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PHYTOPHARMACOLOGICAL EVALUATION OF *FICUS GLOMERATA*, ROXB. FRUIT FOR HYPOGLYCAEMIC ACTIVITY IN NORMAL AND DIABETIC RABBITS

MUHAMMAD SHOAIB AKHTAR and ABDEL QAYUM QURESHI

Department of Physiology and Pharmacology,
University of Agriculture, Faisalabad, Pakistan.

ABSTRACT

The investigation was designed to study effects of powdered *Figas glomerata* fruits on blood glucose levels in groups of normal and alloxan-diabetic rabbits. In normal groups, administration of 1, 2, 3 and 4g/kg body weight of *F. glomerata* pulv lowered the blood glucose levels significantly. The methanolic extract of the drug also produced significant hypoglycaemia but the aqueous extract could not produce this effect. In alloxan-diabetic rabbits the treatment with 2, 3 and 4g/kg body weight of the plant drug produced a significant fall in blood glucose levels. The methoanolic extract of the pulv also produced a significant decrease in the diabetics but the aqueous extract could produce a slight fall in glucose levels in these rabbits. Acetohexamide in 500 mg/kg dose produced a significant decrease in blood glucose levels of the normal rabbits only. Therefore, it is conceivable that the indigenous plant contains more than one type of hypoglycaemic principles which seem to act by producing an organotropic effect on the B-cells resulting in an increased secretion of insulin. In addition, it is also possible that the drug acts by providing certain necessary elements to the beta cells, especially in the alloxan-diabetic rabbits. Furthermore, it may be assumed that the indigenous plant pulv would also help the diabetics by providing certain essential minerals like calcium, phosphorus, zinc, magnesium, manganese, copper and others.

Introduction

The fruits of *Ficus glomera*la, Roxb. (fam. Urticaceae), locally known as Gular, areabundantly available in Pakistan. They have been used since olden times in the ethnomedicine for many varied medicinal purposes including as a remedy of diabetesmellitus (Awan 1981). In addition, they are considered to posses tonic, expectorant, emollient, stomachic and carminative properties (Satyavati et al 1976). The sap extracted from trunk of the tree is also considered curative in diabetes. Moreover, the powdered seeds mixed with pure bee-honey are prescribed $_{o}$ the diabetics in the folklore medicine (Nadkmi 1976, Chopra et al 1956). A study has, therefore, been carried out to investigate the hypoglycaemic activity of the ripe, dried and powdered *Ficus glomerate* fruits and their aqueous and methanolic extracts in normal as well as alloxan-diabetic rabbits. Acute toxicity and behavioral pattern studies were also undertaken to study the safety of the indigenous

plant drug. In addition, its major elemental contents were also determined to know about their possible role in the mechanism of their hypoglycaemic effect.

Materials and Methods

Alpha-D-glucose (anhydrous), methanol and alloxan monohydrate were purchased from B.D.H. Laboratories, Poole, England while glacial acetic acid, benzoic acid (sublimed), O-toluidine, thiourea and trichloracetie acid were obtained from E. Merck, Darmstadt, West Germany. Acetohexamide (DIMELOR) was purchased from ELI LILLY and gum tragacanth was obtained from a local pharmacy.

Adult rabbits of a local strain, weighing 1-2 kg were used. They were fed on green fodder and a rabbit feed prepared by Nutrition Department at University of Agriculture, Faisalabad and tap water ad libitum. The rabbits were randomly divided into 16 groups of 6 animals each. Animals of groups I to VIII were normal while the remaining groups (IX-XVI) were made diabetic by injecting 150 mg/kg body weight of alloxan monohydrate in [ravenously (Butt 1962). Eight days after injecting the alloxan, blood glucose levels of all the surviving rabbits were determined and the rabbits with blood glucose levels of 200-500 mg/100 ml were considered as diabetics and used in the experiments.

Preparation and administration of drug suspensions:

The amount of *Ficus glomerata* (nits pulv required for each rabbit was calculated on body weight basis was weighed on an electric balance. The drug was well triturated with 5 ml of 2% aqueous gum tragacanth solution and the final volume was made upto 15 ml. The drug was administered orally to each animal by using a feeding needle connected to a 20 ml record syringe. Acetohexamide was also administered after suspending in 2% gum solution.

