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Perspective

A Natural Serotonin Stimulant for Appetite Suppression and Targeted Eating as an Alternative to Conventional Obesity Treatments

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Abstract

Recent advances in obesity management reflect the integration of pharmacological, surgical, and behavioral interventions, yet sustainable long-term outcomes remain elusive due to high attrition rates, the complexity of protocol compliance – and for some, costs, risks, and serious side effects. This research combined a patented nutraceutical designed to naturally stimulate serotonin, a biologic hunger agonist, to thereby aid in appetite control and facilitate weight loss through 'Targeted Eating,' a single, unrestricted daily meal protocol. Initial results from this 'real world' user study indicate promising weight management outcomes and compliance with this eating strategy. By exploring the evolutionary biology of perceived hunger and the anatomy associated with episodic versus circadian consumption, the study thus proposes a paradigm shift in obesity treatment and suggests further approaches to provide innovative solutions to the global obesity crisis.

Keywords
Obesity management; appetite appeasement; serotonin; evolutionary biology; targeted eating; nutraceuticals; non-pharmacologic interventions

1. Introduction

The global prevalence of obesity (BMI > 30 kg/m²) and being overweight (BMI 25–30 kg/m²) has escalated in recent decades, affecting both developed and developing nations, catapulting obesity into a health crisis of epidemic proportions [1]. This crisis accelerated post-World War II, with BMIs increasing by 0.5% annually. Notably, since 1980, obesity rates have doubled in over 70 countries, and by 2015, 600 million adults were classified as obese, contributing to 4 million deaths worldwide [2-7]. The rapid rise of obesity, primarily influenced by post-1940s environmental and lifestyle factors, challenges its hereditary attribution [8].

Obesity elevates risks for type 2 diabetes, hypertension, cardiovascular disease, cancers, and musculoskeletal issues, leading to increased mortality [9-12]. The financial burden is significant, with over $190 billion spent annually in the U.S. on obesity-related conditions [13]. Despite these investments, 98% of affected individuals remain untreated due to limited access to effective interventions [14, 15]. Promising treatments, like GLP-1 receptor agonists, have struggled with side effects, high costs, and limited scalability, leaving the epidemic unchecked [16-21]. While pharmaceutical leaders ascend towards trillion-dollar valuations with tantalizing early results [20], and globally renowned clinicians like Dr. Fatima Stanford address waiting lists in the thousands [21], the ultimate measure of success will lie not in shareholder values or patient queues but in the ability to flatten the curve.

Obesity also raises the risk for a host of diseases from childhood onward [22]. The impact of obesity begins early in life, increasing the prevalence of this wide range of diseases, including psychological, neurological, pulmonary, gastrointestinal, renal, musculoskeletal, and endocrine disorders [22, 23]. It complicates the management of several diseases – and increases susceptibility to them, impacting outcomes negatively, as seen in the COVID-19 pandemic [24]. Individuals with a BMI of 30–34.9 kg/m² have a more than 40% higher risk of overall mortality, and this risk doubles for those reaching a BMI > 40 kg/m² [11]. An estimated 4–9% of all cancers are attributed to excess body fat, which is also associated with a decreased life expectancy of up to 20 years, depending on its duration and severity [8, 25-27].

Efforts to treat obesity have been largely resistant to safe, effective solutions. Early medications like amphetamines, while suppressing appetite, posed cardiovascular risks [28]. Numerous approaches followed, including diets, exercise programs, and celebrity endorsements, but were often hindered by logistical challenges like erratic work schedules, cost, and access to healthy foods or exercise facilities. Despite 300,000 years of human existence marked by optimal fitness, the Anthropocene era has seen a paradoxical rise in collective weight gain [26]. Traditional treatments focused on caloric restrictions, increased activity, and behavioral changes. Newer dietary strategies, like Intermittent Fasting (IF) and Time-Restricted Eating (TRE), have shown promise but face challenges in long-term compliance and sustained weight loss [29, 30].

Bariatric surgeries, like sleeve gastrectomy and Roux-en-Y gastric bypass, are effective for weight loss, but complications, costs, and post-surgical weight regain are common barriers [31]. Less invasive methods, such as the intragastric balloon, have shown moderate success but often lead to side effects or require further invasive procedures, like liposuction [32]. Pharmaceutical interventions, including Orlistat (Roche), faced limited acceptance due to side effects [33, 34], while more recent drugs targeting the leptin-melanocortin axis and GLP-1 receptors have shown promise in reducing weight by mimicking natural appetite control pathways [35].

GLP-1 agonists, while effective at diminishing 'food noise' and episodic eating, have shortcomings that have hindered widespread use. Such limitations include chronic administration to manage the underlying triggers of hunger, significant side effects, high costs, and supply issues [16-20]. The need for sustained therapy to prevent weight rebound emphasizes the importance of understanding long-term efficacy and patient compliance, which is challenging due to high dropout rates and unique responses across patient groups [36]. Systematic reviews and meta-analyses reveal that while substantial weight loss through obesity treatments is possible, it is typically unstable without ongoing intervention, contributing to a dearth of dispositive studies, possibly due to inherent research or publication bias compounded by dropout rates not reflected in the final analyses.

