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HYPOGLYCAEMIC EFFECT OF POWDERED ALSTONIA SCHOLARIS (SATONA);

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ABSTRACT

To assess the hypoglycaemic effect of powdered Alstonia scholaris (Satona) leaves, 2 groups of normal (healthy) human volunteers and 4 groups of already diagnosed out-door patients suffering from non-insulin dependent diabetes mellitus (NIDDM) were randomly selected. Groups A and B comprising of 6 normal persons each were treated orally with 30 ml of plain water and 1.0 g of the powdered leaves along with 30 ml water, respectively. Groups C, D and E comprised of 6 NIDDM patients each and were treated orally with 1, 2 and 3 g of the powdered A. scholaris leaves, respectively. For comparison of hypoglycaemic activity, a 2.0 mg tablet of Amaryl (a standard hypoglycaemic sulphonylurea drug) was administered once a day to 6 NIDDM patients of Group F. The 2 hours-postprandial blood glucose levels of all test subjects were determined on the post-treatment days 0, 1, 8 and 15. After intake of 30 ml water only, no significant ($P>0.05$) change in blood glucose was noted while oral administration of Alstonia powder decreased the blood glucose levels of treated normal subjects significantly ($P<0.05$) on days 8 and 15. However, in NIDDM patients, treatment with 3 g of the powder (Group E) showed a highly significant ($P<0.001$) decrease in blood glucose on the days 1, 8 and 15th. In NIDDM patients treated with one 2 mg Amaryl tablet each (Group F) also showed a highly significant ($P<0.001$) decrease in blood glucose levels on the days 1, 8 and 15. It is conceivable, therefore, that powdered Alstonia scholaris leaves exert a consistent hypoglycaemic effect in patients with NIDDM. The mechanism of this hypoglycaemic effect of the plant drug has been already suggested to be insulin triggering and direct insulin-like actions.

KEY WORDS: Hypoglycaemic effect, Alstonia scholaris plant, Satona, NIDDM.

INTRODUCTION

Before the introduction of insulin, treatment of diabetes mellitus relied heavily on dietary measures and the use of traditional plant therapies. Many traditional plant treatments for diabetes exist even today[1,2,3].

In Pakistan, medicinal plants are abundantly available at relatively low cost. There is therefore, every virtue in exploiting such local resources of drugs for human and animal usage. However, only a few have received scientific or medical scrutiny and WHO has recommended that traditional medicinal plant treatments for diabetes warrant further evaluation[4].

Certain pharmacological studies have showed them to even possess interesting hypoglycaemic activities and are even relatively safe and free from side effects[5].

Alstonia scholaris that is commonly known as "Satona" grows wildly and abundantly in Punjab, Pakistan. Its leaves have been used in ethno-medicine for treating many diseases including diabetes mellitus. The bark is prescribed as appetizer, tonic febrifuge, galactagogue, anthelmintic, alterative and antiperiodic. Some plant parts have also been used to treat dyspepsia, liver complaints, diarrhoea and skin diseases[6,7].

An extract of the fresh bark is given with milk in leprosy. The bark juice and oil are used for earache. Infusion of bark is said to be effective in debility after fever and other exhausting diseases. It restores tone of stomach[8] and is used to treat malaria. Recently, Akhtar et al[9] have studied its hypoglycaemic effects in normal and diabetic rabbits after oral administration of powdered Alstonia leaves.

They were found to produce consistent hypoglycaemia in both normal and diabetic rabbits. However, as far as ascertained, no scientific study was available to evaluate its antidiabetic/ hypoglycaemic activity in the diabetic human patients. Therefore, in the present study, powdered Alstonia scholaris leaves were administered orally in various doses to normal subjects and non-insulin dependent diabetic human volunteers.

MATERIALS & METHODS

Two groups of normal (healthy) human volunteers and 4 groups of already diagnosed out-door patients suffering from non-insulin dependent diabetes mellitus (NIDDM) were randomly selected for the study. The groups A and B comprising of 6 normal persons each were treated orally with 30 ml of plain water and 1.0 g of the powdered leaves along with 30 ml water, respectively. Groups C, D and E comprised of 6 NIDDM patients each and were treated orally with 1, 2 and 3 g of the powdered Alstonia scholaris leaves with 30 ml water, respectively. For comparison of hypoglycaemic activity, a 2 mg tablet of Amaryl (glimepiride- a standard hypoglycaemic sulphonyurea drug) was administered once a day to 6 NIDDM patients of group F.

The normal volunteers had no previous history of diabetes and of any other serious disease. The Alstonia scholaris leaves were collected in the month of June 2001 from adjacent lawns of the Administration Block, University of Agriculture, Faisalabad and all the volunteers gave written consent for participation in the trial. Postprandial 2-hours blood samples were drawn from their fingers with a lancet and the blood glucose levels were immediately determined with One Touch Basic Plus Glucometer (Lifescan Company, Milpitas, California, USA). Results obtained were expressed as Means SEM and Student's "t" test was used to check their significance.

The $P<0.05$ values were considered significant while $P<0.001$ as highly significant [10]. Random samples of Alstonia scholaris leaves were also tested for their mutagenecity and carcinogenic potential for living cells at Nuclear Institute of Biology and Genetic Engineering, Faisalabad by the method of Maron and Ames[11].

