

Update Article

TRADITIONAL REMEDIES FOR DIABETES MELLITUS : TRAILS, TRIALS AND TRILATERAL QUEST*

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"It should be remembered that, although estimates will vary, the most commonly quoted figure as to the number of higher plants found growing on planet earth is about 500,000. One often finds quoted educated "guesstimator" that "less than 5% (or 10% or 15%) of plants have been investigated for pharmacological active principles". It should be noted that in many instances, the pharmacological screens did not include animal models to detect the type of activity for which the plant was allegedly used by the natives. As time passed, the pharmacology staff became irritated with thick, sticky extracts that clogged up their syringes and which, for the most part, did not give dramatic activity".

Norman R. Farnsworth

There is currently a significant shift from the state of affairs, indicated by Farnsworth, 14 years back. Our efforts, for many years, were directed towards first finding out clinical activity of medicinal plants and then proceeding for phytochemistry and/or pharmacology^{2,3,4}. There has been a significant impact of this cost-effective clinical to laboratory, approach on the medicinal plant research in India, as well as in other countries. The quest is trilateral-shared by pharmacologists, phytochemists and clinicians. The trails followed up are often picked up from the literature on

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ethnobotany, the books on traditional systems of medicine and the use of the medicinal plants in alternative health care or as folklore remedies claimed to be useful in the treatment of diabetes mellitus, in different parts of the world are of a sizeable number. In India, such plants and remedies mentioned and used for the treatment of diabetes mellitus date back to the ancient authorities like Bhrigu⁵, Charaka, Sushruta and Vagbatta, the last three called Vriddha-trayi of Ayurveda⁶. The text of Ayurveda also describe quite elaborate details on diabetes mellitus-clinical features and complications⁷. A very interesting point is mentioned by Vagbhatta that the diabetic must walk for long distances; it is now that we learn that exercise can induce insulin receptors.

For last several decades, many Indian pharmacologists have tried to study in animals hypoglycaemic activity of plants and traditional remedies⁸. But the claims of presence and/or absence of hypoglycaemic activity in the same plants have resulted because of several factors-improper choice of animal models, no standardisation of the extracts used etc. Rabbits have been used by several investigators⁹; it is known that rabbits are not very suitable for studying the hypoglycaemic activity. Most of the investigations have been with alloxan-induced diabetes; it is now well recognised that strepto-

zotocin-induced diabetes in rats and monkeys provide a better model. Under these circumstances, clinical studies when properly conducted-gain more relevance. Moreover, the degree of hypoglycaemic activity has to be seen in a proper perspective with the high potency of the modern drugs.

The method of the study was as follows :

After a complete glucose tolerance test, diagnostic of diabetes mellitus, the patient with N.D.D.M. was selected. All the anti-diabetic drugs were discontinued. No major changes in diet were advised. The patient was prescribed placebo capsules for one week. At the end of one week, the acute effects of placebo on the fasting blood sugar levels were observed for three hours; the blood samples were drawn at 0, 1, 2 and 3 hours. The patient was put on the ayurvedic drugs for 2 to 12 weeks and the acute response to ayurvedic drug was carried out and blood sugar was measured by Folin-Wu or Nelson-Somogyi method; same method was utilised for a specific plant.

We have conducted placebo-controlled and laboratory-blind studies, on diabetic patients

with properly identified, collected, stored and dispensed ayurvedic plants. We observed that in 85 fasting diabetic patients, placebo perse can reduce the blood sugar at 2 and 3 hours (Fig. 1). The observation further emphasises

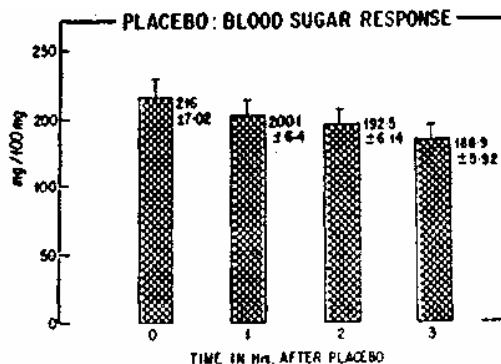


Fig. 1 : Reduction in blood sugar following placebo.

the need to conduct placebo comparisons in clinical studies. The drop in blood sugar was more at three hours than at one hour.

