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Effect of fenugreek fiber flakes on appetite scores and glucose homeostasis in healthy subjects

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Abstract
Background: It is hypothesized that high fiber foods displace energy as they have much lower energy density compared with high fat food. The bulking and viscosity properties of dietary fiber are predominantly responsible for influencing satiation and satiety[1]. The main objective was to determine efficacy and safety of fenugreek fiber flakes (5g and 10g) on appetite scores, glucose homeostasis and insulin response in healthy adult subjects.
Methods: A randomized, single-center, open-label, crossover study in healthy adult subjects (n=18). There were two dosages fenugreek fiber flakes involved 5g and 10g. Fenugreek fiber flakes (5g and 10g) were given along with standard breakfast at each visit. The appetite scores, blood glucose and serum insulin levels were measured at baseline and at each visit.
Results: An analysis of covariance (ANCOVA) performed on primary endpoint change from baseline resulted in significantly lower appetite scores when compared to baseline for both 5g and 10g. On comparison 10g fenugreek fiber flakes resulted in significantly reduced scores compared to 5g fenugreek flakes. Fenugreek fiber flakes 10g resulted in significantly lower (P=0.0001) for desire for consumption of food compared to 5g, the satiety satisfaction scores were found to be significantly high (P=0.0146) compared to 5g. The prospective consumption scores in 10g of fenugreek fiber flakes resulted in significantly lower (P<0.008) for prospective food consumption compared to 5g. The hunger scores was significantly reduced (P=0.0006) with 10g of fenugreek fiber flakes compared to 5g. The fullness scores was significantly greater (P=0.01) with fenugreek fiber flakes of 10g compared to 5g.
Conclusions: Consumption of fenugreek fiber flakes (5g and 10g) with a standard breakfast increased satiety satisfaction and fullness. Fenugreek fiber flakes reduced hunger and desire to consume food and prospective food consumption in 10g significantly compared to 5 g. There were no significant changes observed in glucose homeostasis with fenugreek fiber flakes. Fenugreek fiber flakes 5g and 10g, showed an acceptable safety profile.

Keywords: fenugreek fiber flakes, clinical study, appetite scores, blood glucose, serum insulin

Introduction

Fenugreek (*Trigonella foenum-gracium*) is an annual leguminous herb possessing wonderful medicinal values. The dried seeds are aromatic and bitter, which has been used traditionally in India, China, Egypt and in some parts of Europe for its well-known medical and rejuvenating effects. The major constituents of fenugreek seeds have been identified as proteins (20-25%), dietary fiber (40-45%), mucilaginous soluble finer (20-25%), fixed fatty acids and essential oils (6-8%) and steroidal saponins (2-5%). Since it contains high amount of fiber, number of solvent extraction techniques have been developed to extract fiber from fenugreek [4, 5].

High fiber foods have bulking and viscosity properties which are predominantly responsible for influencing satiation and satiety. Fiber rich foods usually are accompanied by increased efforts and/or time of mastication, which leads to increased satiety through a reduction in rate of ingestion [1].

The effects of dietary fiber on hunger, satiety, energy intake and body weight has been extensively studied. Several types of fibers increase satiety by increasing stomach distension which can slow gastric emptying. Another possible mechanism by which fibers increase satiety is through fermentation in the gut by microflora and the subsequent effects of short-chain fatty acids (SCFA) produced. SCFA interact with G-coupled protein receptors such as GPR41 and GPR43 on enteroendocrine cells and may be part of the mechanism for the effect of fiber on appetite as they increase production of satiety-related hormones from the colon. All in all it has shown to reduce energy density, slowed gastric emptying, altered postprandial glycaemic response and the production and secretion of satiety hormones [2].

Maskarinec *et al.* (2006) reported that plant based food and dietary fiber were most protective against body weight in large and in ethnically diverse population. There are no standardised protocols for conducting studies on dietary fiber and food

intake, which makes it difficult to compare studies and summarize results. Majority of the studies with controlled energy intake reported an increase in post meal satiety and decrease in subsequent hunger with increased fiber [3].

Data on the effects of fenugreek fiber flakes on appetite are non-existent in healthy volunteers. Mathern *et al.* (2009) conducted a study to look at fenugreek fiber on satiety, blood glucose and insulin response in obese subjects [6]. In the changing world where people are conscious on energy intake, it is important first to look at the response of fenugreek fiber flakes in healthy volunteers based on the similar line on the aforesaid study. However, study conducted above did not address the key question on the subjects who had the BMI of less than 30.

A study was planned to examine the effects of fenugreek fiber flakes from fenugreek on satiety, fullness, hunger, desire to consume food and prospective food consumption. It was further important to determine whether fenugreek fiber flakes would reduce glycaemic and insulin response apart from palatability. Some of the changes which the previous studies did not address at all in published literature are especially with normal healthy volunteers. Healthy volunteers are replication of modern healthy people who are keen on maintaining the daily intake and who have little time to take care of their health through physical endurance.

