Effect of 'FenuflakesTM' on 24-hour glycemic variability in adults with type 2 diabetes: A randomized crossover continuous glucose monitoring study

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Pallavi Onkar Deshpande M.Pharm[1], Chinmaya Adwait Gokhale MSc[1], Sunil Bhaskaran B.Tech, Rajagopal Gayathri MSc[2], Kuzhadaivelu Abirami BSc[2], Ranjit Mohan Anjana MD[3], Kamala Krishnaswamy MD[2], Viswanathan Mohan PhD[3], Vasudevan Sudha MSc[2]

[1]Department of Scientific Affairs, Indus Biotech Limited, Pune, Maharashtra, India
[2]Department of Foods, Nutrition & Dietetics Research, Madras Diabetes Research Foundation, Chennai, Tamil Nadu, India
[3]Department of Diabetology, Madras Diabetes Research Foundation, Chennai, Tamil Nadu, India

Authors' email addresses and contributions:
Name:Pallavi Onkar Deshpande
PD: pallavi@indusbiotech.com
Contribution: Overall scientific management, review, and finalization of the manuscript

Name: Chinmaya Adwait Gokhale
CG: chinmaya@indusbiotech.com
Contribution: Overall scientific management, review, and finalization of the manuscript

Name:Sunil Bhaskaran
SB: sunil@indusbiotech.com
Contribution: Concept and design, funding acquisition, finalization of the manuscript

Name: Gayathri Rajagopal
GR: gayathri@mdrf.in
Contribution: Concept and design, experimental, clinical, and data compilation work, preparation of the draft, reviewing and editing of the manuscript

Name: Abirami Kuzhadaivelu
AK: abirami@mdrf.in
Contribution: Software and Formal analysis

Name: Ranjit Mohan Anjana
RA: dranjana@drmohans.com
Contribution: Critically reviewed and helped in finalization of the manuscript

Name: Kamala Krishnaswamy

KK: kamala.krishnaswamy@gmail.com
Contribution: Critically reviewed and helped in finalization of the manuscript

Name: Mohan Viswanathan
MV: drmohans@diabetes.ind.in
Contribution: Critically reviewed and helped in finalization of the manuscript

Name: SudhaVasudevan
SV: s2r_7@mdrf.in
Contribution: Concept and design, data interpretation, critically reviewing and editing of manuscript.

Corresponding Author: Pallavi Deshpande, Department of Scientific Affairs, Indus Biotech Private Limited, 1 Rahul Residency, Off Salunke Vihar Road, Kondhwa, Pune - 411 048, Maharashtra, India. Tel: +91-20-26851239. Email: pallavi@indusbiotech.com

ABSTRACT

Background and Objectives: Evidence suggests that bioactive components present in plant foods have beneficial effects. Fenugreek is commonly used in Indian culinary practices and can help to keep blood sugar levels under control. The objective of this study was to assess the efficacy of defatted fenugreek seed flakes FenuflakesTM on the 24-hour glycaemic response (Incremental Area Under the Curve, iAUC), variability (Mean Amplitude of Glycaemic Excursion assessed by Continuous Glucose Monitoring system) in participants with type 2 diabetes. **Methods and Study Design:** Twenty-one type 2 diabetes participants, aged 42 to 50 years, were provided with 5-day cyclic iso-caloric diets for 14 days without (control diet) and with 30 g of FenuflakesTM (test diet) in a randomized crossover trial. The Abbott Pro sensor recorded interstitial glucose concentration every 15 minutes consecutively for 14 days in the participants. Additionally, fasting plasma glucose and glycated hemoglobin (HbA1c) were assessed at the baseline and end of the study. **Results:** 15 out of 21 participants completed the randomized control and test diet feeding periods as per protocol. There was a significant reduction in 24-hour iAUC (p=0.02) and mean amplitude glycemic excursions (p=0.006). Furthermore, within the test diet, there was a significant reduction in fasting plasma glucose (p=0.01). and HbA1c (p=0.01) at the end of the 14-day intervention period. **Conclusions:** The results suggest that the inclusion of FenuflakesTM, into regular dietary practices may effectively reduce glucose levels and enhance glycemic control in Asian Indian adults with type 2 diabetes.

Key Words: type 2 diabetes, glycemic variability, fasting plasma glucose, glycated hemoglobin, Fenuflakes

INTRODUCTION

The global prevalence of diabetes continues to rise, particularly affecting low- and middle-income countries. A national cross-sectional study in India estimates that approximately 101 million individuals are currently living with diabetes. Furthermore, there has been a significant increase in the prevalence of other metabolic noncommunicable diseases (NCDs) within these populations.[1] A high burden of uncontrolled diabetes persists among patients with type 2 diabetes (T2D) in India, with approximately 76.6% experiencing poor glycemic control.[2] This trend highlights the urgent need for focused public health initiatives to address the challenges posed by diabetes and related metabolic disorders.