The list of medicinal plants and remedies, studied by us, over almost a decade is shown in Table 1. Besides this list, few others were also studied in a preliminary manner-Asanshia, Ficus benghalensis, Trivang-bhasma, Nyctan-

Table 1 : Medical Plants and Remedies Screened Clinically in Patients with Diabetes Mellitus

Ayurvedic/Vern Name	Botanical Name/s etc.	n
1. Shilajieet	Exudation from Himalayan rocks	6
2. Bilwa	Aegle marmelos	6
3. Saptarangi	(a) Salacia prenoidcs	12
	(b) Casearia esculenta	5
4. Daruharjdra	Berberis aristata	10
5- Guduchi	Tinoipera cordifolia	8
6- Ram Udad	Cassia absus	10
7. Neem	Azadirachta indica	6
8. Jambool	Eugenia jambolina	11
9. Tendli	Coccinia indica	20

n=94

thes arbortristis, etc. The results were not conducive to further work.

1. Shilajeet

Six patients studied for 3 to 4 months did not show any hypoglycaemic activity. But, most interestingly, the patients spontaneously reported relief in some of their symptoms bodyache, tingling numbness and weakness. Some patients also reported a relief in polyuria. These observations are to be followed-up with studies on nerve-conduction velocity in diabetic neuropathy. It may also be worthwhile to study the effects of Shilajeet in early autonomic neuropathy. Benzoic acid and hippuric acid are in significant quantities in Suddha Shilajeet 8.5 and 6.1% respectively. Chopra ascribed activity of Shilajeet to benzoic acid but this was questioned by other investigators. The dose of Shilajeet prescribed by Vagbatta is quite large and no safety studies with these doses have been carried out. The present dose was 1/2 teaspoonful twice in a day for 3-4 months.

2. Aegle marmelos

The root powder was administered in a dose of 5 gms b.d. to 3 patients for 4 to 6 weeks. No hypoglycaemic activity was observed. One patient reported relief of body-ache. Three patients received fresh juice of leaves-30 ml. b-d. for 2-3 weeks. There was no hypoglycaemic activity observed; glycosuria was also not affected. There is still a need to conduct studies with higher doses, but traditionally study doses are commonly used-

3. Salacia prenoides

The extract of the root was administered in a dose-equivalent to 25 gms b.d. for continued therapy and 50 gms for acute studies. None

of the twelve patients on *S. prenoides* showed any significant reduction in the fasting or subsequent blood sugar levels as compared to placebo. No adverse reactions, except in one patient, were observed. In one patient even three months therapy did not show any significant reduction in fasting blood sugar. In two patients, constipation was relieved. The individual responses in 12 patients, placebo and *S. prenoides* are shown in Fig. 2.

