

Clinical Evaluation of Antidiabetic Activity of *Trigonella* Seeds and *Aegle marmelos* Leaves

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Abstract: Diabetes mellitus is a heterogenous metabolic disease characterized by altered carbohydrate, lipid and protein metabolism. So many traditional herbs are being used by diabetic patients to control the disease. But very few studies are performed to investigate the efficacy of these herbs clinically. In the present study, an attempt has been made to investigate clinically the antidiabetic activity of Fenugreek seeds (FG) (*Trigonella foenum-graceum* Linn.) and Bael leaves (BL) (*Aegle marmelos*, Corr.) individually and collectively in non insulin dependent diabetes mellitus (NIDDM) patients. Literature survey reveals their antidiabetic activity in animals but no such studies were performed clinically. FG were powdered and used for the study. BL dried in shadow, were powdered and its decoction was used for the study. The study was performed in four different groups for a period of 16 weeks. Each group was having 20 NIDDM patients, whereas five patients were kept as control subjects. Inclusion and exclusion criteria were formed for the study. Written consent was taken from the patients. Initial postprandial blood glucose level (PPBGL) was estimated at the time of enrolment in the study and then after each week during the entire period of the study. At the end of the study, the initial and final readings were compared. There were significant changes in PPBGL of patients who were receiving these two herbs collectively as compared to the other patients who were receiving these herbs individually in comparison to patients who were on their standard oral hypoglycemic therapy. FG powder 20gm and decoction of 5gm BL powder individually once daily orally were found to have antidiabetic effect. It was more markedly observed when these drugs were given in combination.

Key word: Antidiabetic activity • Bael leaves • Fenugreek seeds

INTRODUCTION

Diabetes mellitus (DM) is the commonest endocrine disorder that affects more than 100 million people worldwide (6% of the population) [1]. It is caused by deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. It is found to damage many of the body systems, particularly the blood vessels and nerves [2]. For its therapy, along with the synthetic drugs, many agents of the plant origin are also in use particularly for the treatment of non insulin dependent diabetes mellitus (NIDDM).

Plants are always an exemplary source of drugs; in fact many of the currently available drugs were derived either directly or indirectly from them. According to world ethnobotanical information reports, almost 800 plants may possess antidiabetic potential [3]. In the past decade, research has been focused on scientific evaluation of traditional drugs of plant origin and screening of more

effective and safe hypoglycemic agents has continued to be an important area. In developing countries 80% of population are using traditional medicine in primary medical problems [4]. However, lots of herbs are now being used in the management of DM.

In the present study, an attempt has been made to investigate clinically the antidiabetic activity of Fenugreek seeds (FG) (*Trigonella foenum-graceum* Linn.) and Bael leaves (BL) (*Aegle marmelos*, Corr.) individually and collectively in NIDDM patients. Literature survey reveals their antidiabetic activity in animals but no such studies were performed clinically.

FG commonly known as methi belongs to the family *Leguminosae*, used as food and for medicinal purposes [5]. It is a good source of many essential elements such as iron, phosphorus and sulfur [6]; seeds can inhibit cancer of the liver, lower blood cholesterol levels and also have an antidiabetic effect [7]. It is also used in the treatment of late-onset diabetes, poor digestion (especially in convalescence), insufficient lactation, painful

menstruation, labor pains etc. [5, 8]. Compounds extracted from the plant have been shown cardiogenic, hypoglycemic, diuretic, antiphlogistic, hypotensive activity and hypocholesteremic properties. It may increase plasma insulin level *in vivo* [9, 10]. Its major free amino acid 4- hydroxyisoleucine stimulates insulin secretion from perfused pancreas *in vitro* [11].

BL is a popular plant and cosmopolitan in distribution. It has many medicinal properties such as antifungal, antibacterial, antiprotozoal, hypoglycemic etc. Insulin like action of its leaves on hyperglycemia and their mechanism of action has been reported in the animal studies [12-17].

METHODS

For carrying out the study, clinical protocol was set and was approved by the institutional ethical committee. This study was performed under the supervision of physicians. Inclusion and exclusion criteria were formed for the study. Written consent was taken from the patients. Initial postprandial blood glucose level (PPBGL) was estimated at the time of enrolment in the study and then after each week during the entire period of the study. At the end of the study, the initial and final readings were compared.

Inclusion Criteria:

- Type 2 diabetic patients with fasting plasma glucose level equal to or greater than 140 mg/dl of blood with out any detectable/visible complications [18].
- Type 2 diabetic patients taking oral hypoglycemic agents with history of inadequate control of blood glucose with these agents.
- The patients were of either sex (male or female) between the ages of 35-60 years.

Exclusion Criteria:

- Pregnant or nursing patients.
- Smokers
- Patients with GIT, hepatic, cardiovascular, renal or endocrine disorder (other than diabetes mellitus) which can interfere with the absorption, metabolism and excretion of the study plant.
- Patients with any complication of diabetes mellitus.
- Patients suffering from type 1 (IDDM) diabetes mellitus.