Concerns regarding the side effects of pharmacological treatments have led to increased interest in utilizing plant-based foods and extracts for blood glucose management.[3, 4] Diet therapy is essential for managing T2D,[5] but adhering to restrictive diets can be challenging. Simplifying these dietary modifications can enhance compliance. Various functional food ingredients have been identified as effective in moderating postprandial glycemic responses, making them essential components of dietary management strategies.[6, 7] Especially, dietary fibers have been shown to significantly reduce glycemic responses and may play a crucial role in preventing the onset of diabetic complications.[8, 9]

Trigonella foenum-graecum L. (fenugreek) is a traditional herb characterized by a high dietary fiber content (approximately 48%, comprising 28% insoluble and 20% soluble fiber), protein content (25%), and essential minerals such as iron (8.5 mg%), sodium (40 mg%), calcium (135 mg%), and potassium (891 mg%).[10] Fenugreek is utilized globally not only as a culinary ingredient but also as a functional food, featured in various items, including baked goods and extruded products. Recent studies over the past two decades have demonstrated that fenugreek seeds can effectively lower fasting blood glucose levels and enhance glucose tolerance in adults with diabetes. Fenugreek has also emerged as a nutraceutical with documented hypoglycemic properties.[11] A meta-analysis of ten clinical trials revealed significant reductions in glucose parameters associated with fenugreek seed supplementation.[12] Specifically, doses ranging from 5 to 25 g of fenugreek seed powder have been found to lower postprandial glucose levels. Additionally, a daily intake of 10 g of fenugreek seeds, alongside dietary control and exercise, has shown a synergistic effect, leading to reductions in fasting blood glucose and glycated hemoglobin (HbA1c) levels within a six-month timeframe.[13]

Despite its diverse health benefits, fenugreek's bitter taste often hinders its consumption.[14] To mitigate this limitation, Fenuflakes™, which are 100% natural flakes derived from debittered, defatted fenugreek seeds, have been developed. These flakes are rich in fiber and protein while containing negligible carbohydrates and fats, allowing for easy incorporation into common recipes. Fenuflakes™ can serve as a valuable addition to traditional Indian breakfasts, especially those featuring rice or wheat, as they effectively lower the glycemic index (GI) of these foods.[15] Indian dietary patterns typically consist of 70 to 80% carbohydrates, which constitute a significant proportion of total caloric intake. The predominant carbohydrate sources in these diets are often high GI foods, particularly minimally processed grains such as white rice.16 Therefore, incorporating Fenuflakes™ into meals may help mitigate post-meal blood sugar spikes, which can be particularly beneficial

for individuals managing diabetes or those at risk. Fenuflakes™ further demonstrated significant prebiotic potential by enhancing the production of short-chain fatty acids (SCFA) and promoting the enrichment of beneficial colonic microbiota.[17]

Based on the evidence, the present study aims to evaluate the efficacy of debittered defatted fenugreek seed flakes (Fenuflakes™) on glycemic response, including glycemic variability, over a 14-day period assessed using continuous glucose monitoring (CGM). Additionally, we investigated the changes in fasting plasma glucose (FPG), insulin levels, and HbA1c following supplementation with Fenuflakes™ and compared these outcomes within a crossover study design involving participants with T2D.

MATERIALS AND METHODS

Study participants

Participants were recruited from a volunteer registry at the Madras Diabetes Research Foundation (MDRF) in Chennai, Tamil Nadu, India. In total, 21 individuals aged between 30 and 50 years of both sexes, were included in the study. All participants had T2D with stable dose of oral hypoglycemic agents for a period of 3 months, characterized by FPG levels ranging from 126 to 250 mg/dL, a Body Mass Index (BMI) between 18.5 kg/m² and 30 kg/m², HbA1c levels between 7% and 11%, inclusive, stable dose of anti-hypertensive, lipid-lowering, or thyroid medications or hormone therapy for at least 3 months prior to the screening and agreed to give voluntary informed consent, were included in the study. Exclusion criteria included individuals with allergies to the study medication or any food allergies, those experiencing fluctuations in glucose levels, or participants who had changes in their oral anti-hyperglycaemic agents in the three months preceding the study. Furthermore, individuals with aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) ratio exceeding 2.5 times the upper limit of normal (i.e., AST $\geq$ 100 and ALT $\geq$ 125), serum creatinine levels of 1.5 mg/dL or higher, taking herbals, dietary supplements, or medications, during the past 12 weeks that could profoundly affect blood glucose, those who had participated in any other clinical trial within the last three months, or any conditions deemed ineligible by the investigator, along with clinically significant abnormal laboratory results at the screening visit, were also excluded from the study.

Study design and protocol

The objective of the present study was to investigate the effects of 14 days of Fenuflakes consumption on glycemic response in participants with type 2 diabetes. This study was

designed as a randomized controlled trial with two periods of 14 days each, utilizing a crossover design and a 1-week run-in phase. A 1-week run-in phase was conducted prior to the start of the randomized intervention to evaluate the participants' motivation and compliance. It was conducted at a single study center, the MDRF, in Chennai, India.

