Research Article Open Access

Effects of a 4-week supplementation with novel bioactives N-Trans Caffeoyltyramine (NCT) and N-Trans Feruloyltyramine (NFT) on parameters of continuous glucose monitoring in individuals with prediabetes

Seema Gulati[1,2,3], Anoop Misra[1,2,3,4], Rajneesh Tiwari[2], Michelle L. Zuelch[5], Swati Kalgaonkar[6*]

[1]Diabetes Foundation (India), New Delhi, India; [2]National Diabetes, Obesity and Cholesterol Foundation (N-DOC), New Delhi, India; [3]Center of Nutrition & Metabolic Research (C-NET), New Delhi, India; [4]Fortis C-DOC Centre for Excellence for Diabetes, Metabolic Disease, and Endocrinology, New Delhi, India; [5]Formerly Brightseed, South San Francisco, CA, USA; [6]Brightseed, South San Francisco, CA, USA

***Corresponding Author:** Swati Kalgaonkar, PhD, Brightseed, 310 Utah Ave, Ste 100, South San Francisco, CA 94080, United States.

Submission Date: January 28th, 2026; **Acceptance Date:** February 11th, 2026; **Publication Date:** February 13th, 2026

Please cite this article as: Gulati S., Misra A., Tiwari R., Zuelch M. L., Kalgaonkar S. Effects of a 4-week supplementation with novel bioactives N-Trans Caffeoyltyramine (NCT) and N-Trans Feruloyltyramine (NFT) on parameters of continuous glucose monitoring in individuals with prediabetes. *Bioactive Compounds in Health and Disease* 2026; 9(2): 54 – 64.
DOI: https://doi.org/10.31989/bchd.v9i2.1921

ABSTRACT

Background: Beyond dietary modification, bioactive compounds have emerged as modulators of glycemic regulation. Silico analysis has identified N-trans-caffeoyltyramine (NCT) and N-trans-feruloyltyramine (NFT) as potent modulators of hepatocyte nuclear factor 4α (HNF4α), thereby favorably regulating blood glucose metabolism.

Objective: To evaluate the effects of a proprietary dietary supplement containing novel bioactives, NCT and NFT, on parameters of continuous glucose monitoring in individuals with prediabetes.

Methods: A 4-week randomized, double-blind, placebo-controlled parallel arm trial was conducted in adults (Age: 18-50 years; BMI: 25-30 kg/m^2) with prediabetes (fasting blood glucose ≥100 mg/dL) and abdominal adiposity (waist circumference ≥80cm for females and ≥90 cm for males). A total of 126 participants were randomized to receive either 120 mg/d NCT/NFT (n=63) or placebo (n=63). Glycemic control measures were assessed by continuous glucose monitoring (CGM) and included total 24-hour glucose AUC, mean 24-hour glucose, maximum 24-hour glucose, minimum nighttime glucose, MAGE, MoDD, and basal hyperglycemia AUC. Homeostatic model assessments of insulin resistance (HOMA-IR) and β-cell function (HOMA-β), and quantitative insulin sensitivity check index (QUICKI) were also measured.

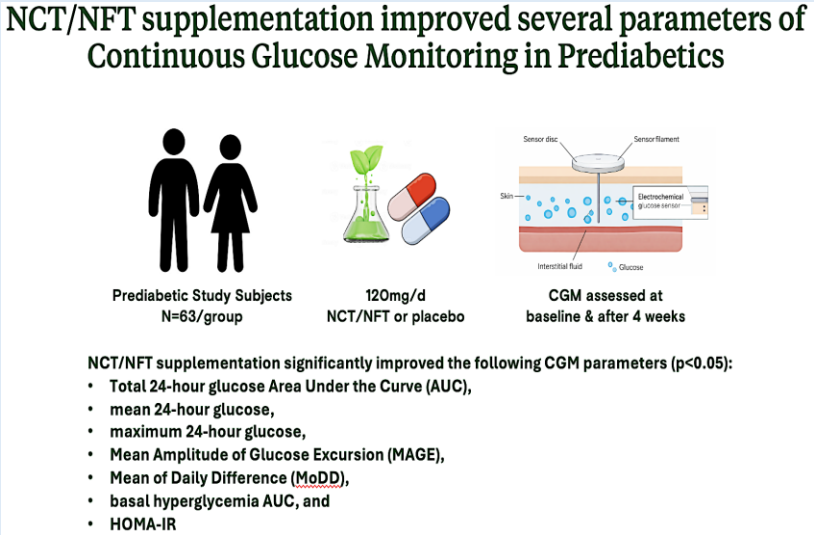
Results: Supplementation with 120 mg/d NCT/NFT for 4-weeks improved measures of glycemic control compared to placebo. Total 24-hour glucose AUC, mean 24-hour glucose, maximum 24-hour glucose, MAGE, MoDD, basal hyperglycemia AUC, and HOMA-IR were all found to improve significantly ($p<0.05$). Minimum nighttime glucose also showed a non-significant trend towards improvement. No changes in HOMA-β or QUICKI were observed.