Preparation and admin stration of aqueous and methanol extracts of ficus glomerata fruits pulv:

Aqueous extract was prepared by maceration and the extract obtained was dried at 40°C. However, the methanolic extract was prepared by continuous extraction technique using Soxhlees apparatus. The alcoholic extract obtained was evaporated by slow heating at 40°C and continuous stirring till complete evaporation of alcohol. Both the dried extracts were administered to rabbits in doses equivalent to 4 g of Fleur glomerata pulv per kg body weight of the animal after suspending in 2% gum solution.

Collection of blood and determination of blood glucose levels:

After drug administration, the animal was held in a wooden rabbit-holder and immediately 0.2 ml of blood was collected from a marginal ear vein (zero hour sample).

Similarly samples of 0.2 ml were also collected at 2, 4, 8, 12 and 24 hours intervals. Exactly, 0.2 ml of blood samples were taken with the help of a special pippet at blood glucose level was determined by the method of Fings et al (1970), using the O-toluidine reagent.

Acute toxicity and behavioural pattern studies:

To study any possible toxic effects or change in the behavioural pattern, all the treated rabbits were kept closely observed for 14 hours daily for a week. The symptoms including awareness, mood, motor activity, CNS excitation, posture, motor incoordination, muscle tone and reflexes were recorded for seven days as described in detail by Laurence and Bacharrach (Laurence and Bacharach 1964). Any mortality occuring during this period was registered.

Elemental analysis *of ficus glomerata fruits pulv:*

In order to determine the level of some major elements in the powdered *F. Glomerata* fruits, the atomic absorption spectroscopy was carried out at the Nuclear Institute for Agriculture and Biology, Faisalabad. Samples for analysis were prepared by wet digestion technique (Volkovic 1975).

Statistical analysis:

The data have been expressed as Means ± SEM (Standard Error of Means) and Student "t" test was used to check their significance (Steel and Torrrie 1980.)

Results and Discussion

Effects of ficus glomerata fruits pulv on blood glucose levels on normal rabbis:

Table-1 shows that the gum tragacanth did not significantly affect the blood glucose levels at 2, 4, 8, 12 and 24 hours intervals. However, treatment with 1 g/kg of *F. glomer*-am fruits (pulv) caused a significant $P < 0.05$) decrease in blood glucose level only at 4 hours after drug administration. Blood glucose levels of the group treated with 2 g/kg dose at 0, 4 and 8 hours intervals were 83.69 ± 2.4, 75.00 ± 0.6, 76.32 ± 3.2 mg/100 ml, respectively. The values at 4 and 8 hours were significantly ($P < 0.05$ or 0.001 lower than at zero hour. The blood glucose at 2, 12 and 24 hours, however, did not differ from zero hour level significantly ($P > 0.05$). Blood glucose of the animals treated with 3 g/kg of the drug at 0, 2, 4, 8, 12 and 24 hours were 89.49 ± 2.4, 82.53 ± 1.2, 73.25 ± 3.2, 71.93 ± 1.8, 75.00 ± 0.6 and 86.64 ± 2.3 mg/100 ml, respectively. A highly significant ($P < 0.001$) reduction was recorded at 4, 8 and 12 hours and the value at 2 hours interval showed a significant ($P < 0.05$) reduction. At 24 hours, blood glucose was not statistically

Table 1: Mean blood glucose levels of normal rabbits experienced in mg/100 ml standard error of means at various time intervals after oral treatment with 2% gum tragacanth and fiats glomerata fruits (pulv.) 1 g, 2g 3g and 4g/kg body weight per 2% gum tragacanth solution.

Time Interval (hour)	Group-I 2% gum tragacanth solution	Group-II Lg/kg Body weight	Group-III $^{2}gA^{g}$ Body Weight	Group-IV 3kg/kg Body Weight	Group-V 4g/kg Body Weight
0	80.70 ± 2.5	91.67 ± 4.5	83.73 ± 2.6	89.49 ± 2.4	79.82 ± 1.6
2	81.58 ± 1.2	81.14 ± 3.8^{NS}	78.95 ± 3.0"^{s}	82.53 ± 12*	72.37 ± 2.4*
4	80.70 ± 2.5	76.32 ± 3.2*	75.00 ± 0.6**	73.25 ± 3.2**	59.21 ± 2.0**
3	8002 ± 1.6	81.58 ± 3.5 ^{NS}	.76.32 ± 3.2*	71.93 ± 1.8**	59.21 ±2.0**
12	78.93 ± 1.7	86.40 ± 8.4^{Ns}	75.06 ± 3.5 ^{NS}	75.00 ± 0.6^{NS}	66.66 ± 0.9**
24	80.70 ± 1.3	88.60 ± 3.9^{N5}	73.20 ± 14.5 ^{NS}	86.84 ± 2.3 ^{NS}	73.68 ± 0.0 ^{NS}