The research adhered to the ethical principles outlined in the Declaration of Helsinki, with the protocol receiving approval from the Ethics Committee of the MDRF (No: ECR/194/Inst/TN/2013/RR-19). All participants gave written informed consent before taking part in the study, which was prospectively registered with the Clinical Trial Registry of India (CTRI) (No: CTRI/2019/08/020654).

In the study, participants adhered to an isocaloric diet, either incorporating FenuflakesTM (test diet) or excluding it (control diet). These FenuflakesTM were supplied by Indus Biotech Limited (India). The samples contained over 25% of both protein and soluble and insoluble fibers, while having negligible amounts of carbohydrates and fats, as determined by AOAC official methods and previously reported.[18]

Both the control and test diet phases each lasted 14 days. The two diets were nearly identical, except that the test diet incorporated 30g of FenuflakesTM (10g added to breakfast, lunch, and dinner) into the daily meals. Participants were randomly assigned to receive one of the diets, with a crossover to the other diet after a one-week washout period. During both phases, all meals for the day—including tea and snacks—were provided at the study center, and participants were restrained from eating outside in order to maintain an iso-caloric feeding during the study. Well-trained research dietitians closely monitored participants' daily food intake and ensured there was no plate wastage. A 5-day cyclic menu for both diets can be found in Supplementary Table 1, while the nutrient composition is detailed in Supplementary Table 2.

Due to its contents, the test diet featuring FenuflakesTM had a significantly higher protein and dietary fiber content compared to the control diet (as noted in Supplementary Table 2). However, no significant differences were found in the amounts of fat, carbohydrates, or total calories, keeping both diets iso-caloric.

Data Collection

Demographic characteristics of participants

Socio-demographic and lifestyle data were collected using an interviewer-administered questionnaire, which assessed participants’ medical histories, family histories of diabetes, medications, demographics (such as education and income), and lifestyle factors such as

exercise, alcohol use, and smoking habits. At baseline, 24-hour diet recalls with two recalls per week during each diet period, totaling four recalls over the 14-day feeding phase, to evaluate diet compliance among participants was collected.

Anthropometric parameters

Body weight (kg) and height (cm) using a digital body composition machine (HBF-224, Omron Health Care Co., Ltd., Kyoto, Japan) and waist circumference (cm) using a non-stretchable measuring tape was measured. BMI was determined by dividing an individual's weight in kilograms by their height in square meters. Blood pressure (BP) and pulse rate were recorded using an electronic BP apparatus (Omron HEM 7120, Tokyo, Japan).

Biochemical parameters

Phlebotomy was conducted by a trained phlebotomist while participants were seated to reduce the risk of vasovagal syncope associated with blood draws. Overnight fasting blood samples were obtained to measure FPG concentrations (using the glucose oxidase peroxidase method in mg/dL), serum insulin (measured with Dako kits, Dako, Glostrup, Denmark, in µg/mL), and HbA1c (%) using a Variant machine (Biorad, Hercules, CA) for all participants. All measurements occurred at baseline (day 1) and at the end of each randomized 14-day diet.

CGM parameters

To analyze interstitial fluid glucose levels, we used the Freestyle Libre Pro™ Flash Glucose Monitoring System (Abbott Diabetes Care, India), which consists of a reader and a sensor. The CGM sensor, positioned on the posterior aspect of the upper arm, collected glucose data at 15-minute intervals over a 24-hour period over 14 consecutive days. Data from the sensor were downloaded using the reader and the FreeStyle Libre software. The mean change in 24-hour interstitial glucose values and the incremental area under the curve (iAUC) from baseline to the end of the study was calculated.

Glycemic variability was evaluated using the Mean Amplitude of Glycemic Excursion (MAGE), which was determined through a validated algorithm. The MAGE represents the simple arithmetic average of the amplitude of all glycemic excursions surpassing a pre-set threshold size (typically one standard deviation). The mean glucose level, Glucose Monitoring Index (GMI), largest amplitude of glycemic excursion (LAGE) and Coefficient of Variation (CV) were recorded. The GMI is derived from the patient's mean glucose level[19] and LAGE was obtained from the maximum range of daily blood glucose fluctuations

obtained by subtracting minimum from maximum value, and the daily maximum range across 14 days was then equilibrated.[20] A series of time intervals concerning glucose concentrations, specifically focusing on the percentage of time spent above 180 mg/dL, above 250 mg/dL, and Time In Range (TIR) of 70-180 mg/dL were documented. The iAUC (mg/dL*15 min), and meal-wise iAUC for breakfast, lunch, and dinner (mg/dL*15 min) were also recorded.