In order to obtain the aforesaid, the objective of this study was planned to evaluate the efficacy and safety of fenugreek fiber flakes (5g and 10g) on appetite, blood glucose and insulin levels in healthy subjects.

Methods

Study group consisted of eighteen healthy subjects between age group of 18 and 65 years of age. The study was carried out at Rajalakshmi hospital and was approved by Rajalakshmi hospital institutional review board. It was confirmed that ethics committee of Rajalakshmi hospital is constituted and functions as per Good Clinical Practice guidelines.

Selection of subjects:

Men and women aged 18 to 65 years with body mass index (BMI) $\leq 25 kg/m^2$ with no other metabolic disorders and those who were willing to give informed consent were included in the study. Subjects with hypertension and diabetes and other unstable medical conditions were excluded from the study. Women who were pregnant, breast feeding and planning pregnancy were excluded from the study.

Study design

Subjects were randomly assigned into two groups (test arm 1 and test arm 2) using blocked randomization method in SAS (version 9.1).

Eighteen healthy, normal weight (BMI 18 to 24.9) subjects, 18-65 years of age participated in the study. All subjects underwent screening procedures after the informed consent process at Visit 1.

Subjects who passed the eligibility criteria were randomized into 2 treatment arms to receive fenugreek fiber flakes either 5 g or 10 g in 1:1 ratio on Visit 2.

The subjects underwent fasting and postprandial blood sugar investigations by standardised glucometer and serum insulin tests at various time points as planned in the study.

Subjects recorded the satiety and palatability ratings on VAS scales (Flint *et al.*, 2000) [7]. The subjects underwent crossover of the treatment arms in the next visit (Visit 3). The subjects who received fenugreek fiber flakes 5 g received 10 g and vice versa. There was a washout period of three days between the crossover visits.

Questionnaires

VAS, 100 mm in length with words anchored at each end, scoring expressing the most positive and the most negative, were used to assess hunger, satiety, fullness, prospective food consumption, desire to consume food and palatability. The questionnaires were given to subjects and were instructed to do the ratings.

Appetite and palatability scores were measured using VAS questionnaires ratings.

Serum insulin levels were assessed using Elecsys insulin assay (electro-chemiluminescence immunoassay method) at the study centre's local laboratory. Around 5 ml blood was drawn at baseline after overnight fasting and after the meal at time points up to 180 minutes post prandial.

Blood glucose levels were assessed using one touch glucometer (batch no: ZA12702, Expiry date: November 2020) at fasting levels and at intervals of 15, 30, 45, 60, 90, 120, 150 and 180 minutes from the start of meal.

Investigational Product

Fenugreek fiber flakes are proprietary products of Bio-gen extracts ltd. The products were defatted and debitterized. The compound is in the form of flakes. The composition of fenugreek fiber flakes is as shown in table.

Table 1: Composition of fenugreek fiber flakes

Parameter	Results
Protein content	32.57 g/100g
Total dietary fiber	49.46 g/100g
Soluble dietary fiber	18.68 g/100g
Insoluble dietary fiber	30.78 g/100g
Total fat content	0.45 g/100g
Iron (Fe)	18.97 mg/100g
Calcium (Ca)	1927.54 mg/100g
Potassium (K)	1321.74 mg/100g
Sodium (Na)	71.40 mg/100g
Magnesium (Mg)	164.39 mg/100g
Total Amino acid	9.05 g/100g
Gluten content	<5 mg/kg

Fenugreek fiber flakes 5g/10g was consumed with water along with a standard meal (breakfast).

Appetite and palatability scores were measured using VAS questionnaires ratings.

Statistical analysis

Data analyses were performed using the following software: SAS® for Windows 95/NT (Version 9.1 or higher, SAS Institute, Cary, North Carolina, USA). Area under the curve (AUC) was calculated using trapezoidal rule using WinNonlin® software (Version 5.3). ANCOVA (Analysis of covariance) was performed for the primary variables using baseline as covariates else paired or independent *t-test* were performed between the treatments. AUC of the VAS satiety scores was calculated using trapezoidal rule

The baseline characteristics were compared among treatment groups. The baseline characteristics which were found to be significant between study groups were accounted in primary analysis model. For continuous variables (age etc.), data was summarized using number of subjects (N), mean, standard deviation (SD), median, minimum and maximum. For categorical variables, data was presented with the number of exposed subjects, number with percentage in various categories of the endpoint, where percentage was based on the exposed subjects. The descriptive variables (gender etc.) were evaluated using Cochran-Mantel-Haenszel test stratified by study center at 0.05 level of significance.

