

The Hypoglycemic Effect of Some Medicinal Plants in Normal and Experimentally Induced Diabetic Rabbits

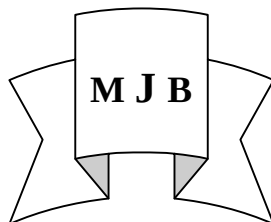
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Abstract

Alloxan (180mg/Kg) I.V is an effective diabetogenic agent that induces diabetes mellitus in rabbits.

Ninety healthy male rabbits were involved in this study. The plasma glucose levels were measured in normal and in diabetic rabbits after giving alloxan and following the administration of glibenclamide, insulin and the aqueous extract of medicinal plants.

Insulin (2IU/Kg) S.C produced a significant reduction in plasma glucose levels in diabetic rabbits ($b = -3.87$ $P < 0.001$). In the mean time, the aqueous extract of *Cinnamomum verum*, *Nigella sativa* and *Olea europea* at a single dose of 0.5g/Kg orally caused a significant lowering of plasma glucose levels in diabetic rabbits with $b = (-2.38)$, (-2.34) and (-1.17) respectively ($P < 0.05$), whereas the aqueous extract of both *Capparis spinos* and *Coriandum sativum* at the same dose produced non significant decrease in plasma glucose levels of diabetic rabbits with $b = (-0.86)$ and (-0.98) respectively ($P > 0.05$).

The aqueous extract of medicinal plants significantly decreased the plasma glucose levels in normal rabbits except with *Capparis spinos*, whereas glibenclamide insignificantly reduced the plasma glucose levels in diabetic rabbits.

الخلاصة

يعتبر الالوكسان (180مغم/كغم) بالزرق بالوريد مادة فعالة لإحداث داء السكر في الأرانب. شملت هذه الدراسة تسعون من ذكور الأرانب السليمة. وتم قياس مستوى السكر في البلازما للأرانب السليمة والأرانب المحدث فيها السكر تجريبياً وكذلك بعد إعطاء الكلينكلمايد والانسولين والمستخلص المائي للنباتات الطبية. نتج إعطاء الانسولين بجرعة (2وحدة دولية/كغم) تحت الجلد انخفاض معنوي في مستوى السكر في البلازما للأرانب المصابة بداء السكر ($b = -3.87$, $P < 0.001$). وفي نفس الوقت فان جرعة مفردة من المستخلص المائي للدارسين والحبّة السوداء والزيتون مقدارها 0,5 غم/كغم بالفم سببت نقصان معنوي في مستوى السكر في البلازما للأرانب المصابة بداء السكر ($b = -2.38$), (-2.34) بالتعاقب ($P < 0.05$), بينما المستخلص المائي لكل من الكبر والكزبرة وبنفس الجرعة أحدث انخفاضاً غير معنوي في مستوى السكر في البلازما للأرانب المصابة بداء السكر ($b = -0.86$) و ($b = -0.98$) بالتعاقب ($P > 0.05$). إن المستخلص المائي للنباتات الطبية المستخدمة في هذه الدراسة أحدثت انخفاضاً معنوياً في مستوى السكر في البلازما للأرانب السليمة ما عدا نبات الكبر، بينما الكلينكلمايد هو الذي لم يحدث انخفاضاً معنوياً في مستوى السكر في البلازما للأرانب المصابة بداء السكر.

Introduction

Diabetes mellitus is a complex metabolic syndrome that is widely distributed in the world with both major types I and II. The world health organization (WHO) expert committee on diabetes 1984, has considered with recommendation that traditional methods of therapy for diabetes should further investigated [1].

The present study aimed to evaluate the possible hypoglycemic effect of an aqueous extract of five selective medicinal plants and compare between their hypoglycemic effect in order to choose the best to be used as an alternative to insulin or as an adjunct in therapy of diabetes type II.

The active parts of these medicinal plants which were used in this study include the leaves of *Capparis spinos* (Kabbar) and *Olea europea* (Olive), the bark of younger branches of *Cinnamomum verum* (Cinnamon), the seeds of *Nigella sativa* (black cumin) and the dried ripe fruits of *Coriandrum sativum* (Coriander).

Materials and Methods

Ninety healthy male rabbits, weighing 1.2- 1.6Kg, they were obtained from the local market of Baghdad city. Each animal was kept in separated cage, which was provided with a wide wire mesh floor. Rabbits fed standard diet (Oxiod pallet) and were given water and food ad libitum.

The possible hypoglycemic effect of the medicinal plants has been examined on two major groups of rabbits (normal and experimentally induced diabetic rabbits).

1st- Normal rabbits grouping:

Fourty two rabbits were divided into 7 equal groups, each group contained 6 rabbits:

Group 1: normal rabbits were given 2ml of distilled water orally (placebo), used as a control.

Group 2: the animals of this group were administered glibenclamide (70µg/Kg) orally.

Group 3, 4, 5, 6, 7: the animals of these groups were given the aqueous extract of Kabbar, Cinnamon, Coriander, black cumin and olive respectively at a single dose of 0.5g/Kg for each animal. This dose was chosen previously after a pilot study.