Safety parameters

Safety outcome measures included adverse events (AEs) or serious adverse events (SAEs) (if any), with description, intensity, duration, outcome, action taken, and opinion about causal relationships recorded. All patient-related original documents, such as informed consent forms and laboratory reports, were collected and maintained at the study center. The study-related data were captured with the allocated code to patients (without identifying information) in the source document and then in case report forms (CRF). Raw CRF data were compiled and verified for accuracy and then archived at the site.

Statistical analysis

The sample size was calculated with a power of 80%, accounting for a 20% expected drop-out rate, a type 1 error rate of 0.05, and a mean difference in iAUC of 21.7 units with a standard deviation of 13.3 for the test group and 13.6 for the control group.[21] All study data were processed using EpiNu software (version 2.0, Chennai, India). Continuous variables are reported as means with standard deviations (SD), and changes in anthropometric and biochemical parameters from baseline were evaluated. The 24-hour interstitial glucose concentration was utilized to compute the iAUC, MAGE, LAGE, and GMI over a 14-day period. Additionally, the interstitial glucose concentration data were analyzed in accordance with the guidelines set forth by the International Consensus on TIR.[22] Differences between the test and control diets were evaluated through a generalized linear model, while comparisons within diets were conducted using a paired t-test. All statistical analyses were carried out utilizing SAS software (Version 9.4, SAS Inc.), with a *p*-value of less than 0.05 considered statistically significant.

RESULTS

Demographic characteristics of participants

Among the 21 individuals who qualified and registered for the study, 15 successfully completed both study periods. One individual had to withdraw after changing his diabetes

medication, while the remaining five dropped out for personal reasons, largely due to restrictions related to the COVID-19 pandemic. Among the 21 participants, 18 finished the control diet period, and 19 completed the test diet period. For this analysis, we focused on the 15 participants who completed both diets (Figure 1).

The average age of those recruited for the study was 46.95 ± 4.02 years, comprising 40% male and 60% female participants (Table 1). No significant differences in clinical and biochemical parameters were detected at the onset of each diet period, regardless of whether analyses were conducted using an intent-to-treat or per-protocol approach. This suggests that the randomization in this crossover trial, combined with a proper washout period, effectively minimized any carryover effects.

Anthropometric parameters

The anthropometric measurements of all study participants are detailed in Table 2. A statistically significant decrease was observed in both the test (p=0.01) and control ($p < 0.05$) diets in waist circumference (cm) compared to baseline measurements. However, no significant differences in waist circumference were observed when comparing the two diets. Additionally, other anthropometric measures, including body weight and BMI, did not exhibit significant changes after either diet. Clinical assessments of BP (mmHg), both systolic and diastolic, showed a non-significant decrease over the 14-day period within each diet when compared to baseline and between the diets.

Biochemical parameters

Following the 14-day intervention, the test diet resulted in a statistically significant reduction in both FPG levels (mg/dL) (p=0.02) and HbA1c (%) (p=0.04) relative to baseline measurements. However, fasting insulin levels showed a non-significant reduction in this test diet. The control diet exhibited no statistically significant changes in FPG levels, HbA1c, or fasting insulin as compared to baseline. Furthermore, no significant differences were observed in FPG and insulin levels and HbA1c between the two diets. Liver function parameters such as total bilirubin (p<0.001), total protein (p=0.01), and albumin (p<0.001) were significantly increased in the test diet , whereas the control diet showed a statistically significant reduction in alkaline phosphatase (ALP) levels (p=0.02) from the baseline. Significant differences were observed in total protein (p=0.02), albumin (p=0.02), and globulin (p=0.04) parameters between the diets. However, the significant increase and decrease in liver function parameters were within the physiological limits (Table 3).

CGM parameters

The test diet showed a significant reduction in glycemic response compared to the control diet, as evidenced by both the iAUC (p=0.02), MAGE (p=0.006), and LAGE (p=0.003). Specifically, the iAUC for iso-caloric meals showed statistically significant reductions at breakfast (p=0.02), lunch (p=0.03), and dinner (p=0.04) in the test diet group. Additionally, the test diet resulted in a significant decrease in mean glucose levels (p=0.007) compared to the control diet. The proportion of time spent within the target glucose range of 70-180 mg/dL was significantly greater on the test diet (64.97 ± 19.85%) compared to the control diet (49.23 ± 24.09%) (p=0.025). The test diet also significantly reduced the duration of hyperglycemia, especially for glucose levels exceeding 180 mg/dL (p=0.004) and 250 mg/dL (p=0.003), in comparison with the control diet. Furthermore, the test diet showed significant reductions in mean glucose levels (p=0.007) and GMI (p=0.007) as compared to the control diet (Table 4).

Safety parameters

Both diets were well tolerated, and there was no incidence of SAE. Five incidences of AEs (stomach pain, stomach upset, common cold, and hypoglycemia) of mild severity were reported in the test diet and recovered in a day without any treatment except for antibiotics prescribed for the common cold. No AEs were observed in the control diet. Additionally, there were no instances of participants withdrawing from the study as a result of any AEs.

