Comparative Study of Fenugreek Seeds on Glycemic Index In High And Medium Dietary Fiber Containing Diets In NIDDM Patients.

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Abstracts: Background: Several studies have reported the hypoglycemic property of Fenugreek seeds (Trigonella foenum graecum), a commonly used condiment in Indian homes, due to its high dietary fiber content. Method: A total of 25 NIDDM patients were given control diets orally consisting of (i)milled rice(boiled rice),(ii) whole wheat (chapati) experimental diets consisting of (iii) boiled rice with fenugreek seed powder and (iv) chapati with fenugreek seed powder given on four consecutive days. Blood was collected at 0, 15, 30,45,60,90 and 120 minutes. Area under curve and glycemic index was calculated for both control and experimental diets. Results: The mean of area under curve of rice with fenugreek and wheat with fenugreek are significantly lower when compared with only rice and only wheat taken orally respectively. Further, the mean glycemic index was significantly lower when fenugreek was given 15 minutes before meal compared to fenugreek given along with meal. Conclusion: Fenugreek has a lowering effect on glycemic index when added to rice and wheat diets, due to delayed gastric emptying and increased intestinal transit time. In addition, fenugreek decreases glucose absorption and inhibits starch digestion due to presence of soluble fiber and galactomannans. Adding fenugreek to the diet of diabetes patients 15 minutes before the meal causes a significant reduction in glycemic index and is beneficial to NIDDM patients for long term control of their blood glucose levels and prevention of hyperglycaemia related complications. [Sampathkumar V NJIRM 2011; 2(3) : 29-37]

Key Words: Fenugreek, glycemic index, Area under curve, control and experimental diets.

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Introduction: Diabetes is the third commonest disease in the world, next to the cardiovascular and oncological disorders[1]. The International Diabetes Federation Directory, in 1994 showed that the global burden of the disease was estimated at 110 million and this figure is likely to increase further to 239 million by 2025[2]. The countries with the largest number of diabetic people will be India, China and USA by 2030. It is estimated that every fifth person with diabetes will be an Indian. The type – II diabetes is non-insulin dependent and is the most common form of diabetes and patients retain endogenous insulin production but exhibit excessive adiposity and resistance to peripheral action of insulin[3].

The development and progression of micro-vascular complications is associated closely with chronic hyperglycaemia. Therefore, tight glycemic control is by far the most effective approach in the prevention of diabetic vascular complications. [4].
Although euglycaemia can be achieved in diabetes patients by conventional insulin and oral hypoglycaemic drug treatment, microvascular and neurological complications cannot be prevented by this[5]. Insulin treatment has also been reported to increase cholesterol synthesis[6] and secretion of very low density lipoproteins[7]. Adherence to long term carbohydrate restricted diet also leads to the development of insulin resistance and thus serum cholesterol levels are raised in diabetic patients[8].

Diet has been recognized as a corner stone in the management of diabetes mellitus. Persons with diabetes may get substantial benefits by increasing their intake of dietary fiber[9]. Fiber present in vegetables, fruits, legumes and fenugreek seed is soluble in nature and more effective in controlling blood sugar and serum lipids than the insoluble fiber present in cereals and millets[10].

Fenugreek is a leguminous herb, commonly cultivated and used as a condiment in India and North African countries. The seeds are yellow in colour, bitter to taste[11] and are a rich source of fiber. It contains mucilaginous fiber and total fiber to the extent of 20% and 50% respectively. In addition it also contains trigonelline, an alkaloid known to reduce blood glucose level. Fenugreek seed powder in the diet reduces blood sugar and urine sugar with concomitant improvement in glucose tolerance and diabetic symptoms in both NIDDM and IDDM. [12].

Different carbohydrates raise the blood sugar to variable extents. Glycaemic index indicates the extent of rise in blood sugar in response to food in comparison with the response to an equivalent amount of glucose. High carbohydrate and high fiber diets improve the glucose tolerance and reduce diabetic symptoms and the dose of oral hypoglycemic drugs required[13].

