HYPOGLYCAEMIC EFFECT OF *BERBERIS ARISTATA* ROOTS, AQUEOUS AND METHANOLIC EXTRACTS IN NORMAL AND ALLOXAN-DIABETIC RABBITS

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Summary

The study was conducted to evaluate the hypoglycaemic effect of dried and powdered root of *Berberis aristata* and its extract in water and methanol on blood glucose levels following oral administration to normal and alloxan treated albino rabbits. Eighty four rabbits were randomly divided into 14 groups of 6 animals each. Group I was untreated and received orally 20 ml of 2 % gum tragacanth solution in water only. The groups II-IV were treated orally with 2, 3 and 4 g/kg body weight (b.w) of dried and powdered roots of *B. aristata* suspended in 2 % gum tragacanth solution in water, respectively. Group V received methanol extract of the roots equivalent (eq.) to 4 g/kg b.w of *B. aristata* while group VI was treated with aqueous extract of the root eq. to 4 g/kg of drug. The control animals of group VII were given gliclazide (500 mg/kg b.w) orally for comparison.

Similar treatments were given to the various groups of the alloxan treated diabetic rabbits. Animals of groups VIII were kept as diabetic control and were given 20ml of 2% gum solution. Groups IX to XI were treated orally with 2, 3 and 4 g/kg b.w of *B. aristata* powdered root suspended in 2 % gum sol, respectively while animals of group XII to XIII were treated orally with methanol and aqueous extracts of the root eq. to 4 g/kg b.w, of crude powder, respectively. Finally the rabbits in animals of group XIV were treated with the control drug, gliclazide (500 mg/kg b.w) orally. It is evident from the data obtained that the roots and their methanolic and aqueous extracts produced significant (P<0.05 & 0.001) decrease in the blood glucose levels at 2, 4 and 8 hours in the normal rabbits and as well as diabetics. It is conceivable, therefore, that *Berberis aristata* roots contain some potent orally effective antidiabetic/hypoglycaemic chemical principle(s) which possess insulin triggering and insulin-like activities.

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Introduction

Innumerable plants have been used empirically to treat diabetic patients and some been clinically proven. If such herbal drugs after thorough investigations are found really effective in controlling blood glucose levels in the diabetics, they may even provide ideal/curative hypoglycaemic principles. Moreover, diabetes has become amongst the commonest disease of the present times and despite considerable progress es in the management o diabetes with the use of synthetic drugs, search for natural agents has now greatly increased all over the globe (1). More than 200 plant species could be added to a folklore list of insulin substitutes including many common plants such as olive leaves, celery, black berry leaves and leaves and roots of banana (2, 3, and 4).

Among the indigenous medicinal plants already screened for antidiabetic/ hypoglycaemic properties, *Vinca rosea* (Sada Bahar) and *Brassica oleraceace* (Ghobi) have been reported to lower the blood glucose levels (5). *Allium cepa* (Onion) and *Allium sativum* (Garlic) decrease the blood glucose levels (6). A large variety of chemical compounds obtained from several plant families have been held responsible for the hypoglycaemic activity (7) while the glycosides isolated from the plant families including Caesalpiniaceae, Papaveraceae, Rhanunculaceae, Rhamnaceae and Scrophuloriaceae contain active principles which lower the blood glucose in test animals. The polysaccharides, oils and vitamins from the family Graminae have also showed pharmacological activity by decreasing blood sugar level in animals. Alkaloids of Apocynaccae, Papaveraceae, Rhamnaceae and Zygophyllaceae particularly are effective in diabetes. Saponins from Araliaceae, glycoproteins from Malvaceae, peptides, amino acids and proteins from Papilionaceae and Rubiaceae have also been reported to be beneficial in reducing the sugar levels (8).