RESULTS

The blood glucose levels of the treated normal and NIDDM diabetic (type II) volunteers before and after oral administration of the powdered Alstonia scholaris leaves on various days intervals are shown in Table-I. Salient features of the results are as follows:

Effect of Alstonia on normal subjects

Table 1 shows that oral administration of 30 ml water did not change the blood glucose levels on all the days checked. However, intake of Alstonia powder in single 1 g dose significantly ($P<0.05$) lowered the blood glucose levels on days 8 and 15th. The means SEM of the blood glucose levels on these days were 82 : 4 and 78 : 3 mg/dl, respectively (Table 1).

Effects of Alstonia on NIDDM patients

Table 1 also shows that powdered Alstonia scholaris leaves in single 2 g oral dose produced significant decrease ($P<0.05$) on day 15 while 3 g on day 1 significantly and on days 5 and 15 highly significantly ($P<0.001$) in the blood glucose levels of the NIDDM patients. The oral intake of 3 g Alstonia scholaris leaves powder by the diabetic patients decreased the blood glucose levels from 298 16 mg/dl on day 0 to 209±13, 144±8 and 126±7 mg/dl on days 1, 8 and 15. However, 1g dose of powder could not reduce the blood glucose levels on any of the days checked.

Effect of Amaryl (glimepiride) on NIDDM patients

Table 1 shows that blood glucose levels after administration of single 2 mg Amaryl tablet were 309±26, 265±21, 192±12 and 130±11 mg/dl on days 0, 1, 8 and 15. The statistically highly significant ($P<0.001$) reductions in blood glucose level were noted on days 8 and 15 after the Amaryl 2 mg tablet orally.

Mutagenecity testing

Ames Plate Incorporation Test and Microlitre Plate Assay (Chromogenic) reports showed the test plant to be non-mutagenic to both the test strains, which points out its possible suitability and safety for human consumption.

Table 1: Postprandial-2 hours mean SEM blood glucose levels of normal and diabetic human volunteers expressed as mg/dl on various days intervals after oral administration of water and 1,2 and 3 g of powdered Alstonia scholaris (Satona) leaves and Amaryl ® 2 mg tablet once daily.

Day(s) interval	Normal Subjects		Diabetetic Subjects			
	Group A Control, 20 ml plain water	Group B 1g of A. scholaris	Group C 1g of A. scholaris	Group D 2g of A. scholaris	Group E 3g of A. scholaris	Group F Amaryl® 2mgTablet
Day 0	103±6	96±4	272±21	319±22	298±16	309±26
Day 1	105±7^{NS}	100±6	225±20^{NS}	301±23^{NS}	209±13*	265±21*
Day 8	113±6^{NS}	82±4*	190±14^{NS}	245±18^{NS}	144±8**	192±12**
Day 15	112±5^{NS}	78±3*	185±12^{NS}	165±13*	126±7**	130±11**

No of test subjects in each group = 6, N.S. = Non-significantly decrease from zero day ($P<0.05$)
* = Significantly decrease from zero day ($P<0.05$), ** = Highly significantly decrease from zero day ($P<0.001$)

DISCUSSION

At the global level, prevalence of diabetes has been reported to be about 120 million people which in the year 2025 would reach about 256 million[12]. In the traditional medicine several plants have been used since ancient times for the treatment of various diseases[1,6]. Modern researches on indigenous medicinal plants have revealed the presence of active principles, which could prove useful for treating many diseases including diabetes[13,14].

In the present study, data summarized in table 1 have shown that significant and consistent reduction in the blood glucose levels of normal (healthy) volunteers was produced by 1 g single oral dose of powdered Alstonia scholaris (Satona) leaves. In addition, a dose dependent hypoglycaemic response was produced by 2 and 3 g single oral doses of Alstonia powder and Amaryl 2 mg tablets in type II (non-insulin dependent) human diabetics. The reductions in blood glucose levels were highly significant ($P<0.001$) with 3 g oral dose of plant drug and Amaryl tablets on days 8 and 15. It is well established that the sulphonylurea oral hypoglycaemic drugs produce hypoglycaemia by stimulating the pancreatic ß-cells to release more insulin in type II diabetics[15]. Therefore, it is possible that Alstonia scholaris leaves act by a similar mechanism. However, they have been reported to contain high amounts of chromium, magnesium, zinc, sodium, potassium, manganese and iron[9]. Thus it is also possible that they act by providing the ß-cells appropriate amounts of certain element(s) as proposed by Leopold[16] and Donsbach[17].

In conclusion, it may be suggested that the hypoglycaemic principles in the Alstonia leaves exert an insulin releasing effect on the ß-cells of both normal and type II diabetics. However, it appears that the powder contains more than one active principles which act not only indirectly by initiating the release of insulin effect but also a direct insulin-like effect in diabetic patients as their ß-cells cannot release insulin. This postulation is, further, supported by the results of an earlier study carried out in the normal and diabetic rabbits[9]. The data discussed above do support that in the type II diabetics.

Alstonia would be sufficiently effective and able to

control their blood glucose levels in appropriate doses in most of the moderately diabetic cases. However, in severely diabetic patients, the plant drug may have to be supplemented with low doses of some oral sulphonylurea drug. In the end, it may be further emphasized that the plant drug may exert a number of other pharmacological actions, which should also be taken care off. Thus the results of this study have validated the folkloric use of this cheap natural remedy of indigenous plant origin for the treatment of non-insulin dependent diabetes mellitus. However, large-scale double blind clinical trials are still required to establish the real usefulness of the indigenous drug.

Similarly activity directed phytochemical studies are required to isolate pure compounds. Such researches may help in finding newer model chemical compounds for the treatment of diabetes.

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