In the present study, an attempt has been made to determine the glycaemic indices of Chapati and Rice (common Indian recipes) with and without fenugreek and also to correlate the values of glycaemic index and its usefulness in the management of NIDDM.

Material and Methods: Selection of subjects: Twenty five non insulin dependent diabetes mellitus (NIDDM) subjects diagnosed since two to ten years, of either sex aged between 40 to 60 years were included in the study. Diabetes was diagnosed on the basis of WHO criteria[14].All the patients were on oral hypoglycaemic drugs. The study was conducted with the approval of the institutional ethical committee. Patients diagnosed as diabetes but suffering from gastro intestinal disorder were excluded from the study.

Nutritive values of Prepared test foods: Milled Rice: 200gm of cooked rice contained 50gm of carbohydrates, 4gm of proteins, 0.5gm fats and provided 220kilo calories[15]. Wheat: 103gm of chapati contained 50gm of carbohydrates, 10gm of proteins, 1.5gm of fats and provided 257 kilo calories[16]. Fenugreek: 12.5gm of ground whole fenugreek seed contained 3.17gm of proteins, 0.987gm of carbohydrates, 6gm of total fiber, 2.5gm of gum and 3.5gm of Natural detergent fiber[17].

Preparation of Fenugreek Seed powder: Fenugreek seeds were soaked overnight and allowed to germinate and to eliminate the bitter taste, and then the seeds were dried after removal from the water, and were ground to a fine powder[18].

Analytical method: Quantitative determination of whole blood glucose from fresh capillary blood was done by the glucometer Accutrend alpha, which is based on glucose – oxidase mediated reaction.[19] Procedure for Meal tolerance test: The Meal tolerance test (MTT) was conducted in patients on overnight fast both with and without addition of ground fenugreek seeds over a period of 5 days.All the studies were begun at 8 am. On the first day, the fasting blood glucose (0 minute) was estimated by glucometer and then 50g of glucose along with 250ml of water was given orally. After the glucose consumption the blood glucose levels were estimated again at 15, 30,45,60,90 and 120minutes. On the following four days control and experimental diets (Rice, Wheat and Rice with fenugreek, wheat with fenugreek) were administered successively which provided 50 grams of carbohydrate.

Day 1 - Oral glucose,
Day 2 - Rice,
Day 3 - Wheat (Chapati),
Day 4 - Rice with fenugreek,
Day 5 - Wheat with fenugreek.

15 subjects were administered Fenugreek seed powder mixed with water and consumed 15minutes before the meal and 10 subjects were given the same along with the meal. All subjects tolerated the fenugreek without difficulty and no side effects were reported. Blood glucose levels were estimated using glucometer by collecting blood samples at 15, 30, 45, 60, 90 and 120minutes.

Calculation of glycaemic index[20]: Area under the glucose curve and glycaemic index of each preparation was calculated as suggested by Wolever and Jenkins. The GI value was calculated to know the extent of rise in the blood sugar in response to the test food in comparison with the response to an equivalent amount of glucose.

$$\text{GI} = \frac{\text{Area under blood glucose response curve for 50g of test carbohydrate food.}}{\text{Area under blood glucose response for 50g of glucose}} \times 100$$

The method used to calculate the incremental area under the blood glucose response curve is illustrated in figure1.

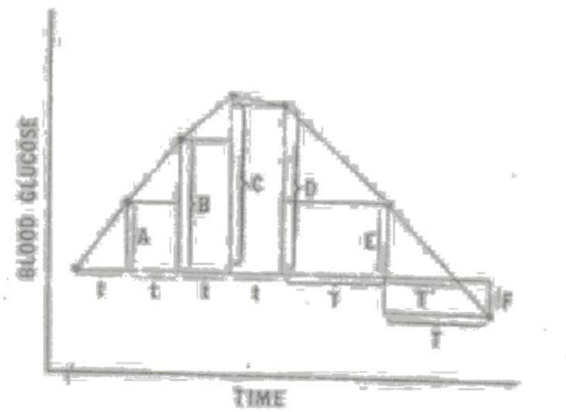

Fig 1: General blood glucose response curve for illustrating the method of calculation of the incremental area under the blood glucose curve.