DISCUSSION

A 14-day crossover study in individuals with type 2 diabetes assessed the effect of daily 30g of 'FenuflakesTM'. The incorporation of FenuflakesTM in the test diet significantly reduced glycemic variability, as measured by a significant decrease in MAGE, FPG, and HbA1c levels. Additionally, participants spent significantly more time within the target interstitial glucose range, indicating improved overall glucose control.The Indian Expert Consensus Recommendations on TIR for glucose monitoring in individuals with diabetes propose a target TIR exceeding 70%. This recommendation accounts for ethnic variations and aligns with the current understanding of optimal glycemic control parameters.[22, 23] The optimal parameters specify a target average glucose level of 173 mg/dL. Moreover, the proportion of time spent above 250 mg/dL should be kept below 5%.22In a comparative analysis, the test diet demonstrated significant improvements in TIR (~65%) and time above 250 mg/dL (~4%) versus the control diet, which had TIR at ~49% and time above 250 mg/dL at ~13%. This

underscores that the Fenuflakes™ intake over a longer duration beyond 14 days may step up, achieving the target percent time of >70%. The test diet exhibited a significant decrease in mean glucose levels, with levels averaging approximately 134 mg/dL. In comparison, the control diet presented with an average glucose level of around 177 mg/dL. These results indicate that the integration of Fenuflakes™ into dietary regimens may offer therapeutic advantages in terms of the amount of fiber and protein to improve the overall quality of Indian diets that are generally lower in fiber and protein.16 Controlling glycemic variability in diabetes is critical for preventing micro and macrovascular problems. This is especially relevant for diabetic people with a higher propensity for the development of cardiovascular diseases.[24, 25] Fenugreek seeds decrease carbohydrate absorption in the intestine, which may reduce postprandial glycemia and insulin demand.[26] A meta-analysis of clinical studies indicated that the consumption of fenugreek seeds led to a statistically significant decrease in fasting blood glucose levels, postprandial glucose at the two-hour mark, and HbA1c levels.[12, 27] The analysis revealed that the mean area under the glucose curve for both rice and wheat consumed with fenugreek was significantly decreased compared to the control diet. This effect appears to be attributable to fenugreek's ability to reduce glucose absorption and retard starch digestion, mediated by its soluble fiber content and galactomannans.[28] In a review of ten clinical studies, the acute postprandial glycemic response modulated by fenugreek seeds is predominantly linked to their dietary fiber composition.[12] The viscosity of fiber in FenuflakesTM of added meals could have prevented the amylolytic enzyme or coated the starch granules in the meal and created a barrier for the amylolytic hydrolysis of starch, resulting in delayed digestion and absorption of glucose into the bloodstream. Debittered FenuflakesTM, being a rich source of soluble fiber with acceptable sensory properties, can be a functional ingredient in healthy foods and can be incorporated into daily diets to achieve favorable health benefits.

Dietary fiber influences postprandial blood glucose levels through three main mechanisms. First, it increases the viscosity of intestinal contents, which slows down glucose diffusion into the bloodstream. Second, fiber binds to glucose, reducing the amount of free glucose available for absorption in the small intestine. Lastly, it inhibits α-amylase, which delays the digestion of starch.[29] Galactomannan, a soluble fiber, has demonstrated the ability to slow the intestinal absorption of sugars.[28] Studies suggest that low-dose interventions, around 1 g daily, can significantly aid in the management of hyperglycemia in patients who have recently been diagnosed with T2D.[30] Notably, galactomannan derived from fenugreek exhibits an exceptional gel-forming capacity, attributed to its optimal galactose-to-mannose ratio of 1:1.[31]

A systematic review and network meta-analysis evaluated the impact of soluble dietary fibers on glycemic and lipid profiles in T2D patients. Galactomannans were found to be the most effective in reducing HbA1c, fasting blood glucose, triglycerides, and LDL cholesterol.[32]

The product Fenuflakes™, known for its high dietary fiber content, requires additional investigation to clarify its mechanism. Preliminary findings indicate that including Fenuflakes™ in the diet leads to a significant reduction in HbA1c levels, which is consistent with previous studies demonstrating similar advantages from various forms of fenugreek supplementation, such as fenugreek extract[33] and powder derived from raw, boiled, and germinated seeds.[32, 34] The CGM data from this study revealed a significant decrease in the MAGE and LAGE among participants who followed a Fenuflakes™-enriched diet. Previous reports indicate that mitigating glycemic variability could play a significant role in reducing the long-term complications associated with diabetes.[35-37] This underscores the potential efficacy of Fenuflakes™ in reducing glycemic variability, which may, in turn, contribute to the prevention of these complications. Additionally, the study found a significant decrease in the iAUC after meals, indicating that incorporating Fenuflakes™ can effectively manage postprandial glycemic responses.