NS = N. significant decrease as compare to zero hour lam (P > 0.05)
* = Significant decrease as compared to zero hour level (P <0.05)
**= Highly significant decrease as compared to ze*ro* hour level (P < 0.0 01)
Number of animals for each observation = 6
t (Tab) values: at P 0.05 (*) 223; at P 0.001 (**) = 4.59
T (Cal) values: Group-II 0 hr. vs. 4 hr. = 2.77
Group-III 0 hr. vs 4 hr.=577 0 hr. vs 8hr.2.77
Group-IV 0 hr. vs 2 hr.258;0hr. vs 4 hr.=4.08; 0 hr. vs 8 hr.= 5.85; 0 hr. vs 12 hr. = 5.77
Group-V 0 hr. vs 2 hr. 2.62; 0 he vs 4 hr.=7.06; 0 hr. vs 8 hr.= 6.40; 0 hr. vs 12 hr.=7.15

different from zero level. Similarly, treatment with 4 g/kg of the drug produced at 4, 8 and 12 hours a highly significant (P < 0.001) decrease in blood glucose levels. ASt 24 hours, the value was non-significant (P > 0.0.5). It was noted that maximum reduction in blood glucose at all the dosage levels was produced at 4 hours intervals and the dose response curve was linear.

Effects of methanolic and aqueous extracts *of ficus glomerata fruits and acetohexamide on blood glucose levels* in *normal rabbits:*

Table 2 shows that rabbits treated with methanolic extract equivalent to 4 g/kg of *Ficus glomerata* fruits pulv exhibited a highly significant reduction of blood glucose at 2, 4 and 8 hours. However, the aqueous extract at the same dosage did not produce this effect. Nevertheless, treatment with 500 mg/kg body weight of acetohexamide caused a significant (P <0.05 or 0.001) reduction in blood glucose levels at 2, 4 and 8 hours only.

Table 2: Mean blood glucose levels of normal rabbits expressed in mg/100 ml ± standard error of means at various time intervals after oral treatment with 2% gum tragacanth, alcholoic and aqueous extracts equivalent to Ficus *glometra* fruit (pulv.) 4g/kg body weight and acetohexamide 500 mg/kg body weight per 2% gum tragacanth solution.

Time interval (hr)	Group-I 2% gumtraga-canth solution	Group-VI methanolic eq. to 4 g/kg dose	Group-VII Aqueous extract eq. to 4 g/kg dose	Group VIII Acetohexamide 500 mg/kg b.w.
0	80.70 ± 2.5	86.85 ± 5.5	83.69 ± 2.4	83.69 ± 2.4
2	81.58 ± 1.2	61.50 ± 4.5**	84.21 ± 2.9 ^{NS}	66.84 ± 5.7*
4	80.70 ± 2.5	53.95 ± 2.7**	79.83 ± 3.4 ^{NS}	70.53 ± 2.8**
8	82.02 ± 1.6	59.21 ± 1.8**	83.77 ± 2.4 ^{NS}	72.10 ±1.6**
12	78.94 ± 1.7	68.86 ± 3.9*	85.09 ± 2.6 ^{NS}	78.42 ± 1.9 ^{NS}
24	80.70 ± 1.3	82.02 ± 4.3^{NS}	85.09 ± 2.2 ^{NS}	79.47 ± 2.8 ^{NS}

NS= N. significant decrease as compared too hear level (P > 0.05)
* = Significant decrease as compared to 0 hour level (P > 0.05)
** = Highly significant decrease as compared to 0 hour level (P < 0001)
Number of animals for each observations = 6
t (Tab) values at P 0.05 (*) = 2.23; at P 0.001 (**) = 4.59
T (cal) values: Group-VT-0 hr. vs 2 hr. = 3.54; 0 hr. vs 4 hr. 5.38; 0 hr. vs 8 hr = 4.67; 0 hr . vs l2 hr =2.67; 0 hr. vs 24 hr = 0.69
Group VIII-0 hr. vs 2 hr. =2.71; 0 hr. vs 4 hr= 3.56; 0 hr. vs 8 hr=3.99

Effect of ficus glmerata fruits pulv on blood glucose levels in *alloxan-diabetic rabbits:*