Conclusions: Overall glycemic burden, as measured using various CGM parameters, was significantly improved in response to treatment with NCT/NFT. Select measures of insulin resistance were also improved. These findings confirm the utility of a proprietary dietary supplement containing NCT/NFT to support glycemic control in individuals with dysglycemia.

Novelty of the Study: This trial is among the first to investigate the effects of novel bioactives NCT and NFT supplementation on glycemic regulation in adults with prediabetes using CGM endpoints. Unlike prior studies relying primarily on point-in-time measures (e.g., fasting glucose or serum insulin), this study integrates both cross-sectional (fasting glucose) and continuous (continuous glucose monitoring) endpoints to enable a more comprehensive evaluation of glycemic control. This second manuscript extends the initial report by focusing specifically on continuous glucose monitoring outcomes alongside previously published findings.

Keywords: glucose regulation, continuous glucose monitoring dietary supplements, Type 2 diabetes, post-prandial glucose, N-trans-Caffeoyltyramine, N-trans-Feruloyltyramine, NCT, NFT, prediabetes, HNF4α

Graphical Abstract: Supplementation with NCT/NFT showed a statistically significant improvement in several CGM parameters in prediabetic subjects within 4 weeks compared to placebo.



INTRODUCTION

Prevalence of Type 2 diabetes (T2D) is high in the US – affecting 38 million (1 in every 10) people - and has been shown to be associated with numerous severe health complications, including dysfunction of the renal and cardiovascular systems and retinopathy [1]. Prediabetes is known to be an intermediary and reversible stage in the development of type 2 diabetes and provides a

unique window of opportunity for treatment intervention. Prediabetes is defined by blood glucose levels that are higher than normal, but not yet high enough to be considered T2D [2]. At this stage of disease progression, return to normoglycemia may still be achieved [2].

Lifestyle modification is the cornerstone of diabetes prevention [2,3]. Behavior change, including nutritional intervention, can reduce the risk of developing T2D by more than 50% [4]. Beyond traditional dietary modifications, the inclusion of select bioactive compounds has been increasingly recognized as a means of furthering glycemic control [5]. These bioactives have been shown to regulate glucose metabolism by modulating pancreatic insulin secretion , glucose uptake by the periphery, and glucose output by the liver [6].

In silico prediction validated by preclinical research has highlighted the role of novel bioactives, N-trans-Caffeoyltyramine (NCT) and N-trans-Feruloyltyramine (NFT), as potent hepatocyte nuclear factor 4 alpha (HNF4α) agonists [7,8]. HNF4α is a key transcription factor involved in both glucose and lipid metabolism [9,10]. Known as the 'master metabolic regulator', HNF4α plays key roles in detecting glucose and facilitating insulin secretion in the pancreas [11,12] and regulating gluconeogenesis, fatty acid oxidation, and lipoprotein assembly in the liver [12,13].

The aim of this study was to evaluate the efficacy of a proprietary dietary supplement containing NCT/NFT on biomarkers of glycemia as assessed by continuous glucose monitoring in individuals with prediabetes. For the purposes of this study, a proprietary blend of these biomimetic plant compounds was produced via precision fermentation intended for human consumption as an ingredient in food, beverage, and supplement applications. The present clinical study seeks to confirm previous preclinical findings, and as such, is entirely novel; the effectiveness of NCT/NFT on blood glucose regulation in humans had not been previously explored. The results of this study can be used to inform potential adjunctive therapies for those with or at risk for developing T2D and is particularly important considering the high prevalence of dysglycemia in the U.S.

MATERIALS AND METHODS

Study design: Detailed methodology has been outlined in a prior publication, along with the Institutional Ethics Committee approved study protocol registration number (Registration Number: ECR/1233/Inst/dl/2019) and the ClinicalTrials.gov reference number (NCT06417840; 05/16/2024) [14].

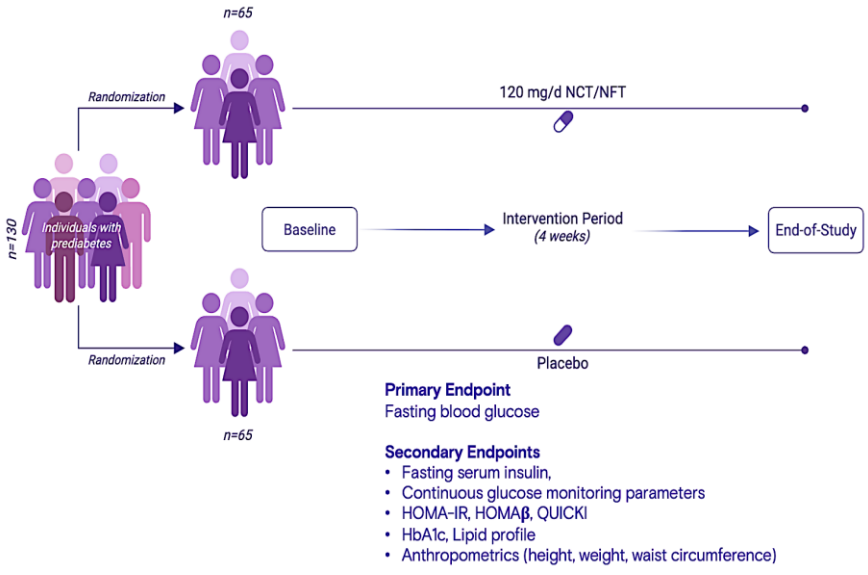


Figure 1. Study Design

Outcome Measures: Given the high volume of data, this study is being published in two phases. The first set of results are published in a previous manuscript [14]. The current manuscript will cover the following endpoints:

Continuous Glucose Monitoring (CGM): Continuous glucose levels were assessed using the Guardian™ 4 CGM system (Medtronic MiniMed, Northridge, CA, USA), which employs electrochemical sensing of glucose in subcutaneous interstitial fluid. Sensors were placed in the upper arm or lateral abdominal wall and worn for three consecutive days at baseline (days 1–3) and during the final study period (days 28–31) to assess the impact of the 4-week treatment intervention. Participants consumed one standardized test meal during each monitoring phase, while all other meals reflected habitual dietary intake. Glucose data were automatically uploaded daily, generating comprehensive glycemic summaries.

CGM data were analyzed to assess the following endpoints:

i. 24-Hour Total Glucose AUC

A comprehensive view of blood glucose levels over a 24-hour period.

ii. 24-Hour Mean Glucose

Average glucose level over a 24-hour period.

iii. Maximum 24-Hour Glucose

Peak glucose level over a 24-hour period.

iv. Minimum Nighttime Glucose

Minimum glucose level over a 24-hour period, which occurs overnight while in a fasted state.

v. Mean Amplitude of Glucose Excursion (MAGE)

A measure of within-day blood glucose fluctuations.

vi. Mean of Daily Difference (MoDD)

A measure of blood glucose variability from day-to-day.

vii. Basal Hyperglycemia AUC

Stable overnight glucose AUC that is not influenced by meals.

Insulin Resistance and β-Cell Function: Insulin resistance and pancreatic β-cell function were measured by Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), Homeostatic Model Assessment of β-Cell Function (HOMA-β), and Quantitative Insulin Sensitivity Check Index (QUICKI). These values are derived based on measures of fasting glucose and insulin and are calculated by the following equations:

HOMA-IR = [Glucose mg/dL X Insulin µU/mL] / 405

HOMA-β = [360 X Insulin µU/mL] / [Glucose mg/dL - 63]

QUICKI = [log10(Insulin µU/mL) + log10(Glucose mg/dL)]-1

Statistical Analysis: Sample size calculations have been previously described [14]. Analysis of covariance (ANCOVA) was applied to evaluate intervention effects on changes from baseline in CGM-derived endpoints, with sex, age, and baseline fasting blood glucose included as covariates and intervention group specified as a fixed effect. Please refer to the previous publication [14] for additional details on statistical analysis.

RESULTS

Subject screening, eligibility, and enrollment details are shared in the previous publication [14].

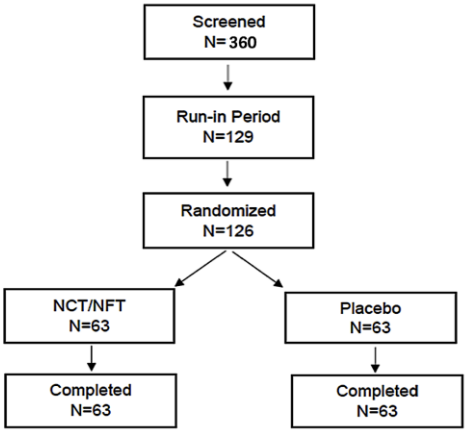


Figure 2. Consort Diagram

Baseline Characteristics: In addition to age, waist circumference, and BMI, the study groups were also comparable in terms of blood glucose measures, like fasting blood glucose and fasting serum insulin at baseline (Table 1). Groups were also similar in terms of energy and macronutrient intake and continued to consume their habitual diet.

Table 1. Baseline Characteristics

	NCT/NFT (n=63)	Placebo (n=63)
Age (years)	43.1 ± 9.4	44.4 ± 9.9
Gender (M:F)	41:22	30:33
Body Mass Index (kg/m^2)	27.2 ± 1.6	27.4 ± 1.5
Waist circumference (cm)	97.7 ± 6.3	97.3 ± 6.5
Fasting blood glucose (mg/dL)	108.4 ± 8.3	108.1 ± 6.4
Fasting serum Insulin (mU/ml)	19.6 ± 11.6	18.2 ± 14.8
HbA1c (%)	5.9 ± 0.4	5.8 ± 0.3

Values are means ± standard deviation. HbA1c: hemoglobin A1c

Continuous Glucose Monitoring: Figure 3 features the pre- and post-intervention values of the average 24-hr continuous glucose measures in treatment and placebo groups. The difference in baseline blood glucose between the two groups was adjusted for prior to data analyses. A summary of CGM outcome results is provided in Table 2. Actual data values of 24hr total AUC glucose (mg/dL*min), 24hr mean blood glucose (mg/dL*min), and postprandial hyperglycemia are presented in tables 3, 4 & 5, respectively.