Primary efficacy analysis

Changes from baseline for all the primary endpoints such as blood glucose levels, satiety, fullness, hunger, desire to consume food and prospective food consumption VAS score and insulin response were evaluated to assess the functional benefits of fenugreek fiber flakes. Descriptive statistics were performed. Sub group analysis was performed for 2 groups by treatment and the data will be presented in appropriate charts. ANCOVA (Analysis of covariance) was performed for the primary variables using baseline as covariates else paired or independent *t-test* were performed between the treatments.

Satiety, fullness, hunger, desire to consume food and prospective food consumption Rating Assessment

Subjects VAS ratings were converted to a numerical score (0 to 100) from the far-left anchor of the scale. Peak scores (mm) as well as area under curve (AUC, mm*h) was calculated. The cut-off for AUC was 3.5 hrs. AUC was calculated using the trapezoidal rule.

- For satiety, ratings of 0 on the scales = I am completely empty. Ratings of 100 = I cannot eat another bite.
- For hunger, ratings of 0 = I am not hungry at all. Ratings of 100 = I have never been more-hungry.
- For fullness, ratings of 0 on the scales = I am not at all full. Ratings of 100 = I am totally full.
- For desire to consume food, ratings of 0 on the scales = I do have desire to eat. Ratings of 100 = I do not have desire to eat food.
- For prospective consumption of food, ratings of 0 on the scales = I do like to eat. Ratings of 100 = I do not like to eat

Secondary efficacy analysis

Post consumption of the IP the effect of fenugreek fiber flakes on the visual, taste, smell and palatability of test products at each visit was compared by paired *t-tests*.

Results

All eighteen subjects completed the study (17 male and 1 female). Their mean age ± SD was 26.44 ± 12.92 years and their mean BMI was 21.15.

Results of appetite ratings for satiety, hunger, fullness and prospective food consumption are listed in table 2

Table 2: Summary of appetite ratings AUC (mm*hr) by treatment

Measurements [AUC (mm*hr)]	Fenugreek Fiber Flakes		p-value [a]
	5 grams (N=18)	10 grams (N=18)	
Desire to consume food score	1062.92 ± 164.35	735.00 ± 188.60	0.0001
Satiety score	1270.83 ± 252.46	1449.16 ± 222.94	0.0146
Prospective food consumption score	993.33 ± 256.28	707.08 ± 252.97	0.0080
Hunger score	970.42 ± 168.28	687.08 ± 211.63	0.0006
Fullness score	1277.16 ± 230.37	1487.50 ± 186.41	0.0101

Mean ± SD

[a] p-value is from paired t-test.

Satiety: For satiety, ratings of 0 on the scale = I am completely empty. Ratings of 100 = I cannot eat another bite.

Mean plot of satiety scores by treatment is presented in Fig. 1.

- Peak satiety scores were found to be higher with fenugreek fiber flakes 10 g compared to 5 g.
- Fenugreek fiber flakes 10 g resulted in a higher AUC (p = 0.0146) for satiety scores compared to 5 g.
- Satiety scores increased from 30 minutes post consumption of fenugreek flakes 5 g and 10 g compared to before consumption score at baseline and steadily reduced over a period of time in the study.

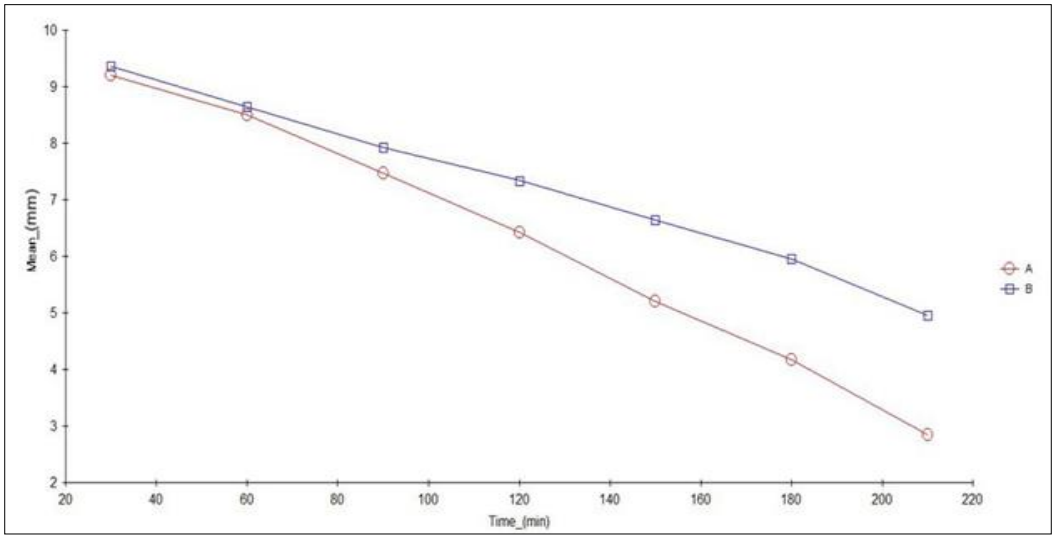

Fig 1: Mean plot of satiety scores by treatment A = 5 g and B = 10 g (N = 18). Mean (mm), time (mins.)