Dietary fiber is known to enhance the synthesis of SCFA in the colon through fermentation by gut bacteria.[40, 41] Numerous studies highlight the positive effects of dietary fiber on obesity and diabetes[42, 43] with meta-analyses providing evidence that SCFA interventions can help lower fasting hyperinsulinemia.[44] Fenuflakes™, in particular, exhibit prebiotic properties by increasing SCFA levels and enhancing the growth of beneficial colon bacteria.[17]

AEs reported, such as stomach pain or discomfort, in the test diet may be attributable to the elevated fiber content of Fenuflakes. An increase in dietary fiber can lead to alterations in gastrointestinal function, particularly during the initial adaptation phase.[45] This may manifest as increased flatulence,[46] changes in stool consistency, abdominal symptoms (including bloating, cramping, and a sensation of fullness), or modifications in bowel habits (such as urgency and defecatory issues).[47] However, there is limited research on the temporal dynamics of early gastrointestinal discomfort. The current study indicates that these AEs resolved spontaneously within a day without necessitating any medical intervention.

The primary strength of this study is its innovative approach. It is the first study to investigate the 24-hour glycemic response to diets including FenuflakesTM. The crossover design allowed participants to act as their controls, reducing intra-individual variability. CGM was effectively used, offering advantages over HbA1c and self-blood glucose testing. Participants reported a favorable acceptance of FenuflakesTM after the bitter flavor of

fenugreek seeds was removed. A detailed analysis of macronutrients and dietary fiber provided a clear comparison between control and test diets, improving the understanding of the mechanisms of the observed outcomes.However, the study has few limitations: while proximate analyses and mineral content of FenuflakesTM were conducted, active components such as galactomannan, saponins, trigonelline, diosgenin, and 4-hydroxy isoleucine remain unexamined. The incorporation of FenuflakesTM in its standard form in dietary preparations may not fully exploit its potential; future research should investigate the incorporation of FenuflakesTM in various forms, possibly enhancing the textural properties of meals.

Conclusion

This crossover study presents compelling evidence that debittered 'FenuflakesTM' can significantly reduce glycemic variability in T2D patients. Employing CGM, the research underscores FenuflakesTM efficacy in enhancing glycemic control throughout the day. It was also found to be safe and well-tolerated by the study participants. Research on FenuflakesTM needs to be explored at different levels in recipes and for a longer study duration to validate their impact on glycemic control and sustainability in T2D management across various populations.