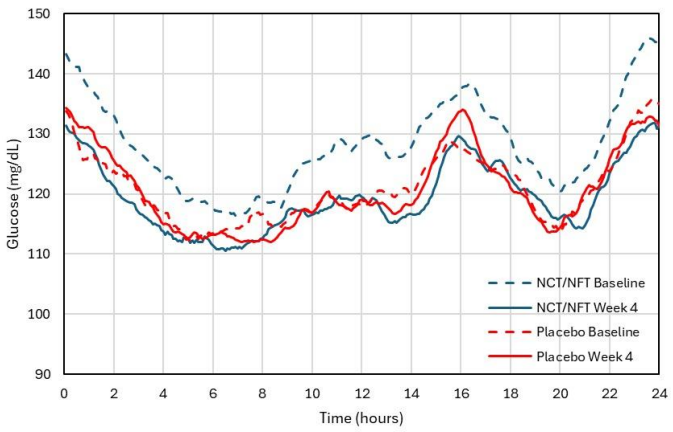


Figure 3: Average 24-Hr Continuous Glucose Measures

Table 2. Summary of Differences in CGM Outcomes between NCT/NFT and Placebo Groups

Outcome	NCT/NFT		Placebo		p-value
	Day 0	Day 28	Day 0	Day 28	
Total Glucose (mg/dL*min) AUC	542,434.7 ± 78,547.8	494,926.1 ± 83331.9	499,322.5 ± 89,411.9	511,575.2 ± 76,956.2	0.0018*
Mean Glucose (mg/dL*min)	127.9 ± 15.9	119.4 ± 15.3	120.6 ± 16.8	120.5 ± 15.6	0.0286*
Maximum Glucose (mg/dL)	189.3 ± 27.3	169.0 ± 22.3	172.9 ± 29.6	175.4 ± 25.8	<0.0001*
Minimum Glucose (mg/dL)	95.2 ± 13.7	89.9 ± 14.7	90.9 ± 13.8	92.0 ± 15.1	0.1697
MAGE (mg/dL)	29.3 ± 16.4	19.8 ± 10.9	21.7 ± 13.1	23.8 ± 14.5	<0.0001*
MoDD (mg/dL)	25.6 ± 7.5	21.3 ± 5.7	21.9 ± 7.8	23.0 ± 7.7	0.0017*
Basal Hyperglycemia (mg/dL) AUC	137,972.7 ± 22,118.8	123,394.3 ± 23,780.9	126,315.2 ± 25,478.5	130,161.0 ± 26,634.6	0.0035*

Values are means ± standard deviations. Asterisk (*) denotes statistical significance ($p<0.05$). MAGE: Mean Amplitude of Glucose Excursion; MoDD: Mean of Daily Difference; AUC: area under the curve

Table 3. 24hr total AUC glucose (mg/dL*min)

	NCT/NFT (N = 63)	Placebo (N = 63)
Baseline		
n	63	63
Mean (SD)	542,434.7 (78,547.76)	499,322.5 (89,411.85)
Median	525,975.0	498,545.0
Min, Max	308,235; 754,490	195,950; 834,460
Post-Intervention (Visit 6)		
n	63	63
Mean (SD)	494,926.1 (83,331.89)	511,575.2 (76,956.17)
Median	485,800.0	500,720.0
Min, Max	263,345; 713,110	289,100; 725,140
Change from Baseline		
n	63	63
Mean (SD)	−47,508.6 (72,052.12)	12,252.7 (85,044.06)
Median	−41,380.0	1,540.0
Min, Max	−211,920; 269,630	−250,430; 269,840
LSM (SE)	−38,519.88 (8,925.966)	2,141.56 (8,740.476)
95% CI	−56,191.180; −20,848.574	−15,162.515; 19,445.641
LSM Treatment Difference (SE)	−40,661.44 (12,739.771)	—
95% CI	−65,883.177; −15,439.703	—
p-value	0.0018	—

Table 4. 24hr Mean Blood Glucose (mg/dL*min)

	NCT/NFT (N = 63)	Placebo (N = 63)
Baseline		
n	63	63
Mean (SD)	127.893 (15.8663)	120.629 (16.7512)
Median	124.196	116.626
Min, Max	104.35; 174.65	73.67; 193.16
Post-Intervention (Visit 6)		
n	63	63
Mean (SD)	119.358 (15.3355)	120.496 (15.5503)
Median	118.159	119.351
Min, Max	92.66; 165.07	97.65; 167.86
Change from Baseline		
n	63	63
Mean (SD)	−8.535 (12.0175)	−0.133 (17.0391)
Median	−7.911	−0.247

