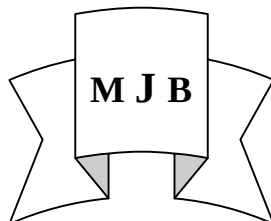


Effect of Aqueous Extract of Some Medicinal Plants on Plasma Lipid Profile in Diabetes Induced Rabbits.

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Abstract

Alloxan (180mg/kg) i.v is a potent diabetogenic agent that induces diabetes mellitus in rabbits with hypercholesterolemia and hypertriglyceridemia .

Fifty-four healthy male rabbits were involved in this study. Both plasma cholesterol and triglyceride levels were measured before and after giving alloxan and following administration of insulin, glibenclamide or aqueous extract of medicinal plants.

Insulin (2 IU/kg) S.C produced a significant reduction in both plasma cholesterol ($b=-1.05$ $p<0.005$) and triglyceride levels ($b=-1.19$ $P<0.01$) whereas glibenclamide (70mg/kg) per Os produced no significant changes in these values. In the mean time the aqueous extract of *Nigella sativa* (0.5g /kg) produced a significant decrease in both cholesterol and triglyceride levels with ($b=-0.65$ $P<0.05$) and ($b=-1.28$ $P<0.05$) whereas *Capparis spinosa* caused a significant decrease in plasma cholesterol levels only with ($b=-0.83$ $P<0.01$). Finally the extract of *Coriandrum sativum* ,*Oleoe uropea* and *Cinnamomum verum* produced a significant reduction in triglyceride levels with ($b=-1.12$ $P<0.05$), ($b=-0.97$ $P<0.05$) and ($b=-1.01$ $P<0.01$) respectively but with no significant change in cholesterol levels.

There is no significant correlation between the hypoglycemic effects of medicinal plants and their hypocholesterlemic & hypotriglyceridemic effect. Also the possibility of using *Nigella sativa* and *Cinnamomum verum* for diabetic patients with type- II but this needs more clinical trials.

Keyword cholesterol, triglyceride, medicinal plants

الخلاصة

يعتبر الالوكسان (180ملغم/كغم) بالزرق بالوريد مادة فعالة لإحداث داء السكري في الأرانب مع فرط الكوليسترول وفرط التراكليراييد في البلازما.

شملت هذه الدراسة أربعة وخمسون من ذكور الأرانب السليمة. وتم قياس مستويات الكوليستيرول والتراكليراييد في البلازما قبل وبعد اعطاء الالوكسان وبعد اعطاء الانسولين والكليبنكلمايد أو المستخلص المائي للنباتات المختلفة.

نتج إعطاء الانسولين بجرعة (2وحدة دولية/كغم) تحت الجلد انخفاضا معنويا في مستويات كل من الكوليستيرول ($b=-1.05$ $p<0.005$) والتراكليراييد ($b=-1.19$, $P < 0.01$) في البلازما بينما الكليبنكلمايد (70ملغم/كغم) بالفم أحدث تغييرا غير معنويا في هذه القيم. وفي نفس الوقت فإن 0.5 غم/كغم من المستخلص المائي للحبة السوداء سبب نقصانا معنويا في مستويات الكوليستيرول ($b=-0.65$ $P<0.05$) والتراكليراييد ($b=-1.28$ $P<0.05$) بينما سبب نبات الكبر انخفاضا معنويا في مستويات الكوليستيرول فقط ($b=-0.83$ $P<0.01$). وأخيرا أحدث المستخلص المائي لكل من الكزبرة والزيتون والدارسين انخفاضا معنويا في مستويات

الترايكليسيرايد , (b=-1.12 P<0.05 b=-0.97 P<0.05) و (b=-1.01 P<0.01) ولكن بدون تغيير معنوي في مستويات الكوليسترول.

لا يوجد ربط معنوي بين التأثير المخفض للسكر للنباتات الطبية المستخدمة مع التأثير المخفض للكوليستيرول والترايكليسيرايد لها. وكذلك إمكانية استخدام الحبة السوداء والدارسين لمرضى السكر من النوع الثاني والذين يعانون من فرط الدهون.

Introduction

Diabetes mellitus is a complex metabolic syndrome characterized by varying degree of insulin deficiency with two well-known type-1 and type-2. Indeed, the hyperglycemia in diabetes mellitus may be associated with or resulted in hypercholesterolemia [1], while the hypertriglyceridemia concerning insulin deficiency in diabetes type -1 is completely reversible with intensive insulin therapy [2].

Some medicinal plants extract (*Nigella sativa* and *Cinnamomum verum*) showed a significant reduction in plasma glucose levels when administered orally in diabetes induced rabbits⁽³⁾.

The current study aimed to explore the possible hypocholesterolemic and hypotriglyceridemic effect of the aqueous extract of these selective medicinal plants and to disclose the relationship between the hypoglycemic effect and lipid lowering effect of these plants in order to choose a safe effective agent or an adjunct in therapy of diabetes type-2 with out raising the lipid profile nor increasing the risk factor.

The active parts of these medicinal plants included, the seeds of *Nigella sativa* (black cumin) the dried ripe fruits of *Coriandrum sativum* (coriander), the leaves of *Olea europea* (olive) and *Capparis spinos* (kabbar) and the bark of younger branches of *Cinnamomum verum* (Cinnamon).

Materials and Methods

Fifty-four healthy male rabbits weighing 1200-1600g were obtained

from local market. Each rabbit was kept in separate cage, which was provided with a wide wire mesh floor. All the rabbits fed standard diet (oxoid) and were given water and food ad libitum. The rabbits were separated in to nine equal groups (each group contained 6 rabbits).

Group 1:- Normal rabbits were given 2ml of distilled water orally as a control.

Group 2:- Normal rabbits were administered alloxan (180mg/kg) I.V to induce diabetes.