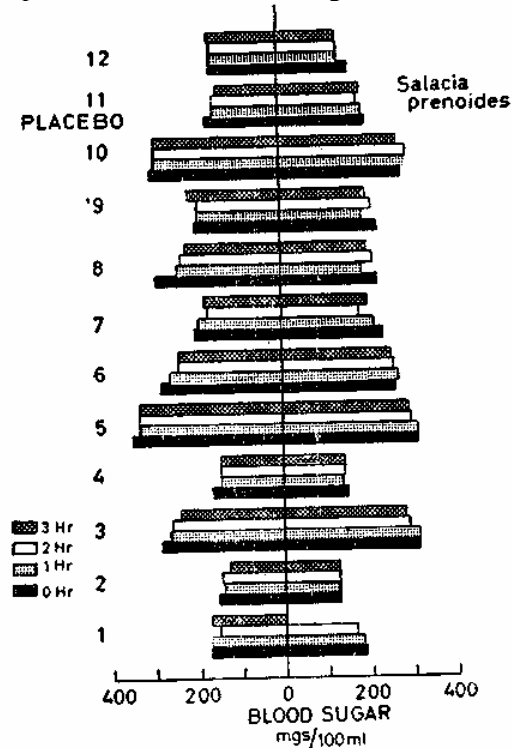


Fig. 2 : Blood sugar values following placebo and *S. prenoides* administration.

4. Caseria esculenta

As *S. prenoides*, as well as *C. esculenta* are known as saptarangi, the latter was also studied. No significant fall in blood sugar was observed. No side-effects were observed.

5. Berberis aristata

Ten patients (3 F and 7 M) received the extract of *B. aristata* root powder, equivalent to 25-50 gms of powder, in divided doses per day, for 2 to 6 weeks. As it can be seen from Fig. 3, there was hardly any significant difference in

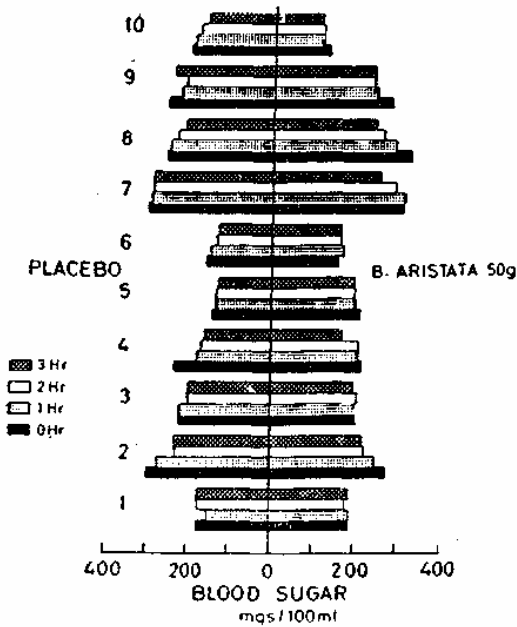


Fig. 3 : Blood sugar values following placebo and *B. aristata* administration.

blood sugar values following placebo or *B. aristata*. Only one patient, No. 10, on a dose of 50 gms equivalent extract per day for two months showed a drop of 70 mg % in the fasting blood sugar and a drop of 60-70 mg % in all one, two and three hourly samples compared to placebo. The duration of diabetes mellitus was only six weeks in this patient, unlike the rest eight patients ranging from 1/2 to 10 years. However, one patient, with a duration of six months, did not show significant reduction. Only one patient reported a

sensation of burning all over the body. Two patients who had elevated blood pressure, basally, showed a reduction from 160/110 to 140/180 mm Hg and from 160/110 to 136/90 mm Hg. This needs to be investigated further because berberine—the active principle of *B. aristata* has been shown to have interesting pharmacological and bio-chemical activities¹⁰.

6. Tinospora cordifolia

T. cordifolia, a very popular Rasayana of ayurveda was given as extract prepared from the stem powder 25 gms b.d. and 50 gms for acute study. There was no significant difference in the blood sugar values after *T. cordifolia* as compared to placebo, in 8 diabetic patients (Fig. 4). Experimentally, Gupta *et al.*