Table 3 gives the blood glucose levels of the diabetic rabbits treated with various drugs. Treatment with 2% gum tragacanth did not significantly reduce the blood glucose at 2, 4, 8, 12 and 24 hours. Similarly, blood glucose of animals treated with 1 g/kg of *F. glomerata* fruits pulv were non-significantly (P > 0.05) different from that at zero hour. However, highly significant (P < 0.001) reductions of the blood glucose levels were produced by 2 g/kg of the powder at 4. 8 and 12 hours but the values at 2 and 24 hours *were* non-significantly (P > 0.05) different from zero hour. Treatment with 3 g/kg of *F. glomerata* produced a highly significant decrease in blood glucose at 4, 8 and 12 hours but at 24 hours interval, the decrease was only significantly lower. The blood highly significantly (P < 0.001) reduced at 4, 8 and 12 hours while at 2 and 24 hours, *they* were found non-significantly different from zero hour level (Table 3).

Blood glucose levels of diabetic rabbits treated with methanolic extract of F. *glomerata* fruits pulv at 4, 8, 12 and 24 hours also showed a highly significant (P < 0.001) decrease. However, the group treated with aqueous extract in the same dosage had blood glucose values at 4 and 8 hours which *were* only significantly (P < 0.05) lower than the

zero hour level. The values at 2, 12 24 hours were non-significantly ($P < 0.05$) less than zero hour level. However, acetohexamide (500 ml/kg) did not alter the blood glucose levels of the alloxan diabetic rabbits.

Table 3: Means blood glucose levels of diabetic rabbits expressed in mg/100 ml ± standard error of means at various intervals after oral treatment with 2% gum tragacanth solution and *Ficus glomerata* fruits (pulv.) 1, 2, 3 and 4g/kg body weight orally per 2 percent gum tragacanth aqueous solution.

Time interval (hr)	Group-IX 2% gum tragacanth	Group-X 1g/kg b.w.	Group-XII 2g/kg b.w.	Group-XII 3g/kg b.w.	Group-XIII 4g/kg b.w.
0	309.21 ± 3.3	312.28 ± 11.5	325.44 ± 5.3	316.67 ± 3.7	311.90 ± 14.5
2	310.97 ± 4.3	301.75 ± 12.8^{NS}	312.25 ± 5.7^{NS}	312.28 ± 3.7^{NS}	281.58 ± 14.4^{NS}
4	314.10 ± 4.7	299.12 ± 15.2^{NS}	281.58 ± 4.0**	280.70 ± 3.5**	267.55 ± 8.9**
8	300.77 ± 4.2	308.77 ± 12.8^{ns}	275.00 ± 3.8**	253.51 ± 7.2**	238.03 ± 8.8**
12	306.58 ± 3.6	308.77 ± 12.3^{NS}	286.81 ± 2.9**	244.74 ± 8.7**	283.00 ± 7.3**
24	309.21 ± 3.3	305.15 ± 12.7^{NS}	315.79 ± 4.1^{NS}	293.86 ± 5.3*	281.58 ± 8.2 ^{NS}

NS = Non significant decrease as compared to 0 hour level ($P > 0.05$)
* = Significant decreae as compared to 0 hour level ($P < 0.05$)
** = Highly significant decrease as compared to 0 hour level ($P < 0.001$)
Numberof animals for each observation = 6
t (tab) values at P 0.05 (*) = 2.23; at P 0.001 (**) = 4.59
to (cal) values Group-XI 0 hr. vs 4 hr. 6.57; 0 hr. vs 8 hr. 7.68; 0 hr. vs12 hr. 6.35
Group-XII 0 hr vs. 4 hr. 7.05; 0 hr. vs 8 hr. 7.77; 0 hr. vs 12 hr. 7.56; 0 hr. vs 24 hr. 3.50
Group-XIII 0 hr. vs 4 hr. 2.61; 0 hr. vs 8 hr.10.64; 0 hr vs. 12 hr. 3.60

Elemental analysis of F. glomerata fruits pulv:

The levels of zinc, calcium, magnesium, manganese, phosphorus, copper and iron in the *F. glomerata* fruits as determined by the atomic absorption sepectroscopy have been given in Table 4. It is clear from the data that the levels of these elements in *F. glomerota* fruits am relatively very high as compared to those found in many other vegetables and fruits as reported by Underwood (1983) and Schroeder (1965).

Acute toxicity of F. glomerata fruits:

Rabbits treated with 2, 4, 6 and 8 g/kg of *F. glomerata* pulv remained alive and did not show any visible symptoms of toxicity. The treated animals showed no restlessness, respiratory distress, convulsions, coma and diarrhoea, etc.