It is the sum of the areas of triangles and rectangles, calculated geometrically as follows.

$$\text{Area} = \frac{At}{2} + At + \frac{(B-A)\,t}{2} + Bt + \frac{(C-B)\,t}{2} \text{ --- etc.}$$

Where A,B,C,D,E and F represents the blood glucose increments, i.e., the differences between the blood glucose concentration fasting , and at times t,2t,3t, 4t, 4t+T and 4t+2T after the start of the meal. 't' and 'T' represent different time intervals between blood samples.

As shown in the above fig. 1 the blood glucose concentration at F is less than the fasting concentration, only the area represented by the triangle ET is above the fating level, and therefore only this portion is included in the 'Total' area. T^1 represents the portion of the time interval T when the blood glucose between E and F is above the fasting level.

Since $E = T^1$, $E+F = T$

Therefore $\frac{E\,T^1}{2} = \frac{E^2\,T}{2\,(E+F)}$

The overall equation simplifies to

$$(A + B + C + D)\,\frac{t}{2} + \frac{(D + E)\,T}{2} + \frac{E^2\,T}{2\,(E + F)}$$

If the last blood glucose concentration, F, is above the fasting level, instead of below as shown here, the last term in the equation (namely E^2 T/ 2 (E+F) becomes E+F) T/2).

Result: Twenty five non-insulin dependent diabetes mellitus patients (13 male and 12 female) aged between 40-60 years (50±4 years) participated in the metabolic study. The diagnosis of diabetes was based on WHO criteria and duration of illness varied from 2 to 10 years (5±1.8 years).

In general, both control diets (Boiled rice and chapati) as well as experimental diets (Boiled rice with fenugreek seed powder and chapati with fenugreek seed powder) were found to be acceptable and the diabetic patients had no difficulty in consuming these diets. Both the control and experimental diets were almost isocaloric and had similar nutrient composition except for the fiber content which was higher in the diets containing fenugreek.

The blood glucose values were analysed at 0, 15, 30,45,60,90 and 120 minutes in NIDDM subjects with control and experimental diets. The mean and standard deviation values were calculated for blood glucose values in both control and experimental diets.

Table.1: Blood glucose in NIDDM subjects with glucose (Standard), control and experimental diets are tabulated as follows.

Time interval (min)	Blood Glucose values(mg/dl) after oral glucose, control and experimental diets in Mean± SD				
	Glucose	Rice	Wheat	Rice with fenugreek	Wheat with fenugreek
0	161±32	168±28	160±32	155±32	160±24
15	184±36	183±28	172±32	166±35	170±26
30	208±35	204±28	190±30	177±38	181±27
45	240±36	229±31	221±39	193±39	196±30
60	260±39	248±32	237±35	216±39	219±35
90	257±35	247±31	232±38	222±37	221±28
120	232±41	230±30	217±33	212±37	211±26

The mean blood glucose values are relatively lower with different control and experimental diets when compared to blood glucose levels after glucose administration at all the time intervals of blood glucose estimation as depicted in Table 1.

The increases in mean blood glucose concentrations and percent increments after carbohydrate load occurred up to 60minutes with glucose, rice and wheat and up to 90minutes with, rice with Fenugreek and wheat with Fenugreek. Highest increments occurred up to 45minutes with glucose, rice and wheat; whereas the same were observed up to 60minutes with rice with Fenugreek and wheat with Fenugreek. Total increments after various diets were less compared to those of glucose and were also less for Fenugreek containing diets compared to those without Fenugreek. Delay in occurrence of peak and relatively longer period for the total increments are observed with diets containing Fenugreek as shown in Table 2.

Table 2: Blood Gucose values in both control and experimental diets at various time intervals are calculated and presented in the following table.