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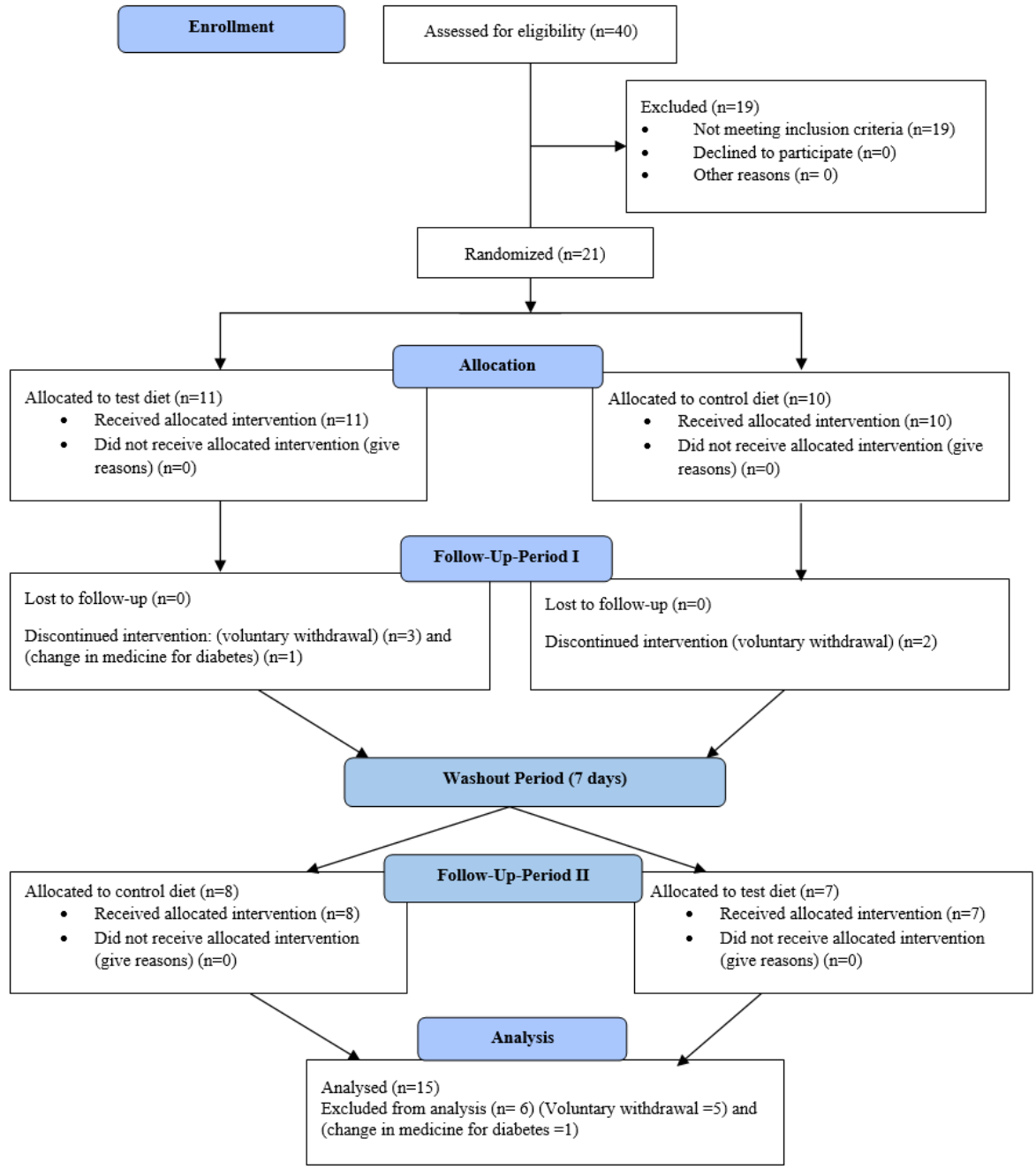
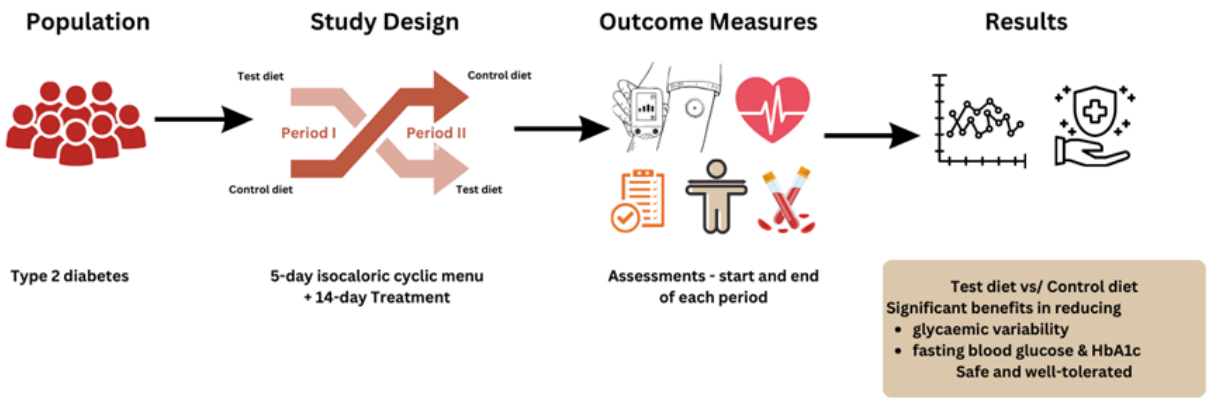


Figure 1. CONSORT chart



Graphical abstract

Table 1. Effect on demographic characteristics

Variables	Total participant (n=15)
Age (years)	46.95 ± 4.02
Sex	
Male n (%)	6 (40)
Female n (%)	9 (60)
Income	
<25000 n (%)	9 (60)
>25000 n (%)	6 (40)
Smoking status n (%)	
Current n (%)	1 (7)
Never n (%)	14 (93)
Alcohol consumption n (%)	
Current n (%)	3 (20)
Never n (%)	12 (80)
Family history of diabetes	
No diabetic parents	6 (40)
One parent with diabetes	8 (53)
Both parents with diabetes	1 (7)
Body weight (kg)	63.83 ± 12.12
BMI (kg/m^2)	26.36 ± 5.08
Waist circumference -WC (cm)	91.21 ± 11.34
Systolic BP -SBP (mmHg)	132.93 ± 18.54
Diastolic pressure BP -DBP (mmHg)	92.03 ± 18.02
FPG (mg/dL)	172.93 ± 37.63
HbA1c (%)	8.71 ± 0.93
Fasting Insulin (µIU/mL)	11.16 ± 6.03

Data presented as mean± SD for continuous variables and n (n%) for categorical variables.

Table 2. Effect on anthropometric parameters

	Test diet (n=15)			Control diet (n=15)			*p* value‡
Variables	Baseline	End study	Change†	Baseline	End study	Change†	
Body weight (kg)	63.93 ± 13.20	63.58 ± 12.85	-0.34 ± 0.89	63.97 ± 12.04	63.92 ± 12.02	-0.05 ± 0.90	0.38
Waist circumference (cm)	91.49 ± 9.87	88.72 ± 11.16	-2.76 ± 3.30**	91.15 ± 12.00	89.29 ± 10.83	-1.86 ± 3.15*	0.45
BMI (kg/m^2)	26.55 ± 5.15	26.42 ± 5.11	-0.13 ± 0.31	26.61 ± 5.00	26.63 ± 5.05	0.02 ± 0.37	0.25
Systolic BP (mmHg)	131.50 ± 18.43	127.70 ± 19.78	-3.8 ± 9.15	130.23 ± 20.15	127.47 ± 21.14	-2.77 ± 19.22	0.85
Diastolic BP (mmHg)	88.80 ± 10.47	84.23 ± 13.25	-4.57 ± 9.61	89.27 ± 18.51	85.47 ± 13.01	-3.80 ± 19.93	0.89

n= number of participants.
Data presented as mean± SD
†Within-diet significance tested using paired t-test.
‡Difference between diet were tested using Generalized Linear Model (GLM)
*p<0.05, **p=0.01.