Subjects: The selected subjects were medically examined and given code numbers and were asked to present

themselves on a specified date for sample collection. Initial postprandial blood glucose level (PPBGL) was estimated at the time of enrolment in the study and then after each week during the entire period of the study.

Blood Sample: Blood samples (3-5 ml) were drawn from each patient and control subject by vene-puncture through plastic disposable syringes. The blood samples were collected in clean oven dried glass bottles which were previously rinsed with 1% sodium fluoride, 3% potassium oxalate solution to prevent coagulation and glycolysis. The plasma was separated after centrifugation. Any sample showing haemolysis was discarded. After separation of plasma, it was transferred to clean, previously acid rinsed, washed and oven dried glass bottles with plastic caps. The plasma glucose estimation was done immediately on the same day by O-toluidine method [19].

Plants: FG and BL were obtained from the local market. They were identified and authenticated by the botanist and then used for the study.

General Plan of Study: FG were powdered and used for the study. BL dried in shadow, were powdered and its decoction was used for the study. A suitable dose was decided by initial randomized study in the first week. The study was performed in four different groups for a period of 16 weeks. Each group was having 20 NIDDM patients.

- Group I received only FG powder 20gm once daily.
- Group II received only decoction of 5gm BL powder once daily.
- Group III received FG powder 20gm + 5gm BL powder once daily.
- Group IV received their regular oral antidiabetic drugs.

Whereas five patients served as control group (without any therapy either the test or standard hypoglycemic agents) in the study

Drop Outs: No dropouts recorded in the study.

Compliance: All participants in the study were showing the compliance and were following the instruction regarding the diet and exercise.

Untoward Effects: Some of the patients they complained about the flatulence. It may be due to the bulking effect of FG where as some others complained about the headache which may be psychological.

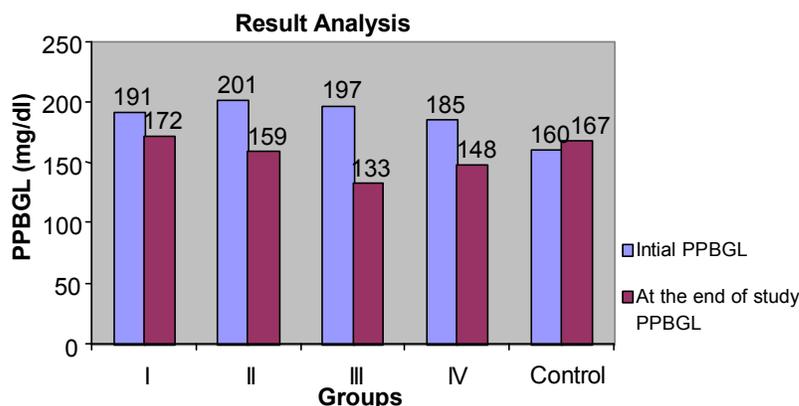


Fig. 1: Comparison of antidiabetic effect on PPBGL in NIDDM patients

Table 1: Showing effects on PPBGL by FG and BL in different study groups (The values are given as Mean \pm SD)

Groups	Initial PPBGL	At the end of study PPBGL
I	191 \pm 10	172 \pm 8
II	201 \pm 6.5	159.4 \pm 5
III	197 \pm 7	133 \pm 8
IV	185 \pm 7	148 \pm 9
Control	160 \pm 5*	167 \pm 7*

(* Non significant changes in PPBGL)

RESULTS

There were significant changes in PPBGL of group III as compared to all other groups. The order of decrease in PPBGL was Group III>II>IV>I, whereas there were no any significant results seen in control patients. The results are summarized in the Table 1 and Fig. 1.

DISCUSSION

A significant decrease was noted in PPBGL sixteen weeks after administration of BL and FG individually and collectively. The fall in PPBGL was more marked in group III where patients were receiving these herbs collectively as compared to other groups whereas in controlled patients the PPBGL changes were nonsignificant.

FG powder 20gm and decoction of 5gm BL powder individually once daily orally were found to have antidiabetic effect. It was more markedly observed when these drugs were given in combination.

The studies suggest that the Bael leaves produce hypoglycemic effect probably by enhancing the peripheral utilization of glucose, correcting the impaired hepatic glycolysis and limiting its gluconeogenic formation similar to insulin [16, 17] whereas fenugreek seeds show hypoglycemic activity due to its fibre content along with other chemical constituents [9].

CONCLUSION

FG and BL can be combined in high dose with oral hypoglycemic agents to bring the blood glucose to normal levels in patients whose diabetes is not controlled with these agents or in those patients in whom these drugs produce adverse effects on dose increments. Our study has opened up a new direction for future large scale clinical research to find an alternative and inexpensive herbal formulation for the NIDDM.

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