared with the effect caused by
the standard drug Glibenclamide (increase of 3.4 %) and the effect of the control
group (increase of 20.1%). On the other hand, 800 mg/kg of the extract caused the glucose to return to its normal level pretreatment with the glucose load, to the effect of the control group.

The effect of 200 mg/kg of the extract was studied on glucose uptake by using the rat hemidiaphragm method. It was found that this dose has a remarkable effect on glucose uptake by cells, when used individually and/or mixed with insulin. Its effect was higher than that attained by the effect of insulin alone. Tables 1&2

Table [1]: Effect of *Olea europaea* leaves ethanolic extract on glucose loaded rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>0 hour</th>
<th>1 hour</th>
<th>2 hour</th>
<th>4 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>97.4 ± 32</td>
<td>164.6 ± 3</td>
<td>123 ± 5</td>
<td>121.8 ± 6</td>
</tr>
<tr>
<td>Glibenclamide (10 mg/kg)</td>
<td>100.58 ± 6</td>
<td>113.12 ± 3.3</td>
<td>119.4 ± 4</td>
<td>104 ± 5.6</td>
</tr>
<tr>
<td>200 mg/kg</td>
<td>88.75 ± 22</td>
<td>90.5 ± 3.3</td>
<td>105.8 ± 12.6</td>
<td>88.75 ± 12</td>
</tr>
<tr>
<td>400 mg/kg</td>
<td>78.5 ± 6</td>
<td>107 ± 3.8</td>
<td>90 ± 20</td>
<td>107 ± 22</td>
</tr>
<tr>
<td>800 mg/kg</td>
<td>74.8 ± 6.8</td>
<td>84.6 ± 14</td>
<td>92.75 ± 12.4</td>
<td>90 ± 17</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n = 6); comparing treatment group with control.

Table [2]: Effect of *Olea europaea* leaves ethanolic extract on glucose uptake by isolated rat diaphragm

<table>
<thead>
<tr>
<th>Incubation medium</th>
<th>Glucose uptake (mg/g/30 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrode solution with glucose (2 g%)</td>
<td>2.92</td>
</tr>
<tr>
<td>Tyrode solution with glucose (2 g%) + insulin (0.25 IU/ml)</td>
<td>9.38</td>
</tr>
<tr>
<td>Tyrode solution with glucose (2 g%) + extract (200 mg/ml)</td>
<td>39.38</td>
</tr>
<tr>
<td>Tyrode solution with glucose (2 g%) + insulin (0.25 IU/ml + extract (200 mg/ml)</td>
<td>42.27</td>
</tr>
</tbody>
</table>
Discussion:

In this study, the effect of three different doses of *Olea europaea* ethanolic extract is evaluated. Dose of 200mg/kg of the ethanolic extract showed the highest hypoglycemic effect in induced hyperglycemia in rats even at four hours after the glucose load compared to the standard drug Glibenclamide. This effect was less attained when using of higher doses of the extract. The above effect was comparable to a previous study conducted on diabetic rats [7] which reported that oral administration of the olive leaves extract (0.1, 0.25 and 0.5 g/kg body wt) for 14 days significantly decreased the serum glucose, total cholesterol, triglycerides while it increased the serum insulin in diabetic rats but not in normal rats (p < 0.05). A comparison was made between the action of olive leaves extract and glibenclamide (600 microg/kg). The antidiabetic effect of the extract was more effective than that observed with glibenclamide.

In another part of the study, 200 mg/kg of the extract was chosen to study the effect of *Olea europaea* glucose uptake by isolated rat hemidiaphragm. Again the above dose showed an increase in the glucose uptake by cells with and without mixing with insulin. An effect found to be higher than that of the insulin alone. These findings may be attributed to the active constituent of the plant, oleuropein which was reported earlier to have an anti-hyperglycemic effect in alloxan diabetic rabbits ([8]). However, a previous study conducted by [9] suggested that both oleuropein and oleanolic acid are involved in the anti-diabetic effect of olive leaves.

References:


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