Table 4: Mean Blood Glucose Levels of Diabetic Rabbits Expressed in mg/ml ± Standard error of means at various time intervals after oral treatment with 2% gum tragacanth, methanolic and Aqueous Extracts equivalent to *Ficus glomerata* Fruit (pulv.) 4g/kg Body weight and acetohexamide 500 mg/kg Body weight per 2% Gum Tragacanth Solution.

Time interval (hr)	Group-IX 2% gum tragacanth	Group XIV Methanolic extract. eq. to 4 g/kg dose	Group XV Aqueous extract eq. tp 4g/kg dose	Group-XVI Acetohexamide 500 mg/kg b.w.
0	309.21 ± 3.3	328.07 ± 4.0	319.30 ± 20.5	307.02 ± 12.4
2	310.97 ± 4.3	322.89 ± 13.6^{NS}	315.80 ± 11.8^{NS}	297.37 ± 15.8^{NS}
4	314.10 ± 4.7	315.88 ±11.9**	264.91 ± 7.2*	294.74 ± 20.7^{NS}
8	308.77 ± 4.2	231.58 ± 8.4**	270.70 ± 6.4*	291.23 ± 7.5^{NS}
12	306.58 ± 3.6	235.09 ± 13.5**	293.25 ± 10.7^{NS}	297.37 ± 13.8
24	309.21 ± 3.3	263.20 ± 10.9**	309.70 ± 20.7^{NS}	289.91 ± 14.6^{NS}

NS = Non significant decrease as compared to 0 hour level (P > 0.05)

* = Significant decrease as compared to 0 hour level (P < 0.05)

** = Highly significant decrease as compared 0 hour level (P < 0.001)

Number of animals for each observation = 6

t (tab) values at P 0.05 (*) = 2.23; at P 0.01 (**) = 4.59

t (cal) values Group-XIV 0 hr. vs. 4 hour = 6.12; 0 hr. vs. 8 hour = 10.64; 0 hr. vs. 12 hour = 7.26; 0 hr. vs. 24 hour = 5.57

Group-XV 0 hr. vs. 4 hour = 2.49; 0 hr. vs. 8 hour = 2.26

Table 5: Some metallic contents of *F. glomerata* as determined by atomic absorption spectroscopy.

Element	Wave length nm	Current mA	Concentration* µg/g
Zinc	213.9	15	28
Calcium	422.7	20	15300
Magnesium	2852	20	9500
Manganese	279.5	25	16
Phosphorous	213.6	20	2700
Copper	324.8	15	12
Ferrum	248.3	25	600

*=Mean values

Discussion

Obviously oral hypoglycaemic drugs are of no value in the treatment of severe disease of any type and in insulin dependant diabetes as their islets have already lost all potential ability to secrete insulin (Guyton 1985). A number of hypoglycaemic plants and herbs am known through folklore (Said 1969, Farnswirth and Segetment 1971) and have been used since centuries in indigenous medicine but their introduction into modem therapy awaits pharmacological testing by modern methods.

Ficus glomerata Roxb. is an indigenous plant whose ripe fruits have been used empirically from the olden times as an anti-diabetic remedy in the ethnomedical practices. Thus pulverized fruits of this plant were administered orally after suspending in 2% gum tragacanth aqueous solution to normal and alloxan diabetic rabbits.

Administration of *F. glomerom* fruits pulv to normal rabbits at the dose levels of 1, 2, 3 and 4 g/kg reduced the blood levels significantly ($P < 0.05$ or 0.001) at different time intervals (Table 1). It is clear that the hypoglycaemic effect of the drug at various dose levels had already started at 2 hours intervals and had reached its maximum at the 4 hour. At the 8 hours, the drug effect persisted and after which the blood glucose levels started increasing and had become statistically non-significant ($P > 0.05$) at 24 hours. The initiation and reaching to its maximum and recovery towards normal was, however, similar, to other doses. From these data, it is evident that administering *F. glomerata* fruits pulv in 1, 2, 3 and 4 g/kg body weight doses had exerted a significant hypoglycaemic effect in the normal rabbits. Previously, production of hypoglycaemic response in normal animals has also been reported for many other medicinal plants (Hassal et al 1954, Shamta et al 1967, Akhtar 1982, Akhtar et al 1984). For the comparison of hypoglycaemic activity, acetohexamide was administered orally which has also been observed to produce significant hypoglycaemic effect in the normal rabbits. The blood glucose levels remained significantly lower at 2, 4 and 8 hours intervals and became non-significant at 12 and 24 hours. The hypoglycaemia produced by 3 and 4 g/kg doses of *F. glomerata* fruits pulv was significant even at 12 hours. It showed that the pulv has got a more prolonged duration as compared to that of acetohexamide.