2nd- Diabetic induced rabbits grouping:

Diabetes was experimentally induced in rabbits by injection of alloxan tetrahydrate (180mg/Kg) [2] I.V through marginal ear vein, sooner the animals were injected with 10ml of 20% glucose solution S.C to reduce alloxan hypoglycemic shock.

Fourty eight rabbits were divided into eight groups, each group contained 6 animals:

Group 1: diabetic rabbits were given 2ml of distilled water orally and used as control.

Group2: diabetic rabbits were treated with a single dose of insulin (2IU/Kg) S.C.

Group3: diabetic rabbits were treated with glibenclamide (70µg/Kg) orally.

Group 4,5,6,7,8: diabetic rabbits were treated with the aqueous extract of Kabbar, Cinnamon, Coriander, black cumin and olive respectively at a single dose of 0.5g/Kg for each animal. The duration of treatment to all tested groups was four successive weeks.

Medicinal plants were collected (kabbar, olive leaves in May and June], bought from the local market (Cinnamon, Coriander and Black cumin), crushed, minced thoroughly and hot aqueous extract were prepared. The aqueous extract of these plants was given per Os via stainless steel tube.

Blood samples were collected from the marginal ear vein of each rabbit after 12 hours of fasting. These samples were taken before starting the experiment and two hours after giving glibenclamide and aqueous extract of medicinal plants to normal rabbits and once weekly after different treatment in diabetic rabbits. In addition to glibenclamide and aqueous extracts insulin was given to diabetic rabbits after the induction of diabetes with alloxan. The plasma glucose levels were determined by Barham & Trinder method [3]. The analysis of variance was conducted by using complete randomized design (CRD) and least significant difference (LSD) at 1% and 5% levels to compare between the means of the plasma glucose levels in treated groups of normal rabbits. The association between the means of blood glucose levels and days of treatment was presented as regression coefficient (b). All statistical manipulations, which were employed, depend on method of Snederos & Cochran [4].

Results and Discussion

The results of this study revealed that the plasma glucose levels of normal rabbits (group 1) were within the normal range along the period of the study, but administration of glibenclamide and the aqueous extract of the five selective medicinal plants (groups 2-6) produced a significant decrease in plasma glucose levels of normal rabbits as compared with placebo except *Capparis spinos*

which produced non significant decrease in plasma glucose levels (table 1).

The hypoglycemic effect of glibenclamide was related to stimulation of insulin release from the beta cells of the pancreas [5], associated with lowering of plasma glucose levels in normal rabbits.

Insulin is released in response to a variety of stimuli e.g the amino acid leucine [6], and *Nigella sativa* contains leucine in its constituents [7], therefore it may stimulate the release of insulin and decrease the plasma glucose levels in normal rabbits.

Medicinal plants have shown to contain saponins, glycosides and alkaloids in their structures [8,9], these active compounds may reduce significantly the plasma glucose levels in normal rabbits.

Glibenclamide was more effective than the aqueous extract of *Capparis spinos*, *Coriandrum sativum* and *Olea europea* in reducing plasma glucose levels, whereas the aqueous extract of *Cinnamomum verum* and *Nigella sativa* were more effective than glibenclamide in decreasing plasma glucose levels in normal rabbits after 2 hours of administration of 0.5mg/Kg orally.

Alloxan is a potent diabetogenic agent that produced prominent hypoglycemia, these results are similar to Jimenez et. al results [10]. This hypoglycemic action is due to destruction of beta cells of pancreatic islets with cessation of the glycolysis process and catalyzation of both gluconeogenesis and glycogenolysis [11].

The results in table 2 showed that the treatment of diabetic rabbits with insulin (group 2) produced highly significant reduction in plasma glucose levels ($P < 0.001$) but does not reach to

the normal values. This reduction is related to increase the rate of glucose uptake by the cell [12]. Whereas the diabetic rabbits in group 3 showed non significant decrease in plasma glucose levels ($P>0.05$) throughout the four weeks of treatment with glibenclamide. This is due to the destruction of beta cells by alloxan and no functional cells remain to respond.

The aqueous extract of *Nigella sativa* (group 7) produced a significant decrease in plasma glucose levels of diabetic rabbits during four weeks of treatment ($P<0.05$) as compared with the diabetic control (group 1). It has been shown that *Nigella sativa* decreased the elevated glucose and malondialdehyde concentration [13] producing hypoglycemia in rats. The hypoglycemic effects of *Nigella sativa* may be mediated through decreasing hepatic gluconeogenesis [14].

There was no significant reduction of plasma glucose levels in diabetic rabbits treated with aqueous extract of both *Capparis spinos* (group 4) and coriander (group 6) throughout the four weeks of treatment ($P>0.05$) as

compared with plasma glucose levels of diabetic control (table 2, figure 1).

The aqueous extract of cinnamon contain methylhydroxy chalcone polymer (MHCP) which has an important role in dropping high glucose levels in diabetic mice [15]. MHCP is an effective mimetic of insulin in which may be useful in treatment of insulin resistance and changing the glucose utilization in the cells [16].