Therefore, an investigation was carried out to evaluate the hypoglycaemic effect of dried and powdered *Berberis aristata* roots; allegedly used very commonly in folklore as a curative remedy for diabetes mellitus and some other diseases (9). The blood glucose levels were determined in normal and alloxan treated diabetic albino rabbits before and after oral treatment with powdered root and its extract in water and methanol.

Materials and Methods

Medicinal Plant Used and Its Parts:
Bark of roots of *Berberis aristata* locally known as Sumlu were collected from Rawalakot (AJ&K). The roots were completely dried under the shade, powdered finely with the china herb grinder in the laboratory of the Department of Physiology and Pharmacology. The powdered material was stored in well closed cellophane bags at 4°C in the refrigerator.

Experimental Animals Used:

Healthy male and female adult rabbits (*Oryctolagus cuniculus*) of a local strain, weighing 1000-1500 g were used in these experiments. The animals were kept under observation for one week before experimentation under usual managemental conditions in the animal room of the Department of Physiology and Pharmacology, University of Agriculture, Faisalabad. The animals were fed green fodder *ad libitum* and a rabbit feed prepared by the Nutrition Department of the University of Agriculture, Faisalabad. Fresh and whole-some water was supplied *ad libitum.*

Grouping of Rabbits:

Eighty four rabbits were randomly divided into 14 groups of 6 animals each. Animals of group I to VII were kept as normal (non-diabetic) while those of groups VIII to XIV were artificially made diabetic by administering 150 mg/kg of alloxan-monohydrate.

Group I served as untreated control as they received orally 20 ml of 2 per cent gum tragacanth solution in water only. The animals of group II to IV were treated orally with 2, 3 and 4 g/kg body weight of powdered roots of *Berberis aristata* suspended in 2 per cent gum tragacanth aqueous solution respectively.

The animals in group V received methanol extract of the roots equivalent to 4 g/kg dose of *Berberis aristata*. Similarly, the rabbits of group VI were treated with aqueous extract of the plant equivalent to 4 g/kg dose of *Berberis aristata*. The animals of group VII were administered Gliclazide (500 mg/kg body weight) orally for comparison.

Similar treatments were given to the various groups of the alloxan-diabetic rabbits. Animals of groups VIII were kept as diabetic control and were administered with 20ml of 2 per cent gum solution. The groups IX to XI were treated orally with 2, 3 and 4 g/kg body weight of *Berberis aristata* powder suspended in 2 per cent gum tragacanth aqueous solution respectively while animals of group XII to XIII were treated orally with Methanol and aqueous extracts of the whole plant equivalent to 4 g/kg dose of *Berberis aristata* powder respectively. Finally the animals of group XIV were treated with Gliclazide (500 mg/kg body weight) orally.

Preparation of alloxan-Diabetic Rabbits

A group of rabbits, weighing 1000-1500g were made diabetic by injecting 150 mg/kg body weight of alloxan monohydrate intravenously (10). Eight days after injecting the alloxan-monohydrate, blood glucose levels of all the surviving rabbits were determined by the Glucose PAP fluid monoreagent. Rabbits with blood glucose levels of 300-500 mg/100 ml were considered as diabetic and were employed for further study.

Preparation and Administration of Plant Drug Suspension

The amount of powdered roots of *Berberis aristata* (Sumlu) required for each animal on body weight basis was weighed with an electric balance. The same was triturated with about 10 ml of 2 percent aqueous gum tragacanth solution and the final volume was always made up to 20 ml. The drug was administered orally to each animal by using a stomach tube connected with a 50 ml BD-record syringe (7). Control drug gliclazide was also administered after suspending in 2 percent aqueous gum tragacanth solution.

Preparation and Administration of Methanol and Aqueous Extracts of *Berberis aristata* (powdered roots)

Methanol Extract:
Known amounts of powdered roots were put into the thimbles made of special filter paper and 250 ml of methanol was taken into the glass flasks. The extract obtained was evaporated by slow heating at 40°C and continuous stirring. The process of evaporation was continued till complete evaporation of methanol was ensured. The dried methanol extract so obtained was dissolved in distilled water just before administration to rabbits. Methanolic extract yielded by 4 g/kg body weight of the powdered *Berberis aristata* (Sumlu) was administered to each rabbit of the group.