	NCT/NFT (N = 63)	Placebo (N = 63)
Min, Max	−48.81; 15.71	−57.97; 47.60
LSM (SE)	−7.00 (1.671)	−1.74 (1.639)
95% CI	−10.309; −3.694	−4.982; 1.507
LSM Treatment Difference (SE)	−5.26 (2.376)	—
95% CI	−9.968; −0.560	—
p-value	0.0286	—

Table 5. Postprandial Hyperglycemia (mg/dL) AUC

	NCT/NFT (N = 63)	Placebo (N = 63)
Baseline		
n	63	63
Mean (SD)	108,673.2 (25,856.84)	97,145.2 (20,976.45)
Median	102,930.0	94,975.0
Min, Max	55,520; 190,700	38,535; 139,260
Post-Intervention (Visit 6)		
n	63	63
Mean (SD)	95,389.6 (23,457.63)	103,398.7 (20,905.85)
Median	93,245.0	103,400.0
Min, Max	31,220; 161,380	60,580; 149,985
Change from Baseline		
n	63	63
Mean (SD)	−13,283.6 (19,549.12)	6,253.6 (24,073.85)
Median	−10,915.0	7,870.0
Min, Max	−63,925; 24,980	−48,550; 67,440
LSM (SE)	−10,686.75 (2,459.661)	3,585.17 (2,408.300)
95% CI	−15,556.295; −5,817.200	−1,182.699; 8,353.030
LSM Treatment Difference (SE)	−14,271.91 (3,505.026)	—
95% CI	−21,211.037; −7,332.790	—
p-value	0.0001	—

Insulin Resistance and β-Cell Function

HOMA-IR: Insulin resistance, as assessed by HOMA-IR, was significantly improved with treatment (NCT/NFT: -0.4 ± 2.5 vs placebo: 0.7 ± 2.3; p=0.0028). From baseline, HOMA-IR was significantly increased in the placebo group (+0.71), whereas it was decreased in the NCT/NFT group (-0.47).

HOMA-β & QUICKI: No change between the treatment and placebo groups was observed in pancreatic β-cell function, as assessed by HOMA-β.

No change was observed in either group with regards to insulin sensitivity, as assessed by QUICKI.

DISCUSSION: Nutrition is the foundation of blood glucose management [2]. Emerging research has highlighted the role of dietary bioactives in supporting glycemic control [5]. Novel bioactives NCT and NFT have proven to be HNF4α agonists [7,8], which promote its gluco-regulatory functions [10-12]. The present study confirmed preclinical evidence that supplementation with NCT/NFT supports healthy blood glucose regulation. Whereas the preclinical research on NCT/NFT helped confirm the predicted mechanism of action and demonstrated that these bioactives do indeed induce HNF4α agonism, the current study helps join the remaining dots and demonstrates how induction of that mechanism results in improvements of glycemic endpoints. Daily supplementation with a proprietary , sustained release formulation containing 120 mg NCT/NFT for 4 weeks resulted in significant improvements in several biomarkers of glycemia in individuals with prediabetes, including 24-hour total glucose AUC, 24-hour mean

glucose, 24-hour maximum glucose, MAGE, MoDD, and basal hyperglycemia AUC. No changes in minimum nighttime glucose were observed.

Continuous glucose monitoring provides continuous, real-time data on glucose trends, offering insights beyond traditional point-in-time measurements [15]. Interpretation of CGM data should consider several quantitative metrics and indices of variability to provide a comprehensive characterization of overall glycemic control.

In the current study, mean 24-hour glucose concentrations were significantly reduced in response to the 4-week intervention, indicating reduced glucose exposure, but not necessarily reflecting variability. Total 24-hour glucose AUC, which accounts for both the magnitude and duration of excursions, was also reduced with NCT/NFT treatment over the intervention duration, substantiating evidence of improved overall glycemic control, including mitigated fluctuations. This is supported by the significant reductions observed in both peak glucose and MAGE, which reflects the extent of within-day variability, including peaks and troughs. Variability in mean glucose between consecutive days was also stabilized with the 4-week treatment, as demonstrated by significantly reduced MoDD in the treatment group. Independent of postprandial excursions, basal hyperglycemia AUC was also attenuated, further exemplifying both improved glycemic stability and a lower glycemic burden. Finally, the minimum glucose achieved during the overnight (fasted) period was reduced, albeit not significantly. This could be for a variety of reasons, including nocturnal shifts in metabolism to support a prolonged fasting state (eg. increased hepatic glucose production).[16] Still, the decreasing trend in the NCT/NFT group, along with the significant improvement in other indices, suggests that improvements may be more pronounced with a longer intervention period. While this study was designed with a 4-week intervention period because the endpoints did not require longer intervention time, a 12-week intervention duration is generally recommended for exploratory research. For additional endpoints, like hemoglobin A1c, a 4-week intervention presents as a limitation and a longer intervention should be considered for future studies assessing such outcomes.