Time interval (min)	Glucose mg/dl (%)	Rice mg/dl (%)	Wheat mg/dl (%)	Rice with Fenugreek mg/dl (%)	Wheat with Fenugreek mg/dl (%)
15	23(14)	18 (9)	12 (8)	11 (7)	10 (6)
30	24 (13)	21(11)	18 (10)	11 (7)	11 (6)
45	32 (15)	25 (12)	31 (16)	16 (9)	15 (8)
60	20 (8)	19 (8)	16 (7)	23 (12)	23 (12)
90	-	-	-	6 (3)	2 (1)
Total incre-ments	99	83	77	77	61

In order to assess the glycaemic responses of various carbohydrate loads, blood glucose area under the curve is calculated by using the formula of Wolever and Jenkins. The mean and standard deviation values are calculated. The data is statistically analyzed by using student ‘t’- test. The mean AUC values with all control and experimental diets are lower than AUC of glucose, and this difference is statistically significant as depicted in table 3.

Table 3: Comparison of mean±SD of area under curve (AUC) (mg/dl/min) of glucose (standard) with control and experimental diets.

Food	Mean	SD	P
Glucose	8468	648	-
Rice	6731	633	<0.001
Wheat	6313	587	<0.001
Rice with Fenugreek	5246	888	<0.001
Wheat with Fenugreek	4887	773	<0.001

In order to assess and classify the glycaemic response to various foods, the glycaemic indices for control and experimental foods are calculated using glucose as standard and presented in Table 4. Rice has highest while wheat with fenugreek has lowest glycaemic index compared with other diets as shown in Table 4.

Table 4: Mean±SD of glycaemic indices of control and experimental diets.

S. No.	Name of Recipe	Mean±SD glycaemic index
1	Rice	79.25±3.05
2	Wheat	74.39±2.79
3	Rice with Fenugreek	62.79±6.97
4	Wheat with fenugreek	57.42±5.64

To assess effectiveness and tolerance of fenugreek when given prior to and along with food, fenugreek powder was given in the form of a drink 15minutes before the meal in 15 cases and along with the meal in the other 10 cases. Fenugreek is well tolerated in both the forms by the patients. The glycaemic indices between these groups were compared. There is no significant difference between glycaemic indices of rice and wheat in both groups, whereas, the mean of glycaemic indices in the group who had taken fenugreek 15minutes before food were significantly low, when compared with the group who had taken fenugreek along with food (with both rice and wheat) as shown in Table 5.

Table 5: Mean ± SD , 't' and 'p' values of glycaemic indices of control(rice/wheat) and experimental diet containing fenugreek administrated along with food and 15 minutes before food

Recipe	Fenugreek along with food		Fenugreek 15 minutes before food		P
	Mean	SD	Mean	SD	
Rice	79.33	2.12	79.22	3.61	NS
Rice with fenugreek	69.47	4.21	58.33	4.31	<0.001
Wheat	73.61	2.53	74.91	2.92	NS
Wheat with fenugreek	61.69	4.95	54.57	4.13	<0.001

Discussion: Diabetes mellitus is a group of metabolic disease characterized by hypergr lycaemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycaemia of diabetes mellitus is associated with long term dysfunction, damage and failure of various organs especially eyes, kidneys, nerves, heart and blood vessels. United Kingdom prospective diabetes study conclusively demonstrated that improved blood glucose control reduces the risk of developing microvascular complications like retinopathy and neuropathy and possibly decreases the neuropathy in the type II DM. Medical nutrition therapy is integral to total diabetic care and management, One of its important goals is maintenance of as near normal blood glucose level as possible by balancing food intake with exogenous insulin, or oral glucose lowering medications and physical activity.