Hunger scores

For hunger ratings of 0 = I am not hungry at all. Ratings of 100 = I have never been more hungry.

Mean plot of hunger scores by treatment Figure 2.

- Peak hunger scores were found to be reduced with fenugreek fiber flakes 10 g compared to 5 g.
- Fenugreek fiber flakes 10 g resulted in significantly lower AUC (*p=0.0006*) for hunger scores compared to 5 g.
- Hunger scores reduced from 30 minutes post consumption of fenugreek fiber flakes 5 g and 10 g compared to before consumption score at baseline and steadily increased over a period of time in the study.

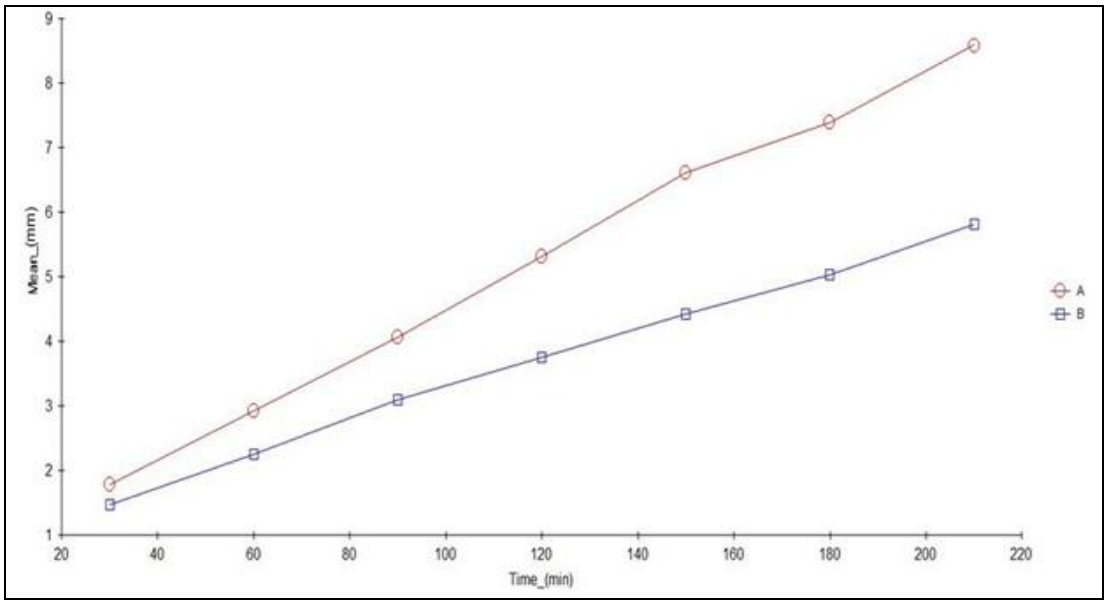

Fig 2: Mean plot of hunger scores by treatment A = 5 g and B = 10 g (N = 18) Mean (mm), time (minutes.)

Fullness

For fullness, ratings of 0 on the scale = I am not at all full. Ratings of 100 = I am totally full.

Mean plot of fullness scores by treatment is presented in Figure 3.

- Peak fullness scores were found to be higher with fenugreek fiber flakes 10 g compared to 5 g.
- Fenugreek fiber flakes 10 g resulted in significantly higher AUC (*p= 0.01*) fullness scores compared to 5 g.
- Fullness scores increased from 30 minutes post consumption of fenugreek flakes 5 g and 10 g compared to before consumption score at baseline and steadily reduced over a period of time in the study.