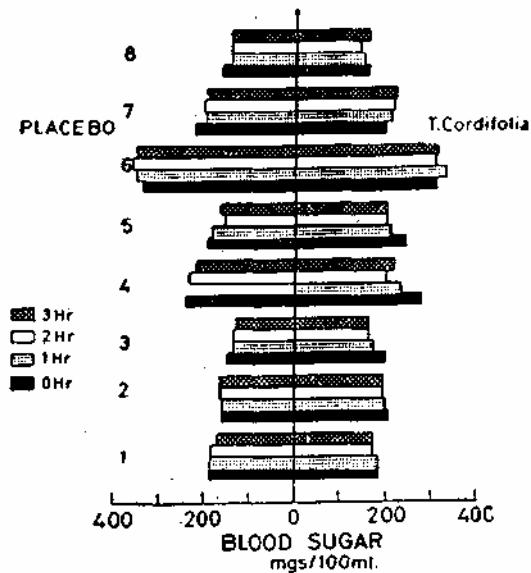


Fig. 4 : Blood sugar values following placebo and *T. cordifolia* administration

have shown hypoglycaemic activity of *T. cordifolia*; adrenaline—induced hyperglycaemia was counteracted and glucose uptake by rat diaphragm induced by insulin was potentiated¹¹. This has not been confirmed by others.

One patient complained of loss of appetite, constipation, flatulence, nausea with a dose of 25 mg b.d. These side-effects were relieved by reduction of dose to 12.5 gms b.d.

7. *Azadirachta indica*

Six patients studied with *A. indica* did not show any significant reduction in blood sugar as compared with placebo. The dose used was 2.5 gms of leaf powder b d. Two patients complained of diarrhoea; in one patient this was transient and self-limiting; in another one a reduction of the dose to 1.25 gm b.d. led to relief. The latter patient also reported relief in pruritus with *A. indica*. This plant needs to be studied further as experimental studies have shown hypoglycaemic activity.

8. *Eugenia jambolina*

The root powder was administered in a dose of 5 gms b.d. to 8 diabetic patients. The fasting blood sugar was reduced significantly only in 2 patients. However, there was no statistically significant difference between the placebo and *E. jambolina* groups in acute studies. Relief of cramps, pruritus, polyphagia and polyuria were reported in 5 patients. The side-effects observed were dryness of mouth, nausea and diarrhoea in one patient each. There is a need to study higher doses of this plant.

9. *Coccinia indica*

The leaf powder (lyophilized) was studied in two doses 5 gms and 10 gms p.o. for acute studies in 6 volunteers for hypoglycaemic activity and tolerability. The powder was well tolerated and no hypoglycaemic activity was observed. Azad-Khan¹² *et al.* showed that *C. indica* as compared to placebo reduced the fasting sugar (195±53 mg % to 181 ±51 mg %

with placebo and 179±51 rag % to 122±48.5 mg with *C. indica*). At the dose of 1.2 g p.o. of the leaf powder in 3 diabetic patients, no reduction in fasting blood sugar was observed by us. The maximum changes observed with placebo and *C. indica* were coparable. With the dose of 1.8 g p.o. an increase in fasting blood sugar was observed in one patient from 272 to 336 mg %. The highest dose used was 2.4 g; this did not have any significant effect on the fasting blood sugar. However, with this dose, in 3 patients of NIDDM, the acute studies showed consistently more hypoglycaemia than with the placebo. This dose and higher doses need to be studied on a larger sample size. *C. indica* was well tolerated. Acute toxicity of *C. indica* in rats and mice showed LD 50 > 3 gms/kg and in dogs 1 g/kg induced no emesis.

10. Other plants

*Curcuma longa*¹³, *Momordica charatia*, *Eucalyptus*¹⁴, *Allium cepa*, *Allium sativum*¹⁵, *Dolichos biflorus*, *Ficus benghalomis*, *Ficus glomerata*, *Gymnema sylvestre*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Rieva cunata*, etc have studies—experimental and uncontrolled clinical, showing hypoglycaemic activity. Recently, *Trigonella foenum-graecum* (Methi)¹⁶ has been shown to have hypoglycaemic activity both at the National Institute of Nutrition (ICMR) and Swami Prakashananda Ayurveda Research Centre in preliminary studies. This lead needs to be followed up like Guar gum, which has adjuvant use in NIDDM patients. There is a need to establish a clinical screening unit for placebo controlled studies.

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