Aqueous Extract:
        Weighed amount of properly comminuted drug was kept for Maceration in a suitable Menstrum (distilled water) in round neck well stopper flask and agitated it occasionally for a period of one day. The drug was then filtered through a fine filter and marc was pressed in order to avoid the loss and filter the mixed liquids. The process of maceration was done at room temperature. The extract thus obtained was then dried in Petri dish in an oven at temperature not more than 40°C and drug was then administered to the rabbit in amounts equivalents to 4 gram/kg body weight of powdered plant individually to all the animals of the group.
H) Collection of blood samples
After administration, the animals were held in a wooden rabbit holder and immediately 0.2 ml of blood was collected from an ear vein. Similar samples of 0.2 ml were collected at 0, 2, 4,8,12 and 24 hours time intervals. After collecting blood, methylated alcohol was applied on the pricked site to protect the ear against infection.

Determination of blood glucose
Blood glucose was determined by using kit-method, peridichrom. Glucose GOD-PAP (Centronic GmBH, Germany). The results obtained are very accurate by the glucose oxidase method used for true glucose determination. Presently the kit-method has been found to be one of the most widely used manual method. Due to these reasons, it was selected for these experiments.

Statistical analysis and arrangement of data:
The data was expressed as means ± SEM (Standard Error of Means).Student "t" test was used to check the significance of the data (11).

Results

Standard curve for blood glucose determination
The standard curve for glucose estimation drawn by plotting the absorbance on the ordinate against the glucose concentration as abscissae was found to be linear up to 300 mg/100ml of glucose.

STDIES ON NORMAL RABBITS

Effect of *Berberis aristata* roots on blood glucose levels in normal rabbits
The mean blood glucose concentration ± SEM of control and drug treated animals after oral administration of different doses of *Berberis aristata* at various time intervals are summarized in Table 1. The following results have been drawn from these data:

Group-I: Rabbits treated with 2% gum solution
Table1 shows that blood glucose levels of the control group administered with 15 ml of the 2 percent gum tragacanth aqueous solution was determined to be 91.08 ± 1.9 mg /100 ml at zero hours. The gum tragacanth did not affect the blood glucose levels as there was no statistical difference at 2, 4, 8, 12 and 24 hours intervals.

Table 1: Mean blood glucose levels of normal rabbits expressed in mg/100 ml ± standard error of means at various time interval after oral administration with 2 % gum tragacanth and *Berberis aristata* (Powdered roots) 2, 3 and 4 g/kg b. weight.

Time Interval (Hours)	Group-I 2 % Gum Tragacanth solution.	Group-II 2 g/ kg^{-1} b. wt.	Group-III 3 g kg^{-1} b. Wt.	Group-IV 4g kg^{-1} b. Wt.
0	91.08 ± 1.9	93.95 ± 1.4	95.74 ± 1.7	86..38 ± 3.6
2	89.59 ± 2.2	91.20 ± 2.5 NS	94.80 ± 3.2 NS	84.11 ± 2.9 NS
4	91.50 ± 2.1	91.65 ± 2.4 NS	85.58 ± 3.1**	80.42±1.7*
8	92.50 ± 2.0	85.50 ± 2.0 *	80.91 ± 1.6**	72.20 ± 2.0**
12	90.33 ± 2.2	83.82 ± 2.5*	78.64 ± 4.7**	71.78 ± 3.8**
24	90.18± 4.0	92.34 ± 2.5 NS	95.50 ± 4.3 NS	85.43 ± 2.2 NS

NS   =   Non-significant decrease as compared to Zero hour level (P> 0.05)
*   =   Significant decrease as compared to zero hour level (P < 0.05)
**   =   Highly significant decrease as compared to zero hour level (P < 0.001)
No. of animals for each observation = 6