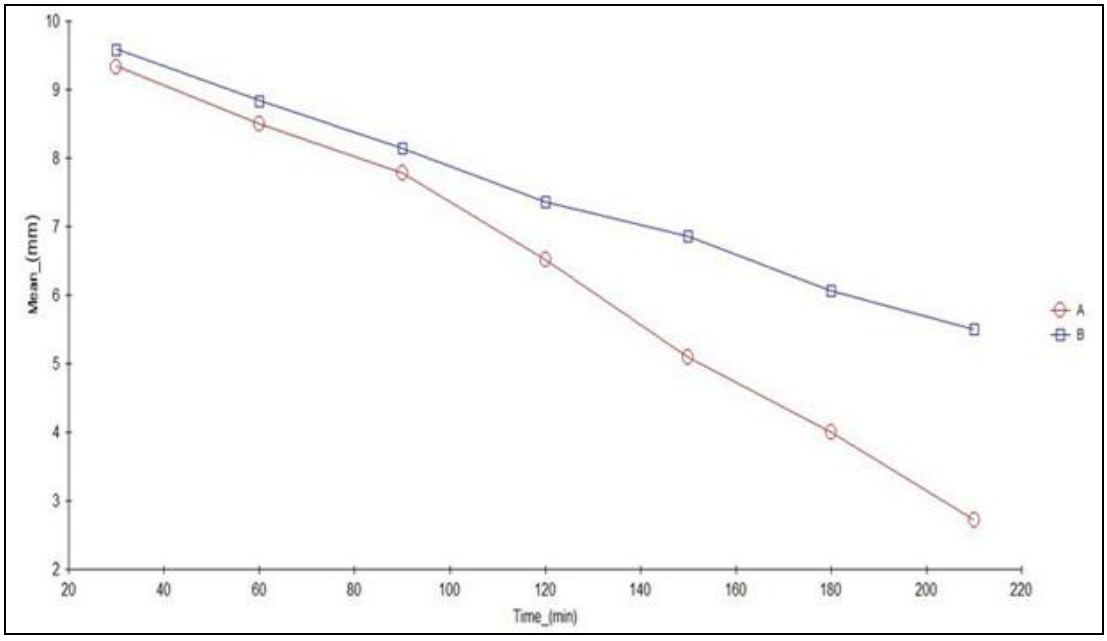

Fig 3: Mean plot of fullness scores by treatment A=5 g and B=10 g (N=18) Mean (mm), time (minutes)

Prospective food consumption

For prospective food consumption, ratings of 0 on scales = I can eat nothing at all. Ratings of 100 = I can eat a lot.

Mean plot of prospective food consumption scores by treatment is presented in Figure 4

- Peak prospective consumption of food scores was found to be lower with fenugreek fiber flakes 10 g compared to 5 g.
- Fenugreek fiber flakes 10 g resulted in significantly lower AUC ($p<0.008$) for prospective food consumption compared to 5 g.
- Prospective consumption of food scores reduced from 30 minutes post consumption of fenugreek fiber flakes 5 g and 10g compared to before consumption score at baseline and steadily increased over a period of time in the study.

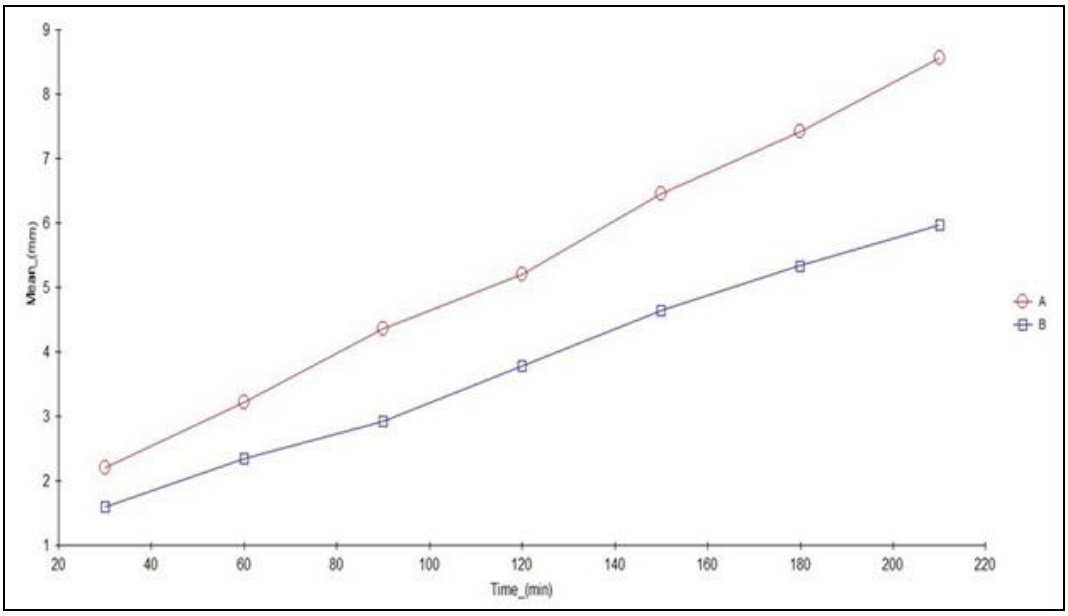

Fig 4: Mean plot of prospective food consumption scores by treatment A=5 g and B=10 g (N=18). Mean (mm), time (minutes.)

Desire to consume food

Mean plot of desire to consume food scores by treatment is presented in Figure 5. Error! Reference source not found.

- Peak desire for consumption of food scores were found to be lower with fenugreek fiber flakes 10 g compared to 5g.
- Fenugreek fiber flakes 10 g resulted in a significantly lower AUC (*p=0.0001*) for desire after consumption of food scores compared to 5g.
- Desire for consumption of food scores reduced from 30 minutes post consumption of fenugreek fiber flakes 5g and 10g compared to before consumption score at baseline and steadily increased over the period of time in the study.