It has been shown that various plant products may act on blood glucose through different mechanisms. Some have insulin like activity[21] and others may increase number of Beta cells in the pancreas by activating regeneration of these cells[22,23.] The plant fiber may interfere with digestion, absorption and metabolism of the carbohydrates[24]. Over the past two decades of intensive research in dietary fiber, its necessity to the human diet and the positive effects on several diseases have been firmly established and its use in the treatment of several diseases including diabetes is now routine[25]

Fenugreek seeds are commonly used as a condiment in India for culinary purposes and as an herbal medicine. The toxicological studies conducted in experimental animals[26,27] and humans[28]established it to be safe. Several short term and long term metabolic studies have demonstrated hypoglycaemic effect of fenugreek seed in normal[29] and diabetic patients[30, 31, 32]. It associated with lower incidence of diabetes mellitus[33]. In recent years, glycaemic index of foods received considerable attention because of its usefulness in formulating diets for diabetics[34].

In the present study glycaemic index of two common fenugreek recipes, which are acceptable to diabetics, was determined and an attempt made, to assess the role of various nutrients, particularly dietary fiber, on glycaemic index of these preparations. In accordance with studies conducted by other authors it was observed that in addition to being acceptable, there were no side effects in any of the patients studied.

The recent dietary recommendations of diabetics include high carbohydrate diets. Cereal grains, predominantly carbohydrate containing foods are a major component of human diet throughout the world. The major cereal grains are wheat and rice, forms of wheat and rice used in India are chapatti and boiled rice respectively. In the present study the control and experimental diets selected were wheat and rice based preparations.

We observed that the post control and experimental diet blood glucose levels are lower at all time intervals compared to post glucose load blood glucose values. It has been shown that different carbohydrate sources raise the blood glucose to different extent when fed in equivalent amounts[35]. It has been suggested that the difference is due to differences in digestion and absorption of the various foods. Wheat and Rice, being complex carbohydrates are expected to give lower post prandial blood glucose values.

The effect of glucose and other carbohydrates on blood glucose concentrations during tolerance tests is represented by their glycaemic responses, which are defined as the incremental area under the blood glucose response curves. It has been known for many years that different carbohydrate foods, with the same macro nutrient composition, produce different glycaemic responses[36]. In the present study also we found that Rice and Wheat diets produced different glycaemic responses, wheat having a significantly lower glycaemic response than that of rice and both having lower glycaemic responses compared to glucose. We also observed lowering effects of fenugreek on glycaemic responses, when added to rice and wheat diets.

As reported earlier by different authors, we also observed a significant difference in the GI of different foods containing equivalent amount of carbohydrate. It has suggested that several factors such as physical form of the preparation, nature of cooking, presence of anti nutrients, fat, protein, and dietary fiber influence the GI of the particular food, although the role of some of these factors is doubtful. Wheat and rice differ in their constituent proteins and lipids[37].

It has been shown earlier that there is no correlation between GI and nutrient protein and fat content of various preparations which indicates that these nutrients cannot influence the GI. Recently, it has been suggested that the effect of protein and fat on GI are not observed unless they are present in amounts of 25g/50g of carbohydrate[38]. All the dietary preparations used in the study contained less than 25grams of protein or fat/50grams of carbohydrate. Hence the significant differences in GI observed between rice and wheat are not due to the differences in their composition but due to the different configuration and different modes of preparation. The unavailable carbohydrate (Dietary fiber) is lower in rice than that in wheat. The wheat preparation (chapatti) is partially cooked whereas the rice preparation (Boiled rice) is completely cooked[39].

The metabolic effects of fenugreek seeds may be divided into acute and chronic ones. Several authors reported the post prandial glucose lowering effects of fenugreek when administered concurrently and used for some time along with the diets. In the present study we observed the acute effects of fenugreek on glycaemic response of wheat and rice. As reported earlier we also found significant lowering in GI values of both the foods tested when fenugreek is given along with them. The delayed and reduced rise in plasma glucose, hence the lower glycaemic response and GI values may be due to delayed gastric emptying[40], delayed intra luminal glucose diffusion[41, 42] leading to decreased intestinal transit time[43,44] or delayed nutrient absorption. All these are shown to be the causes of low GI exhibited by various foods in the presence of soluble fiber. Whole fenugreek seeds are the rich sources of soluble fiber in the form of galactomannans, which resemble guar gum in chemical structure and viscosity. Subsequently, it has been shown in experimental studies that galactomannans derived from fenugreek seeds has an inhibitory effect on starch digestion. Based on this information, it has been postulated that galactomannan, present in the fenugreek seeds, may be responsible for its hypoglycaemic effect[45]. Recently a French group isolated 4-hydroxyleucine, a novel amino acid from fenugreek seeds, which is not present in mammalian tissues.