Group-II
Rabbits treated with powdered *Berberis aristata* roots 2 g/kg body weight orally:
Table 1 shows that the blood glucose levels of group-II animals treated with 2 g/kg dose of *Berberis aristata* roots at zero hour before drug administration was recorded to be 93.95 ± 1.4 mg /100 ml. As compared to zero hour level there was a significant (P < 0.05) decrease glucose level at 8 hour and 12 hours intervals after plant drug administration. The blood glucose level at 2 and 24 hours intervals of drug administration was also lower then at zero hour but difference was found to be statistically non-significant (P > 0.05).
Group-III
Rabbits Treated with powdered *Berberis aristata* roots 3 body weight orally:
The mean blood glucose levels ± SEM of group III treated with 3g/kg dose of the drug at zero 2, 4, 8 and 12 hours intervals were 95.74 ± 1.7, 94.80 ±3.2, 85.58 ± 3.1,80.91 ± 1.6, 78.64 ± 4.7 mg/100 ml, respectively. The values at 4 hour interval were found to be

highly significant (P < 0.001) and also at 8 and 12 hours were found to be highly significant (P < 0.001). The mean blood glucose levels at 2 and 24 hours intervals were found to be 94.80 ±3.2, 95.50 ± 4.3 mg/100 ml, and do not differ from zero hour level significantly (P> 0.05).

Group-IV
Rabbits treated with powdered *Berberis aristata* roots 4 g/kg body weight (orally):
Table 1 shows the mean ± SEM blood glucose level of group-IV animals treated with 4 g/kg dose of drug at zero 2, 4, 8, 12 and 24 hours intervals were found to be 86.38 ± 3.6, 84.11 ± 2.9, 80.42 ± 1.7, 72.20 ± 2.0, 71.78 ± 3.8 and 85.43 ± 2.2 mg/100 ml, respectively. A highly significant (P < 0.001) reduction was recorded at 8 and 12 hours intervals and significant reduction recorded at 4 hour interval. At 2 and 24 hours the mean blood glucose level were not different statistically (P > 0.05) from zero hour level (Table 1).

Group-V
Rabbits treated with methanolic extract equivalent to 4 g/kg dose of the powdered *Berberis aristata* roots:
Table 2 shows mean ± SEM blood glucose level of group-V to be 88.77 ± 1.5 mg/100 ml at zero hour. However, the values at 2, 4, 8, 12 and 24 were found to be 84.83 ± 6.2, 82.85 ± 2.8, 75.84 ± 2.9, 72.76 ± 3.4, 87.48 ± 4.4 mg/100 ml. The values at 8 and 12 hours interval showed a highly significant (P < 0.001) decrease and at 4 hour interval showed a significant (P<0.05) decrease from zero hour.

Group-VI
Rabbits treated with aqueous extract equivalent to 4g/kg dose of powdered *Berberis aristata* roots:
Table 2 shows mean ± SEM blood glucose levels of group-VI to be 85.88 ± 2.5 mg/100 ml at zero hour. The reducing in glucose levels at 4 hour interval as appears in values 80.78 ± 2.9 and exhibits a significant effect (P < 0.05) at 8 and 12 hours intervals. However, the values at 2 and 24 hours intervals showed a non-significant (P > 0.05) decrease in blood glucose level.

Group VII
Rabbits treated with the Gliclazide 500 mg/kg body weight:
In table 2 the blood glucose level group treated with 500 mg/kg b. wt. of Gliclazide at zero hour was found to be 85.78 ± 3.9 mg/100 ml. A statistically significant (P < 0.05) reduction in blood glucose level is indicated at 2, 4 and 8 hours interval. However, at 12 hours and 24 hours interval the blood glucose levels was found to be statistically non-significant (P> 0.05) when compared with the zero hour level.