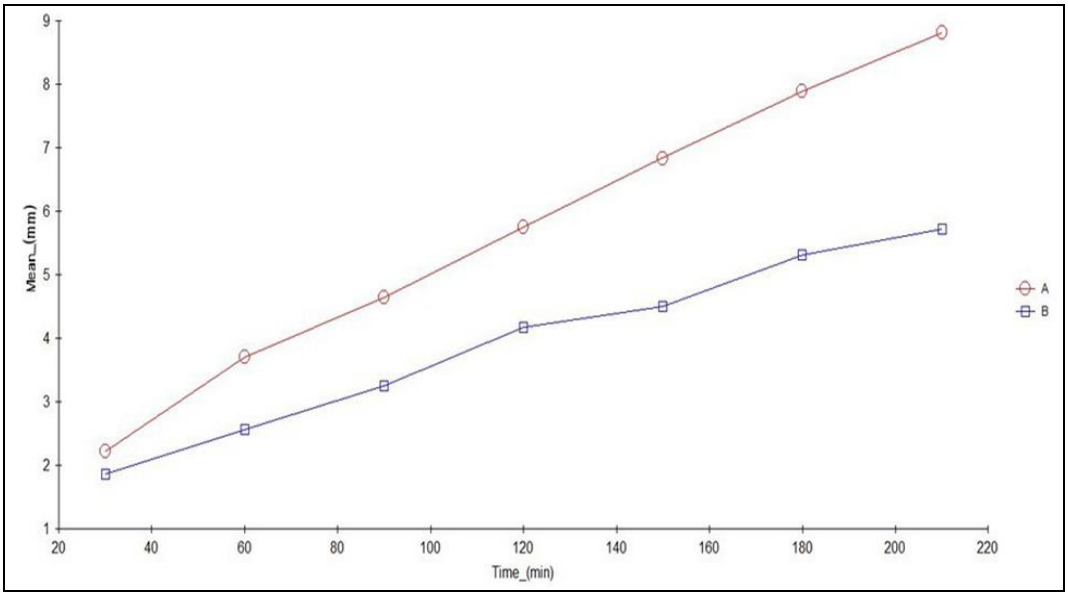

Fig 5: Mean plot of desire to consume food by treatment A=5 g and B=10 g (N=18) Mean (mm), time (mins.)

Palatability

Palatability of the test products were assessed using visual analogue scales. Subjects rated the visual appeal, smell, taste, aftertaste and overall palatability of the test products. Lower scores meant better palatability than higher scores, since on the scale 0 = good and 10 = bad.

Summary of palatability of the fenugreek fiber flakes (5g or 10g) are presented in figure 6.

Visual appeal, smell, taste scores were found to be better with fenugreek flakes fiber 10 g and aftertaste and palatability scores were found to be better with fenugreek flakes fiber 10g. Overall, total palatability scores were found to be better with fenugreek flakes fiber 10 g compared to 5g.

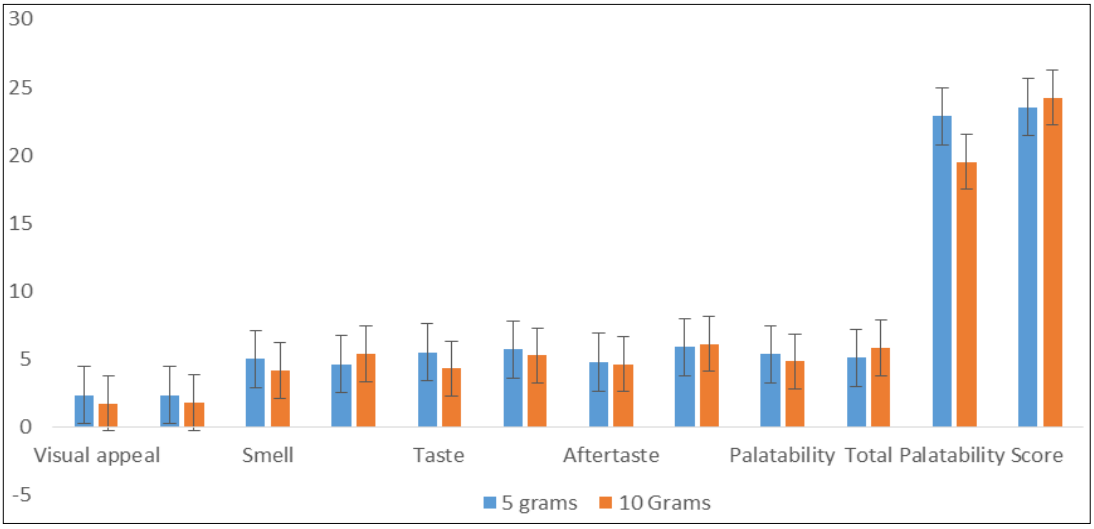

Fig 6: Mean of palatability score measurements by visit and treatment

Blood parameters

Blood Sugar And Serum Insulin Response Results

A trend of reduction in serum insulin after consumption of fenugreek fiber flakes was observed and the reduction was found to be more with 10 g compared to 5g. There were no significant changes in glucose levels. The summary of blood glucose and serum insulin is represented in Table 3 and figure 7 and figure 8.