The study population was insulin resistant (median HOMA-IR: 4.5; median QUICKI: 0.31) with preserved β-cell function (median HOMA-β: 135.9) at baseline, characteristics which are consistent with a group having prediabetes [16,17]. The significant improvement in HOMA-IR observed in the NCT/NFT treatment group is consistent with the reductions in fasting glucose and insulin that were seen following the intervention. This measure is reflective of the body's ability to maintain insulin-mediated glucose homeostasis. Insulin resistance develops prior to overt hyperglycemia and is therefore an early marker of metabolic dysfunction [18]. Despite statistically significant changes in HOMA-IR, QUICKI - another surrogate marker for insulin sensitivity - remained unchanged. Improvements in HOMA-IR may not necessarily be reflected by QUICKI due to the logarithmic nature of its calculation, which makes it less sensitive to modest improvements in fasting glucose and/or insulin levels. Pancreatic β-cells were not significantly compromised at baseline and, therefore, did not experience further improvements related to the intervention.

Collectively, these findings demonstrate substantial improvements in glycemia and reduced glycemic burden. This is meaningful because chronic elevations and exaggerated fluctuations in glucose contribute to the risk of severe health complications. . Acutely, hyperglycemia presents symptoms such as polydipsia, polyuria, fatigue, headache, and blurred vision [19]. Chronic hyperglycemia damages both the macro- and micro-vasculature, resulting in nerve damage, vision loss, and adverse cardiorenal outcomes [20]. Frequent, pronounced oscillations in blood glucose levels are linked to oxidative

stress and inflammation [21]. Moreover, sharp spikes in blood glucose trigger an exaggerated insulinemic response, resulting in a substantial and abrupt decrease in circulating glucose levels. This reactive hypoglycemia impairs appetite regulation and energy balance, causing excessive hunger, lethargy, difficulty concentrating, and mood disturbances [22]. Attenuating the glucose response and lessening glycemic variability preserves organ-system function (cardiovascular, renal, etc.), decreases systemic oxidative stress, and prevents the acute discomfort associated with hypoglycemia.

Continuous glucose monitoring has become increasingly popular, regardless of diabetes status. In those with abnormal glucose regulation, monitoring glucose continuously helps manage circulating levels and reduce complications associated with dysregulation [23]. In a non-diabetic population, it allows for a personalized snapshot into the inner workings of the body [23]. In both cases, CGMs showcase the influence of external stimuli on internal metabolic processes [24]. Specific to blood glucose regulation, CGMs support sustained metabolic health. Circulating glucose levels fluctuate as part of normal physiological function, including in individuals without diabetes. By understanding the glycemic response elicited by different variables, blood glucose concentrations can be better stabilized, thereby reducing the risk of complications associated with high glycemic load and instability [23]. Insights gained from CGM data can also help detect subtle deviations from usual blood glucose patterns that may signal early signs of metabolic dysregulation and thus support the prevention of T2D [26].

Personalized nutrition, including CGM, is at the forefront of healthcare. New omics technologies have underscored the importance of individualized approaches to health, including in the nutrition and metabolism space (eg. metabolomics) [25]. While other robust, conventional methods continue to be used in mainstream clinical research to assess glycemic regulation [27, 28], the immediate feedback offered by personalized biomonitoring devices like CGM inform lifestyle choices (diet, exercise, sleep, etc.), support optimized metabolism (enhancing glycemic control), and can be a powerful motivator for adopting healthier habits [24].

Healthy blood glucose regulation is key to optimal metabolic health. The role of novel dietary bioactives, NCT and NFT, in achieving this had not previously been explored. The results of this study demonstrate the efficacy of a proprietary dietary supplement containing NCT/NFT in enhancing glycemic control in individuals with prediabetes. A core strength of this study is that it aligns with multiple steps of the FFC Functional Food Development Model, including but not limited to rigorous, evidence-based research that identified a specific health target using in silico predictions and validated them with the help of this human clinical trial. A 4-week treatment with 120 mg/d NCT/NFT yielded significant improvements in several biomarkers of glycemia as assessed by CGM, reducing both glycemic variability and overall glycemic burden. Monitoring glucose concentrations, regardless of diabetes status, can be helpful to inform dietary and lifestyle choices and to mitigate the deleterious complications of abnormal glucose regulation.

Scientific Innovation: This study is the first human clinical trial that utilized a rigorous clinical study design to evaluate a proprietary supplement containing bioactives NCT and NFT, targeting several parameters of continuous glucose monitoring in addition to the point-in-time measurements showcased in the previous publication from this study [14]. The statistically significant improvements in the CGM endpoints represent clinically meaningful outcomes, especially when coupled with the unsolicited testimonials provided by the study subjects, wherein they reported feeling better energy levels throughout the day (secondary to reduced blood glucose level fluctuations) with NCT/NFT supplementation. These

results, combined with those showcased in the earlier publication (improved fasting blood glucose, fasting serum insulin, postprandial glucose, and time out of range), help support the role of NCT/NFT as potent ingredients for cutting edge formulations in the functional food as well as the nutraceutical space for ongoing support of healthy blood glucose regulation, as in the case of those weaning off GLP-1 drugs.