The aqueous extract of *Oleo europea* (group 8) contains active compounds that could explain the significant hypoglycemic effect of this extract ($P<0.05$) throughout the four weeks of treatment (table 2, figure 1).

Insulin was more effective than the aqueous extract of the five medicinal plants in reducing plasma glucose levels in diabetic rabbits.

The obtained results in the present study show that both *Nigella sativa* and *Cinnamomum verum* were the most effective hypoglycemic plants in experimental animals and they possibly be used in diabetic patient with type II.

References

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Table 1 The fasting plasma glucose levels before and two hours after administration of glibenclamide and the aqueous extract of medicinal plants in normal rabbits.

group	Fasting plasma glucose (mmol/ml)	
	Before treatment	After treatment
Placebo	4.96 ± 0.86	4.86 ± 0.66
Glibenclamide	5.64 ± 0.79	3.86 ± 0.65
<i>Capparis spinos</i>	5.58 ± 0.81	4.58 ± 0.81
<i>Cinnamomum verum</i>	5.25 ± 0.66	2.83 ± 0.54
<i>Coriandum sativum</i>	5.65 ± 0.65	3.95 ± 0.61
<i>Nigella sativa</i>	5.82 ± 0.41	3.18 ± 0.66
<i>Olea europea</i>	5.38 ± 0.48	4.20 ± 0.58

Table 2] Regression coefficient (b) of the plasma glucose levels (mmol/ml) in diabetes induced rabbits after administration of insulin, glibenclamide and aqueous extract of five medicinal plants for four weeks.

Treatment	Effect on serum glucose	(b)	Significant
Insulin	Decrease	-3.87	$P < 0.001$
Glibenclamide	Decrease	-0.52	NS
<i>Capparis spinos</i>	Decrease	-0.86	NS
<i>Cinnamomum verum</i>	Decrease	-2.38	$P < 0.05$
<i>Coriandrum sativum</i>	Decrease	-0.98	NS
<i>Nigella sativa</i>	Decrease	-2.34	$P < 0.05$
<i>Olea europea</i>	Decrease	-1.17	$P < 0.05$

NS = non-significant, $P > 0.05$.

$P < 0.05$ = significant level 0.05.

$P < 0.01$ significant level 0.01.

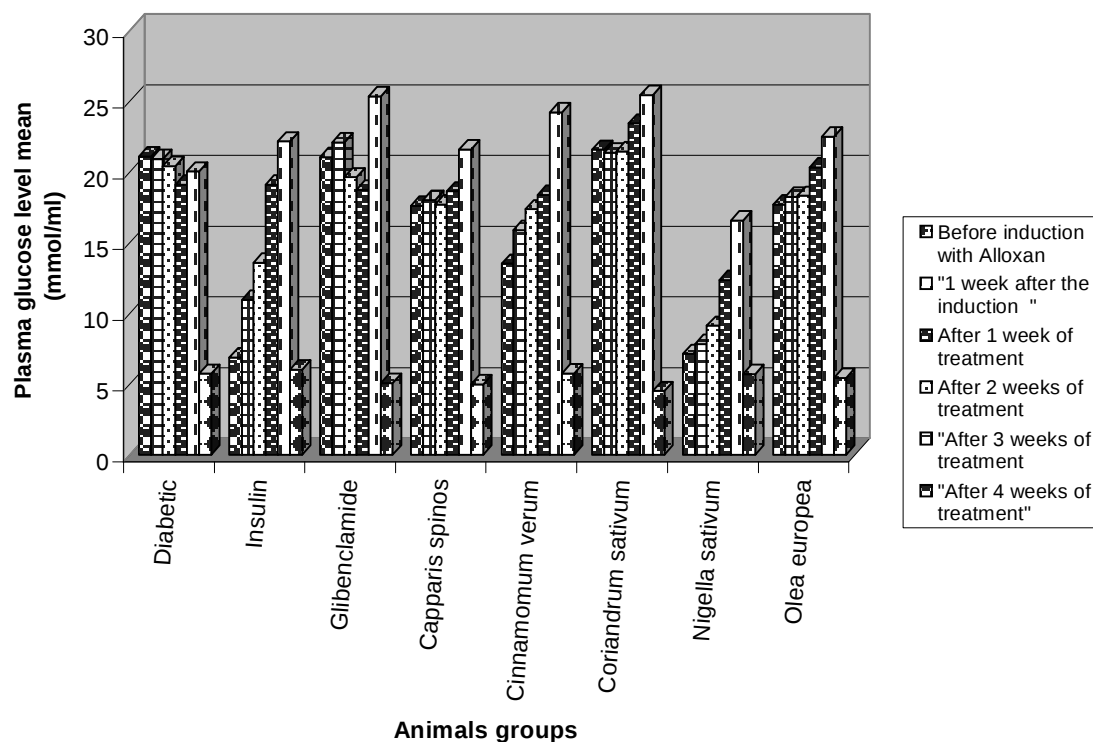


Figure 1 Fasting plasma glucose levels in diabetes induced rabbits after administration of insulin, Glibenclamide and the aqueous extract of five medicinal plants for four weeks.