Table 3. Effect on biochemical parameters

	Test diet (n=15)			Control diet (n=15)			*p* value‡
Variables	Baseline	End study	Change†	Baseline	End study	Change†	
FPG (mg/dL)	186.93 ± 54.72	163.60 ± 44.47	-23.33 ± 33.23*	160.07 ± 48.56	156.87 ± 46.87	-3.20 ± 26.06	0.08
HbA1c (%)	8.91 ± 1.13	8.74 ± 1.15	-0.17 ± 0.29*	8.86 ± 1.52	8.79 ± 1.38	-0.07 ± 0.61	0.60
Fasting Insulin (µIU/mL)	12.49 ± 7.26	10.14 ± 4.92	-2.4 ± 4.4	12.39 ± 7.00	13.19 ± 8.48	0.80 ± 4.74	0.07
Total bilirubin (mg/dL)	0.55 ± 0.36	0.73 ± 0.50	0.17 ± 0.15***	0.59 ± 0.33	0.65 ± 0.30	0.06 ± 0.19	0.09
Total protein (g/dL)	7.26 ± 0.29	7.49 ± 0.35	0.23 ± 0.26**	7.38 ± 0.41	7.29 ± 0.35	-0.09 ± 0.36	0.02
Albumin (g/dL)	4.09 ± 0.27	4.26 ± 0.25	0.17 ± 0.13***	4.13 ± 0.20	4.14 ± 0.26	0.01 ± 0.23	0.02
Globulin (g/dL)	3.17 ± 0.36	3.23 ± 0.40	0.05 ± 0.17	3.25 ± 0.43	3.15 ± 0.37	-0.09 ± 0.19	0.04
SGOT (IU/L)	24.13 ± 19.38	22.33 ± 9.00	-1.80 ± 11.97	22.93 ± 9.95	27.60 ± 36.37	4.67 ± 32.05	0.47
SGPT (IU/L)	21.73 ± 16.35	21.87 ± 10.04	0.13 ± 9.97	21.53 ± 8.78	27.33 ± 38.85	5.80 ± 37.71	0.58
ALP (IU/L)	98.07 ± 34.11	96.20 ± 29.19	-1.87 ± 15.67	106.53 ± 31.76	98.60 ± 30.27	-7.93 ± 11.22*	0.23
GGT (IU/L)	32.07 ± 20.21	32.53 ± 25.91	0.47 ± 9.98	36.07 ± 17.95	40.33 ± 40.64	4.27 ± 28.36	0.63

n= number of participants; FPG: xxxxx; HbA1c: xxxxx; SGOT: xxxx; SGPT: xxxxx; ALP: xxxxx; GGT: xxxx
Data presented as mean± SD
†Within-diet significance tested using paired t-test.
‡Difference between diet were tested using Generalized Linear Model (GLM)
*p<0.05, ***p<0.001.

Table 4. Effect on CGM Parameters

Variables	Test diet (n=15)	Control diet (n=15)	p value†
Mean glucose level (mg/dL)	134.10 ± 43.03	177.22 ± 45.01	0.007
GMI	6.52 ± 1.03	7.55 ± 1.08	0.007
CV	31.18 ± 8.26	27.88 ± 8.00	0.291
Time above range 180 mg/dL (%)	21.71 ± 22.93	47.55 ± 28.55	0.004
Time above range 250 mg/dL (%)	3.58 ± 5.61	13.37 ± 12.47	0.003
TIR 70-180 mg/dL (%)	64.97 ± 19.85	49.23 ± 24.09	0.025
IAUC mg/dL*15 min[1]	473.05 ± 165.16	678.87 ± 277.01	0.02
Meal wise IAUC mg/dL*15 min			
Breakfast	246.88 ± 69.89	329.70 ± 102.97	0.02
Lunch	226.03 ± 112.31	347.44 ± 165.41	0.03
Dinner	386.26 ± 128.10	498.38 ± 152.03	0.04
MAGE	93.35 ± 21.13	114.99 ± 25.80	0.006
LAGE	119.22 ± 29.72	156.36 ± 32.38	0.003

n= number of participants; CMI: XXXX; CV: XXXX; IAUC: XXXX; MAGE: XXXXX; LAGE: XXXXX
Data presented as mean± SD.
†Difference between diet were tested using Generalized Linear Model (GLM)
*p<0.05.