Table 2:Mean blood glucose levels of normal rabbits expressed in mg/100 ml ± standard error of means at various item interval after oral treatment with 2 % gum tragacanth, methanolic and aqueous extracts equivalent to *Berberis aristata* (powdered roots) 4 g/kg b. wt and Gliclazide 500 mg/kg Body weight.

Time Interval (Hours)	Group-I 2 % Gum Tragacanth Solution	Group-V Methanolic Extract	Group- VI Aqueous Extract	Group-VII Gliclazide
0	91.08 ± 1.9	88.77 ± 1.5	85.88 ± 2.5	85.78 ± 3.9
2	89.59 ± 2.2	84.83 ± 6.2 NS	83.34 ± 2.8 NS	71.17 ± 8.2 *
4	91.50 ± 2.1	82.85 ± 2.8 *	80.78 ± 2.9 *	70.61 ± 8.7 *
8	92.50 ± 2.0	75.84 ± 2.9 **	74.61 ± 2.8 **	75.08 ± 4.0 *
12	90. 33 ± 2.2	72.76 ± 3.4 **	70.77 ± 1.9 **	82.57 ± 1.3 NS
24	90.18 ± 4.0	87.48 ± 4.4 NS	86.38 ± 3.6 NS	85.93 ± 4.7 NS

NS   =Non-significant decrease as compared to zero hour level (P>0.05)
*   =Significant decrease as compared to zero hour level (P < 0.05)
**   =Highly significant decrease as compared to zero hour (P<0.001)
No. of animals fro each observation   =   6

STUDIES ON DIABETIC RABBITS

Effects of alloxan-monohydrate administration to rabbits:
The administration of alloxan monohydrate to experimental rabbits was carried out very slowly and proper care was taken to avoid death in receiving alloxan injection died after 24 hours. The blood glucose concentrations of the surviving rabbits were determined after eight days of injections. The rabbits with blood glucose levels above 200-400 mg/100 ml were selected and divided in to 7 groups (VIII-XIV), of six animals each. The mean blood glucose concentrations ± SEM of animals are summarized in Table 3. The results of these experiments are in agreement with other who has also reported that alloxan treated produced a severe persistent hyperglycemia in rabbits and rats (Marquis *et al.* 1977).
Effect of powdered *Berberis aristata* roots on blood glucose levels in diabetic rabbits:
Mean blood glucose concentration ± SEM of control and alloxan diabetic rabbits after administration of different doses of powdered Berberis aristata roots at various time intervals are summarized in Table 3. The results obtained have been deduced as follows:

Group-VIII:
Diabetic rabbits treated with 2% gum tragacanth aqueous solution (15 ml):
As dedicated in Table 3 the mean ± SEM blood glucose level of group-VIII animals treated with 2% gum tragacanth solution at zero hour of administration was found to be 325.91±5.1 mg/100 ml. The gum did not reduce the blood glucose levels at 2, 4, 8, 12 and 24 hours as the values obtained are statistically non-significant (P > 0.05) compared to that at zero hour. The means ± SEM of blood glucose level have been summarized in the table 3.

Group IX
Diabetic rabbits treated with Powdered *Berberis aristata* roots 2 g/kg body weight (orally):
The mean ± SEM blood glucose of group-IX animals treated with 2 g/kg dose of powdered *Berberis aristata* roots was found to be 341.58±9.6 at zero hour (Table 3). The mean ± SEM values obtained at 2, 4 and 8 hours are non-significant (P > 0.05) different from that at zero hour while the mean ± SEM at 12 hour interval (306 ± 6.6) was found to be highly significant decrease when compared to zero hour interval (P> 0.001) Fig. 4.

Table 3:   Mean blood glucose levels of diabetic rabbits expressed in mg/100 ± standard error of means at various time intervals after oral treatment with 2% gum tragacanth solution and *Berberis aristata* (powdered roots) 2, 3 and 4 g/kg b. weight.