Group 3:- Diabetic rabbits were treated with insulin (2IU/kg) S.C as a single dose.

Group 4:- Diabetic rabbits were treated with glibenclamide (70mg/kg) orally as a single dose.

Group5, Group6, Group7, Group8 and Group9:- Diabetic rabbits were treated with aqueous extract of black cumin, coriander, olive, kabbar and cinnamon at a single dose of 0.5g/kg by oral route respectively. All the groups were treated for interval of four successive weeks.

Medicinal plants were collected, crushed, minced thoroughly and hot aqueous extract were prepared. The aqueous extract of these plants was given orally via stainless steel tube.

Blood samples were obtained from marginal ear vein of each rabbit after 12 hours of fasting. These samples were taken before starting the experiment and once weekly after different treatment. The plasma cholesterol and triglyceride levels were determined by Allain et al method [4].

Results were expressed as mean $\pm$ SD. 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 cholesterol & triglyceride levels after different treatment. The association between the means of cholesterol & triglyceride levels and weeks of treatment was presented as regression coefficient (b). These calculations depend on method of Snederos and Cochran[5].

Results & Discussion

The result of the current study revealed that the plasma cholesterol and triglyceride levels of normal rabbits (Group1) were within the normal ranges throughout the four weeks of treatment (Figure 1 & 2).

Administration of alloxan as a diabetogenic agent (Group2) produced marked elevation of plasma cholesterol and triglyceride levels after one week as compared with (Group 1), this elevation lasted a long the period of this study. The hypercholesterolemia that occurred in diabetes is related to increased fatty acid degradation and conversion to the main product acetyl-CoA which has an important role in cholesterol synthesis [6]. The hypertriglyceridemia associated with hypercholesterolemia may be related to impaired adipose tissue lipoprotein lipase activity with failure of excretion from circulation [7]. The treatment of diabetic rabbits with insulin (Group 3) produced highly significant decrease in plasma cholesterol levels ($P<0.05$) and triglyceride levels ($P<0.01$) throughout the four weeks of treatment as compared with (Group 2) (figure 1&2). The reduction in plasma cholesterol levels is related to stimulation of the lipogenesis and inhibition of lipolysis [8] while the

reduction in plasma triglyceride levels is related to activation of lipoprotein lipase activity by insulin [9]

The oral hypoglycemic drug glibenclamide (Group 4) produced no significant change in lowering plasma cholesterol and triglyceride levels through out four weeks of treatment.

The treatment of diabetic rabbits with aqueous extract of black cumin (Group 5) showed a significant decrease in both plasma cholesterol levels and triglyceride levels ($P<0.05$) as compared with diabetic rabbits in group 2 (tables 1&2). The hypocholesterolemic and hypotriglyceridemic effect of this plant may be related to its constituents of active compounds (glycosides, alkaloids]. Black cumin has previously been reported to be effective in lowering plasma cholesterol levels of diabetic rats [10] and plasma triglyceride levels of rats with carbon tetra chloride induced hepatotoxicity after four weeks of treatment [11].

The aqueous extract of kabbar (Group5) caused a significant reduction in plasma cholesterol levels ($P<0.01$) with non significant change in triglyceride levels. This effect may be related to steroid-saponins presenting in the plant which can decrease the total plasma cholesterol without any change in triglyceride levels of normal and diabetic rats [12].

The effect of coriander, olive and cinnamon (Group6, 7, 9) on plasma cholesterol levels in diabetic rabbits caused non significant change ($p>0.05$) as compared with (Group 2) whereas these three plants produced a significant decrease in plasma triglyceride levels with $P<0.01$, $P<0.05$ and $P<0.05$ respectively (Table 2).

There is no available data referring to the hypotriglyceridemic effect of these

plants but this effect may be related to antioxidant effect of cinnamon and coriander and to the changes in the lipid metabolism [13, 14].

Finally, it is difficult to conclude that most the aqueous extract of medicinal plants with hypoglycemic effect may have hypocholesterolemic & hypotriglyceridemic effect. We also conclude the possibility of using black cumin and cinnamon in hypercholesterolemic and hypertriglyceridemic diabetic patients with type-II especially when the primary results showed the significant hypoglycemic effect of these plants [3] but these need more clinical trials for confirmation.

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Table 1 Regression coefficient (b) of the plasma cholesterol levels (mmol /ml) throughout the four weeks of the treatment in diabetes induced rabbits.

Treatment	Effect on serum cholesterol	(b)	Significant
Insulin	Decrease	-1.05	P<0.05
Glibenclamide	Decrease	-0.33	N.S
<i>Nigella sativa</i>	Decrease	-0.65	P<0.05
<i>Coriandrum sativum</i>	Decrease	-0.45	N.S
<i>Olea europea</i>	Decrease	-0.60	N.S
<i>Capparis spinos</i>	Decrease	-0.83	P<0.01
<i>Cinnamomum verum</i>	Decrease	-0.52	N.S

Table 2 Regression coefficient (b) of the plasma triglyceride levels (mmol/ml) throughout the four weeks of the treatment in diabetes induced rabbits

Treatment	Effect on serum cholesterol	(b)	Significant
Insulin	Decrease	-1.19	P<0.01
Glibenclamide	Decrease	-0.64	N.S
<i>Nigella sativa</i>	Decrease	-1.28	P<0.05
<i>Coriandrum sativum</i>	Decrease	-1.12	P<0.05
<i>Olea europea</i>	Decrease	-0.97	P<0.05
<i>Capparis spinos</i>	Decrease	-0.47	N.S
<i>Cinnamomum verum</i>	Decrease	-1.01	P<0.01

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

$P < 0.05$ = significant level 0.05.

$P < 0.01$ significant level 0.01.