It is reported that 4-hydroxy leucine simulates insulin secretion through a direct action on pancreatic β- cells in experimental animals and in humans[46]. The stimulating effect of 4-hydroxy leucine is strictly glucose dependent and is devoid of any secretory effect under normal concentrations of glucose, hence the absence of risk of hypoglycaemia. Besides insulinotrophic effects, experimental studies conducted in Zucker fa/fa rats demonstrated that 4- hydroxyl isoleucine can reduce insulin resistance through activation of the early steps of insulin signaling in peripheral tissues and liver, and extend a direct effect by improving sensitivity to insulin. This may be especially important in NIDDM patients in whom insulin resistance predominates. Our present study supports the beneficial effects of fenugreek in lowering of GI through its constituents of soluble fiber, mainly the galactomannans and 4-hydroxyleucine.

We observed relatively delayed and comparatively lower peak and lower total increments of blood glucose concentrations when fenugreek was taken with wheat and rice diets as compared to only wheat or rice. This may indicate that fenugreek not only decreases the hyperglycaemic effect of that particular meal but also of the subsequent meals which will be advantageous to diabetics on treatment[47].

Although significant changes in glycaemic responses are noted when fenugreek is added to the diet, the glycaemic responses however never completely returned to normal. Hence we strongly support the view that fenugreek can only act as an adjuvant to therapy and cannot replace the insulin or oral hypoglycaemic drugs.

As it has been shown earlier, addition of fenugreek to prescribed diets in diabetics decreased the requirement of insulin and oral anti diabetic drugs. It has been reported that the euglycaemia achieved by conventional insulin and oral hypoglycaemic drug treatment could not completely prevent microvascular and neurological complications. It has been reported that insulin increases cholesterol synthesis and secretion of very low density lipoprotein[48]. Several earlier reports have shown the beneficial effects of fenugreek including those on lipid metabolism. Hence fenugreek supplementation may be much more beneficial to the diabetics.

The Indian Council of Medical Research in 1987 suggested that fenugreek be consumed in the form of a drink 15minutes before the meals, as it led to a significantly higher effect on blood glucose response than fenugreek given along with the food. In the present study we observed a significant lowering of glycaemic index of both rice and wheat when fenugreek is administered 15minutes before the meal compared to fenugreek given along with the diet. However, there is no statistically significant difference in glycaemic index of rice and wheat in these two groups. This indicates that these two groups of diabetic patients are comparable and hence the significant difference observed with fenugreek diets is due to the time of fenugreek administration. It has been reported that certain dietary fibers like Guargum, pectin and Fenugreek fiber form intra luminal gels. This leads to delayed carbohydrate absorption as a result of slower absorption through these intraluminal gels. Hence we also confirm and recommend that the administration of fenugreek before the regular meal is better than fenugreek taken along with the meal.

Conclusion: In the present study, it has been observed that different carbohydrate diets like rice and wheat give different glycaemic indices. Wheat (chapati) has a significantly lower glycaemic response when compared to rice because of the higher unavailable carbohydrate content in wheat and also as it is partially cooked. Fenugreek has a lowering effect on GI when added to rice and wheat diets which is attributed to delayed gastric emptying and increased intestinal transit time, decreased glucose absorption and inhibition of starch digestion due to the presence of soluble fiber and galactomannans. Significant lowering of GI of both rice and wheat were observed when fenugreek was administered 15minutes before the meal, when compared to fenugreek given along with the diet as this provided time for the formation of intraluminal gels.

The present study concludes that adding fenugreek to the diet of diabetic patients 15 minutes before the meal causes a significant reduction in GI and is beneficial to NIDDM patients for long term control of their blood glucose levels and prevention of hyperglycaemic related complications.

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