Time Interval (Hours)	Group-VIII 2 % Gum Tragacanth solution	Group-IX 2 g/kg b. wt.	Group- X 3 g/kg b. wt.	Group-XI 4 g/kg b. wt.
0	325.91 ± 5.1	341.58 ± 9.6	349.65 ± 11.5	373.29 ± 9.9
2	325. 32 ± 12.7	336.78 ± 6.2 NS	345.22 ± 12.6 NS	364.25 ± 13.8 NS
4	325.35 ± 11.4	337.64 ± 14.4NS	333.45 ± 7.3 *	350.59 ± 6.2 *
8	324.22 ± 6.0	336.35 ± 18.1NS	330.61 ± 4.4 *	332.54 ± 6.8 **
12	322.30 ± 8.9	306.45 ± 6.6 **	311.19 ± 7.4 **	300.19 ± 7.3 **
24	326.62 ± 5.3	340.50 ± 6.9NS	348.65 ± 4.7 NS	373.45 ± 13.2 NS

NS   =   Non-significant decrease as compared to zero hour level (P> 0.05)
*   =   Significant decrease as compared to zero hour level (P < 0.05)
**   =   Highly significant decrease as compared to zero hour level (P < 0.001)
No. ob animals of each observation   = 6

Group X

Diabetic rabbits treated with powdered *Berberis aristata* roots 3 g/kg body weight:
The mean ± SEM blood glucose level of group-x treated with 3 g/kg body weight dose of powdered *Berberis aristata* roots was found to be 349.65 ± 11.5 at zero hour (Table 3). The drug produced a significant decrease (P < 0.05) in blood glucose at 4, and 8 hours' intervals and the highly significant decrease (P < 0.001) was found at 12 hours interval.

Group - XI

Diabetic rabbits treated with powdered *Berberis aristata* roots 4 g/kg body weight:
The mean ± SEM blood glucose of animals treated with 4 g/kg of powdered *Berberis aristata* roots at zero hour was found to be 373.29 ± 9.9 mg/100 ml. The drug produced a statistically significant decrease (P < 0.05) in blood glucose at 4 hour interval and found to be 350.59±6.2 but the highly significant decrease (P < 0.001) was found to be at 8 and 12 hour intervals, respectively. The blood glucose values at 2 and 24 hours intervals were statistically not different from that at zero hour.

Effect of methanolic and aqueous extracts of the *Berberis aristata* roots and Gliclazide on blood glucose levels in diabetic rabbits:
Mean blood glucose concentration ± SEM of diabetic control and aqueous extracts and these diabetic rabbits treated with alcoholic and aqueous extracts and Gliclazide after administration at various time intervals are summarized in Table 4. The results deduced are as follows.

Group-XII

Diabetic rabbits treated with methanolic extract equivalent to 4 g/kg dose of *Berberis aristata* roots:
As shown in the Table 4 the blood glucose levels of group-XII animals treated with methanolic extract at zero hour was found to be 301.43±5.8 mg/100 ml. The glucose levels at 4 and 8 hours showed a highly significant (P < 0.001) decrease and at 12 hour interval showed a significant (P < 0.05) decrease when compared with the zero hour level.

Group XIII

Diabetic rabbits treated with aqueous extract equivalent to 4 g/kg dose of *Berberis aristata* roots:
The mean ± SEM blood glucose value at zero hour of the group treated with aqueous extract equivalent to 4 g/kg dose of *Berberis aristata* was found to be 317.31±5.0 mg/100 ml. The values at 4, 8 and 12 hours intervals were found to be highly significant (P < 0.001). The values at 2 and 24 hours intervals were non-significantly (P > 0.05) lower when compared with zero hour level.

Group XIV

Diabetic rabbits treated with Gliclazide,500 mg/kg body weight orally:
As shown in table 4, the blood glucose level at zero hour after administration of Gliclazide, 500 mg/kg body weight was found to be 319.60±7.4 mg/100 ml however, the values obtained at 2, 4, 8, 12 and 24 hours was non-significant (P > 0.05) from zero hour interval.