Table 3: Summary of change from baseline of glucose and insulin response by treatment

Parameter(Units)	Statistic[a]	Fenugreek Fiber Flakes		p-value [b]
		5 grams	10 grams	
Serum Insulin Response (µU/ml)	LS Mean ± SD	29.03± 21.34	21.85± 21.34	0.0003
Blood Glucose Levels (mg/dl)	LS Mean ± SD	31.63± 5.47	31.09± 5.47	<0.001

[a] Estimated LS Means and Standard Deviation from Repeated Measures ANCOVA model.
[b] P-value is from Overall F-test of Repeated measures ANCOVA.

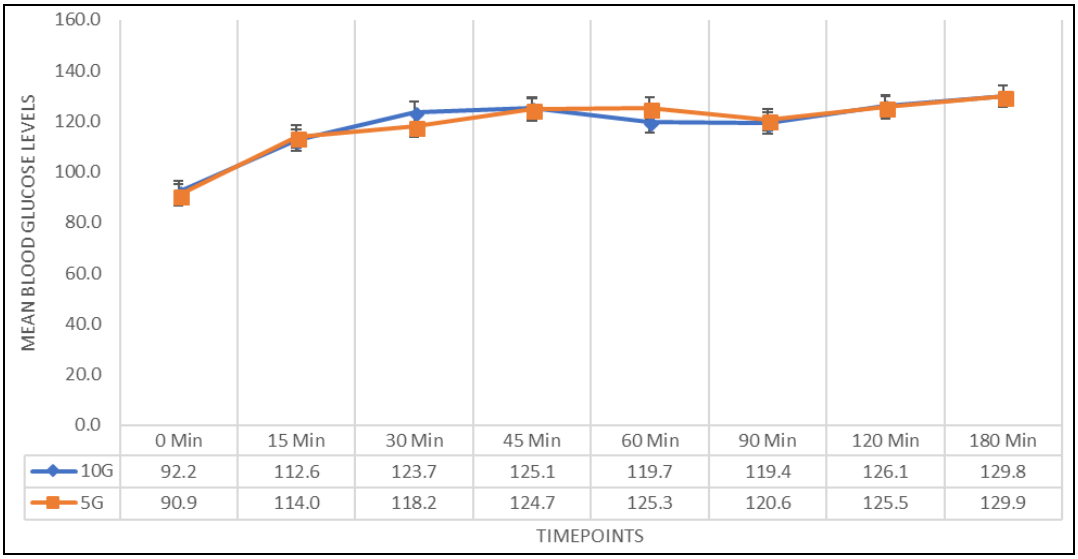

Fig 7: LS mean plot of blood glucose levels by treatment A=5 g and B=10 g (N=18)