In order to fractionate the hypoglycaemic activity of the plant drug, its methanolic and aqueous extracts were also administered to normal rabbits. The methanolic extract could cause a highly significant reduction in the blood glucose level (Table 2) but aqueous extract of the plant did not produce a significant decrease in glucose levels; suggesting that its hypoglycaemic principles are extractable in methanol but not in the water.

In an effort to determine possible mechanism of the hypoglycaemic action of *F. glomerata* fruit pulv, it was also administered to the alloxan-diabetic rabbits. Table 3 shows that in the diabetic rabbits, oral administration of 2, 3 and 4 g/kg of pulv has also produced a significant ($P < 0.05$ and 0.001) decrease in blood glucose levels. A significant effect was also produced by the methanolic extract of the drug. Interestingly, aqueous extract of the plant could also produce hypoglycaemia in diabetic rabbits. The acetohexamide (500 mg/kg), however, did not produce any significant hypoglycaemia in the

alloxan-diabetic rabbits. It is well known that acetohexamide stimulates the pancreatic beta cells to produce more insulin and increase glycogen deposition in liver (Goth 1985). In addition, alloxan is also known to cause a selective beta cytotoxicity. The sulfonylureas do not decrease blood glucose levels of alloxan-diabetic animals and it is only insulin that can lower than blood glucose levels (Gilman et al 1985). It is reported that the biguanides produce hypoglycaemia by increasing the glycolysis and uptake of glucose in muscles and by decreasing gluconeogenesis in the liver and absorption of glucose in the intestines (Gilman et al 1985). Furthermore the biguanides do not produce hypoglycaemia in the normal subjects because the increase in peripheral glucose utilization is compensated by an increase in hepatic glucose output. Thus, it is conceivable that *Ficus glomerata* fruits pulv contains more than one types of hypoglycaemic principles. Some one acts by stimulating the release of insulin while some other ingredient exerts an insulin-like action. However, its active principles do not seem to act like biguanides as the blood glucose levels have decreased in both normal and alloxa-diabetic rabbits. In this regard, a phytosterolin isolated from *F. religiosa* has been reported to produce similar results (Bever and Zahnd 1979). A bengalenoside, isolated from *F. bengalensis* has produced similar hypoglycaemic effect. However, these compounds were unable to reduce the blood glucose levels of the totally depancreatized animals. A fall of the blood glucose levels of alloxan-diabetic rabbits after oral administration of F. *religiosa* and I/V administration of *F. bengalensis* extracts have also been reported (Bever and Zahnd 1979). Since *F. glomerata* belongs to the same genus, it may also be supposed to contain similar glucosides.

Ficus glomertota fruits have also been found to contain high amounts of minerals including magnesium, phosphorous, calcium and other trace elements (Table 4). It may be, therefore, hypothesized that in normal rabbits the fruits pulv might have also produced hypoglycaemic effects by facilitating glucose uptake by the cells and by increasing the rate of phosphorylation of glucose. Furthermore, it has been reported that alloxan causes complexation with biological metals in P-cells producing their deficiency. Since *F. glom*erata pulv has exerted rapid hypoglycaemic action in normal and diabetic rabbits, it may be hypothesized that it could have also acted by providing the p-cells appropriate amounts of *these elements.* Accordingly, this plant drug might have initiated the release of insulin due to its trace minerals which deblock the enzymatic processes as already proposed by Leopold (1978) and Donsbach (1982). The term "hypoglycaemic elements" has, therefore, been coined for such minerals in the biological matter.

In conclusion, these data have suggested that there are more than one type of hypoglycaemic principles, both organic and inorganic, in *F. glomerata* fruits which produce a significant fall in blood glucose levels in normal and alloxan-diabetic rabbits by producing an organotropic effect on the B-cells which results in an increased release of insulin from the pancreatic beta cells. *F. glomerata* fruits pulv may, in the long run after more detailed studies, prove to be a more valuable antidiabetic agent as in addition to its insulin releasing and insulin-like activities, it also compensates the mineral deficiency that occurs in the diabetics due to osmotic diuresis. Remineralization could correct the effect of volume depletion and thus a decrease the release of stress hormones stimulated

through general adaptation syndrome described by Selyc (1976).

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