Table 4: Mean blood glucose levels of diabetic rabbits expressed in mg/100 ± standard error of means at various time intervals: after oral treatment with 2% gum tragacanth, methanolic and aqueous extracts equivalent to *Berberis aristata* (powdered roots) 4 g/kg b. wt. and Gliclazide 500 ml/kg body weight.

Time Interval (Hours)	Group-VIII 2% Gum Tragacanth solution	Group-XII Methanolic extract	Group- XIII Aqueous Extract	Group-XIV Gliclazide
0	325.91 ± 5.1	301.43 ± 5.8	317.31 ± 5.0	319.60 ± 7.4
2	325. 32 ± 12.7	310.63 ± 14.8 NS	316.75 ± 14.0 NS	314.70 ± 7.2 NS
4	325.35 ± 11.4	325.01 ± 7.3 **	286.46 ± 4.1 **	310.90± 6.3 NS
8	324.22 ± 6.0	315.01 ± 5.3 **	274.28 ± 3.3 **	307.31 ± 3.9 NS
12	322.30 ± 8.9	310.50 ± 4.2*	261.32 ± 3.3 **	312.27 ± 2.7 NS
24	326.62 ± 5.3	302.88 ± 5.1 NS	315.77 ± 6.8 NS	318.47 ± 9.6 NS

NS   =   Non-significant decrease as compared to zero hour level (P> 0.05)
*   =   Significant decrease as compared to zero hour level (P < 0.05)
**   =   Highly significant decrease as compared to zero hour level (P < 0.001)
Number of animals for each observation = 6

Discussion

A considerably large number of hypoglycaemic/antidiabetic plants and herbs are known through folklore but their introduction into modern therapy waits pharmacological testing by modern methods. Several studies have already been carried out in the recent years on plants including *Momordica charantia* (2) Opuntia fuliginosa (12), *Lagerstroemia speciosa* (13), *Cleome droserifolia* (14) *Polygala senega* (15) and *Trigonella foenum-graecum* (16). However, a large number of medicinal plants still need testing by the modern scientific techniques.

It is clear that the hypoglycaemic effect of the tested plant drug at various levels had already started at 4 hour intervals and had reached its maximum at the 8 and I2th hours' intervals after drug administration. The drug effect persisted and then became statistically non-significant (P>0.05) at 24 hours. The initiation and reaching to its maximum and recovery towards normal were similar to all the doses.

It is well known that sulphonylureas including gliclazide produce hypoglycaemia in normal animals by stimulating the pancreatic beta cells to release more insulin (17). They do not, however, lower blood glucose in alloxan-induced diabetics as their beta cells are destroyed and are not able to secrete insulin. Thus in the present study gliclazide was found devoid of significant effect on blood glucose levels in diabetic rabbits (Table 4). Therefore, it is unlikely that *B. aristata* root do not act only like sulphonylureas because the blood levels were also decreased in alloxan-diabetic rabbits; showing that the plant

possesses some insulin-like activity as well. Other hypoglycaemic compounds like biguanides act by increasing the glycolysis and uptake of glucose in muscles and also by decreasing glyconeogenesis in liver and absorption of glucose from the intestines. However, the biguanides do not produce hypoglycaemia in normal subjects because the decrease in peripheral glucose utilization is compensated by an increase in hepatic glucose output (18). Therefore, it would appear that the active principles in the plant drug do not act like biguanides as blood glucose levels have been lowered in both normal and alloxan-diabetic rabbits. Thus it is conceivable that *Berberis aristata* roots possess potent and orally effective antidiabetic/hypoglycaemic active principle(s) which probably possess insulin triggering and insulin-like activities. However, further comprehensive chemical and pharmacological investigations are needed to elucidate the exact mechanism of hypoglycaemic effect and to isolate the active principles of the *Berberis aristata* plant.

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