Practical Implications: The incidence of prediabetes and type 2 diabetes continues to rise worldwide. Once targeted blood glucose control is achieved with a pharmaceutical intervention, adjunctive use of functional food ingredients or nutraceuticals that support ongoing healthy blood glucose regulation is warranted. Four weeks of NCT/NFT supplementation resulted in significant improvements across multiple CGM-derived endpoints in adults with prediabetes. This proprietary formulation demonstrates promise as a non-pharmacological dietary supplement for supporting glycemic regulation, supporting its further development as a commercial nutraceutical for metabolic health.

Acknowledgments: The authors would like to acknowledge CLINFINITY, LLC, and Susan Spruill, MS, PStat®, of Applied Statistics and Consulting for their work on statistical analysis. The authors would also like to acknowledge Rajashekhar Reddy Palavalli for their contribution to the study of CGMS data, Intazamul Haque Shamshad Ahmad, and Ashok Kumar Gaur for helping in data collection. The authors' responsibilities were as follows: SK, AM, SG: designed research; AM, SG, RT: conducted research; MZ: co-drafted the manuscript; SK: co-drafted the manuscript and had primary responsibility for final content. All authors have read and approved the final manuscript.

Data Availability: Data described in the manuscript, code book, and analytic code will be made available upon request to the corresponding author.

Funding: This study was funded by Brightseed®. Study sponsors were not involved in either the conduct of the trial or the analysis of the data.

Conflicts of Interest: Swati Kalgaonkar is an employee of Brightseed®.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). A Report Card: Diabetes in the United States Infographic. *Diabetes*. 2024 Sep 26 [Retrieved on 2025 May 29]. https://www.cdc.gov/diabetes/communication-resources/diabetes-statistics.html
2. Echouffo-Tcheugui JB, Perreault L, Ji L, Dagogo-Jack S. Diagnosis and management of prediabetes: A review. *JAMA*. 2023;329(14):1206–1216. DOI: https://doi.org/10.1001/jama.2023.4063
3. Islam K, Islam R, Nguyen I, Malik H, Pirzadah H, Shreshta B, et al. Diabetes mellitus and associated vascular disease: Pathogenesis, complications, and evolving treatments. *Adv Ther*. 2025;42(6):2659–2678. DOI: https://doi.org/10.1007/s12325-025-03185-9
4. Centers for Disease Control and Prevention (CDC). Health and Economic Benefits of Diabetes Interventions. National Center for Chronic *Disease Prevention and Health Promotion*. 2024 May 24 [Retrieved on 2025 June 27] https://www.cdc.gov/nccdphp/priorities/diabetes-interventions.html
5. Pelczyńska M, Szymon S, Konieczny M, Bączyk H, Szyszko J, Cholewa K, et al. Influence of certain natural bioactive compounds on glycemic control. *Nutrients*. 2025;18(1):52. DOI: https://doi.org/10.3390/nu18010052
6. Chahroor JA, Baki ZA, Badan DE, Nasser G, Maresca M, Hijazi A, et al. Herbal medicines in the management of diabetes mellitus: Plants, bioactive compounds, and mechanisms of action. *Biomolecules*. 2025;15(12):1674. DOI: https://doi.org/10.3390/biom15121674
7. Lee SH, Veeriah V, Levine F. Liver fat storage is controlled by HNF4α through induction of lipophagy and is reversed by a potent HNF4α agonist. *Cell Death Dis*. 2021;12(6):603. DOI: https://doi.org/10.1038/s41419-021-03862-x
8. Veeriah V, Lee SH, Levine F. Long-term oral administration of an HNF4α agonist prevents weight gain and hepatic steatosis by promoting increased mitochondrial mass and function. *Cell Death Dis*. 2022;13(1):89. DOI: https://doi.org/10.1038/s41419-022-04521-5