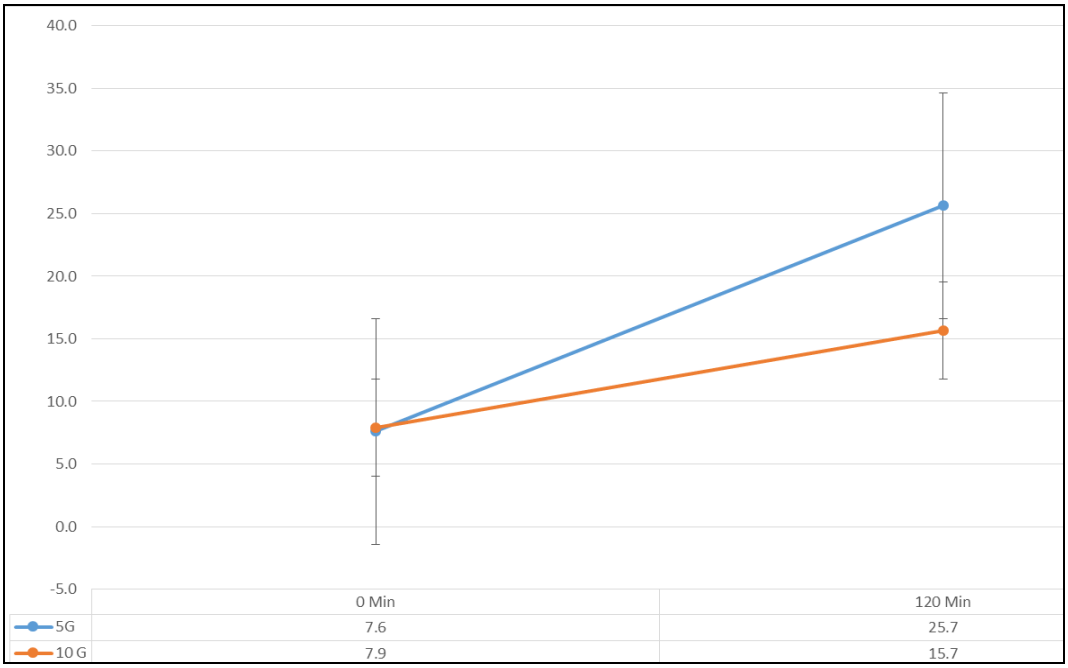

Fig 8: LS Mean plot of insulin response by treatment A=5 g and B=10 g (N=18)

Discussion

Consumption of 10 g of fenugreek fiber flakes in addition to a standard breakfast increased satiety, fullness and reduced hunger desire to consume food and prospective food consumption compared to 5g of fenugreek fiber flakes. In a similar study conducted by Mathern *et al.* (2009) [6], fenugreek fiber, given at a breakfast meal, did not influence energy intake for the remainder of the day, suggesting effects on satiety are short term. The presence of viscous fiber from fenugreek may have played a role in promoting satiety by slowing the rates of gastric emptying. This could be due to extensive gel formation leading to low viscosity of the resulting gels inside the intestine. This may delay the gastric emptying and decrease the intestinal transit time of the food mass. Glucose trapped inside the gel leaches out slowly and prevents the sudden raise of blood glucose level, which may also help to avoid fatigue and over eating. Fenugreek galactomannan (mixture of galactose and mannose) has been shown to slow gastric emptying in animal models [8]. Viscosity and gel-forming property of soluble dietary fiber inhibit macronutrient absorption, reduce postprandial glucose response and may benefit changes in the body metabolism.

However, in our study the increase in satiety was not related to reduced absorption of glucose as our study did not find any effects of fenugreek fiber flakes on postprandial blood glucose concentrations. A previous study by Madar *et al.* (1988) found significant reductions in postprandial blood glucose in response to a mixed meal supplemented with 15 g fenugreek seeds [9]. However, the subjects with Type 2 diabetes with altered glucose metabolism. A study by Sharma and Raghuram (1990) found that 5 g of fenugreek gum significantly reduced postprandial blood glucose in normal subjects, when given with a large dose (100 g) of glucose [10]. The amount and type of carbohydrates consumed are largely responsible for postprandial blood glucose and insulin responses to meals and large amounts of fat or protein (> 50 g) are needed to significantly impact the glucose and insulin response to a meal [11]. In our study, we did not have diabetic or obese patients who consumed high amount of glucose and hence we did not find any changes in the glucose metabolism. Therefore, it would be interesting to investigate whether fenugreek fiber flakes would have significant effects on postprandial blood glucose in response to a larger meal or high energy meal or subjects with high BMI.

The postprandial insulin AUC was decreased with the addition of 10 g of fenugreek fiber powder, which is in line with other studies, which have found decreased insulin response with fiber [12], and a previous study showing that fenugreek gum can lower postprandial insulin response [10].

During the study, a single incidence of nausea and vomiting was reported by a subject which was mild in nature and assessed by investigator as not related to the IP. No death or SAE was reported during the entire duration of study.

The current proof of concept study was conducted on healthy subjects and had limitations of being an open-label, having a short duration of consumption of investigational product and a small sample size. A larger population study on fenugreek fiber flakes looking at different BMI, obese, prediabetic and diabetic population is ongoing. This may answer many of the unknown questions of fenugreek fiber flakes with this larger population.

Conclusions

Fenugreek fiber flakes 5 g and 10 g showed an acceptable safety profile and a positive efficacy trend in improving the satiety in healthy adult subjects. 10 g dose of fenugreek fiber flakes added to a meal increased satiety and fullness and decreased hunger and prospective need of food in VAS scores. This study did not provide evidence that addition of fenugreek fiber flakes to a meal altered carbohydrate metabolism, as no effects were seen on postprandial glycaemia. Insulin response was significantly increased with 10 g fenugreek fiber flakes

and requires further study. The total palatability scores were found to be better with fenugreek fiber flakes 10 g than 5g though not significantly. Though the study was a comparison of fenugreek fiber flakes of 5g versus 10g, compared to baseline there was a significant change in reported scores of satiety, fullness, hunger, desire to consume food and prospective need of food amongst subjects on fenugreek flakes of 5g and 10g. Our study results suggests that fenugreek fiber flakes has a role in the control of food intake in normal individuals who want to use diet as a method to control energy intake through their effects on appetite suppression and food intake.

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