9. Abdel-Rasol MA, El-Sayed WM. Nuclear receptors in metabolic, inflammatory, and oncologic diseases: Mechanisms, therapeutic advances, and future directions. *Eur J Med Res*. 2025; 30:843. DOI: https://doi.org/10.1186/s40001-025-03073-6
10. Hamdy H, Shen C, Xu J, Fan D, Zhang Y, Li H, et al. Hepatocyte nuclear factor 4-alpha: A key regulator in liver carcinogenesis. *Front Endocrinol*. 2025; 48:885–897. DOI: https://doi.org/10.1007/s13402-025-01064-7
11. Ng NHJ, Ghosh S, Bok CM, Ching C, Low BSJ, Chen JT, et al. HNF4A and HNF1A exhibit tissue-specific target gene regulation in pancreatic beta cells and hepatocytes. *Nat Commun*. 2025;15(1):4288. DOI: https://doi.org/10.1038/s41467-024-48647-w
12. Ghanem SS, Al-Barazenji T, Badi R, Abdelalim EM. Bridging pancreatic and hepatic development: Overlapping genes and their role in diabetes. *Cell Mol Biol Lett*. 2025; 30: 113. DOI: https://doi.org/10.1186/s11658-025-00790-y
13. Van Dender C, Vandewalle J, Libert C. Balancing metabolism and regeneration in liver diseases through HNF4α targeting. *Trends Endocrinol Metab*. 2026;37(1):83–98. DOI: https://doi.org/10.1016/j.tem.2025.04.003
14. Gulati S, Misra A, Tiwari R, Zuelch ML, Kalgaonkar S. Effect of supplementation with *n*-trans caffeoyltyramine and *n*-trans feruloyltyramine on glycemia in prediabetic individuals: A randomized, double-blind, placebo-controlled trial. *Bioactive Comp Health Dis*. 2025;8(11):489–504. DOI: https://doi.org/10.31989/bchd.v8i11.1828
15. Son H, Moon SJ, Cho YM. The expanding role of continuous glucose monitoring in the management and prevention of type 2 diabetes. *Diabetes Ther*. 2025. DOI: https://doi.org/10.1007/s13300-025-01830-8
16. Unni US, Bril F, Mugler JP, Carter RE, Basu A, Basu R. Role of hepatic glycogen on nocturnal gluconeogenesis in type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2025;110(10):2790–2799. DOI: https://doi.org/10.1210/clinem/dgaf044
17. Bkaily G, Jazzar A, Abou-Aichi A, Jacques D. Pathophysiology of prediabetes hyperinsulinemia and insulin resistance in the cardiovascular system. *Biomedicines*. 2025;13(8):1842. DOI: https://doi.org/10.3390/biomedicines13081842
18. Davoodian N, Lotfaliany M, Huxley RR, Lee CMY, Pasco JA, Adams RJ, et al. Prediabetes transitions to normoglycemia or type 2 diabetes and associated risk factors in the obesity, diabetes and cardiovascular disease collaboration: An individual-level pooled analysis of 19 prospective cohort studies. *Lancet Glob Health*. 2025;13(9): E1533–E1542.
19. Dhatariya K, Mustafa O, Stathi D. Hyperglycemic crisis. In: *NIH Endotext*..;2000 [updated 2025]. DOI: https://www.ncbi.nlm.nih.gov/books/NBK279052/
20. Mohammed S, Muhammed H, Shetty TV, Shanavas S. Micro and macrovascular complications in diabetes mellitus. *Yangtze Med*. 2025;9(1):96–123. DOI: https://doi.org/10.4236/ym.2025.91009
21. Wang X, Cao Y. A narrative review: Relationship between glycemic variability and emerging complications of diabetes mellitus. *Biomolecules*. 2025;15(2):188. DOI: https://doi.org/10.3390/biom15020188
22. Gonzalez JT, Lolli L, Veasey RC, Rumbold PLS, Betts JA, Atkinson G, et al. Are there interindividual differences in the reactive hypoglycaemia response to breakfast? A replicate crossover trial. *Eur J Nutr*. 2024; 63:2897–2909. DOI: https://doi.org/10.1007/s00394-024-03467
23. Wilczek F, Van Der Stouwe JG, Petrasch G, Niederseer D. Non-invasive continuous glucose monitoring in patients without diabetes: Use in cardiovascular prevention—A systematic review. *Sensors*. 2025;25(1):187. DOI: https://doi.org/10.3390/s25010187
24. Schembre SM, Liao Y, Jospe MR. Continuous glucose monitors as wearable lifestyle behavior change tools in obesity and diabetes. In: Faintuch J, Faintuch S, eds. *Obesity and Diabetes*. Springer; 2020:591–603. DOI: https://doi.org/10.1007/978-3-030-53370-0_43
25. LeVatte M, Keshteli AH, Zarei P, Wishart DS. Applications of metabolomics to precision nutrition. *Lifestyle Genomics*. 2022;15(1):1–9. DOI: https://doi.org/10.1159/000518489
26. Richardson KM, Schembre SM, Da Silva V, Blew RM, Behrens N, Roe DJ, et al. Adding a brief continuous glucose monitoring intervention to the National Diabetes Prevention Program: A multimethod feasibility study. *J Diabetes Res*. 2024; 2024:7687694. DOI: https://doi.org/10.1155/2024/7687694
27. Babiker R, Ali IA, Merghani TH, Banaga AS, Hashim NT, Ahmed MS, et al. Gum acacia supplementation improves adiponectin levels and HbA1c/adiponectin ratio in women with type 2 diabetes: A randomized controlled trial. *Funct Foods Health Dis*. 2025;15(3):176–190. DOI: https://doi.org/10.31989/ffhd.v15i3.1568
28. Taga M, Yohizumi K, Kobayashi H, Iwamoto N. The second-meal effect of *Undaria pinnatifida* sporophylls (mekabu) in healthy young women: An open-label crossover study. *Funct Foods Health Dis*. 2025;15(12):882–892. DOI: https://doi.org/10.31989/ffhd.v15i12.1807