These treatments align with a broader understanding of appetite control mechanisms, including the role of serotonin, which is primarily produced in the gut and helps regulate hunger and mood. Stimulating serotonin production, especially through a natural nutraceutical targeting the GLP-1 and serotonin pathways in the gut, can serve as an effective appetite suppressant, reducing cravings and promoting a single-meal-per-day approach [37-42]. Functional Magnetic Resonance Imaging (fMRI) analysis has revealed that during extended fasting, the activity of the prefrontal cortex – responsible for logic, reasoning, and planning – is diminished [38]. This eventually shifts focus to the limbic system, which includes the hypothalamus, thalamus, and nucleus accumbens. This shift can stimulate hunger perceptions, linking behavioral responses to biological needs and perceptions of food scarcity.

The brain, especially the limbic region, thus modulates food intake by sensing various molecules and metabolic signals. After food ingestion, intestinal sites stimulate neural pathways, transmitting nutritional signals from the gut to the brain, influencing perceptions of well-being or equilibrium. Food intake is managed through two primary brain mechanisms: the homeostatic circuit, which aligns energy intake with output, and a hormonal pathway linked to reward mechanisms, both influenced by serotonin levels [39, 40]. Although brain serotonin production is modest, up to 90% of endogenous serotonin production occurs in the gastrointestinal tract, essential for synaptic communication between the brain and gut [41]. However, maintaining balanced serotonin levels is crucial, as imbalances are often linked to various disorders.

These dynamics inspired the patent for an approach that leverages the use of a natural, affordable nutraceutical when combined with an ancestral eating strategy. The nutraceutical formulation and delivery mechanisms are designed to act at the distal end of the small intestine, where the GLP-1 hormone, essential for satiety, is also predominantly produced. The densely compacted capsule is taken on an empty stomach to deliver tryptophan to the ileum, where it converts to the neurotransmitter, serotonin, and is immediately accessible to the Vagus nerve to act as a natural appetite suppressant.

Such stimulation of serotonin can reduce cravings and enhance perceived energy and mental acuity while the patient migrates from counter-productive eating habits to a single, unrestricted

meal each day with respect to quantities and food group choices. The impetus for adopting this approach, or 'Targeted Eating', is centered on the principle of maximizing the salubrious effects of cellular quiescence and DNA regulation that can be achieved in the absence of nutrient uptake, and therefore, adenosine triphosphate (ATP) synthesis in the mitochondria during glucose metabolism by oxidative phosphorylation [42]. As such, following a circadian rhythm that includes a single meal per cycle also has substantial paleoanthropologic evidentiary support as a critical evolutionary advantage. And, once the adaptation has been habituated, the nutraceutical may be discontinued without risk of rebounding.

2. Materials and Methods

2.1 Description and Composition of the Supplement

The serotonin stimulant nutraceutical used in this user study comprised a synergistic combination of natural ingredients. The core components include proteins sourced from milk and egg sources, constituting 34.5-38.5% of the capsule. Essential amino acids such as Tryptophan, as well as Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, and Valine, along with non-essential amino acids, contribute to the nutritional profile.

The total carbohydrate content of each capsule ranges from 19-21%, consisting of Lactose, Glucose, and Galactose. Lipids make up 33-37.5%, with saturated fats representing approximately 25-27.5% of the total fat content. Monounsaturated fats contribute 24-25.5%, while polyunsaturated fats constitute approximately 4.5-6% of the total fat content. Trans fats are present in trace amounts.

The vitamins and minerals in each capsule include: Vitamin A (1.5 to 2.4 IU), Vitamin D (0.36 to 0.72 IU), Riboflavin (B2) (0.0024 to 0.0033 mg), Niacin (B3) (0.0009 to 0.0018 mg), Folic Acid (B9) (0.075 to 0.12 µg), Vitamin B12 (0.0057 to 0.0099 µg), Pantothenic Acid (B5) (0.0057 to 0.0072 mg), Calcium (2.85 to 3.9 mg), Phosphorus (3.0 to 3.75 mg), Magnesium (0.33 to 0.42 mg), Zinc (0.015 to 0.021 mg), Potassium (4.95 to 5.58 mg), Sodium (1.65 to 2.55 mg), and Iron (0.0033 to 0.0066 mg).

The capsule also contains other bioactive components and enzymes. These include: Antioxidants (Lutein, Zeaxanthin; 0.018 mg); Avidin (0.05%); Choline (1.5 to 3.0 mg); Conjugated Linoleic Acid (CLA) comprising 0.5 to 1% of total fatty acids; Growth Factors (IGF, TGF; trace); Immunoglobulins (0.3 to 0.6 mg); Lactoferrin (0.012 to 0.12 mg); Lactoperoxidase (18.0 mg); Lysozyme (2.1 mg); Oligosaccharides (0.6 mg); Omega-3 Fatty Acids (0.1 to 0.3%); and Sphingolipids (<1% of total lipids). The supplement contains lyophilized whole (bovine) milk and whole (avian) egg products, compressed in an organic capsule.

2.2 Study Design

In this user study, participants were enrolled for a period ranging from 12 to 16 weeks to assess the impact of a natural serotonin stimulant for appetite appeasement to facilitate adoption of a single meal per day. Conducted at the Hughes Medical Center in The Valley, Anguilla, a 'real world' protocol was used to explore the integration of a newly patented, oral nutraceutical designed to leverage gut-brain axial signaling and its appetite regulation. The user study followed the premise that patient engagement and behavioral motivation are essential components of any weight management approach because the food they eat cannot be 'blinded' like a clinical trial comparing

a new compound to a placebo. The participants in this study understood the objective of migrating to a single meal per day, and while given capsule administration schedules, each was briefed on the intended utility of the nutraceutical and knew that all were given the patented supplements.

This investigation aligned with the concept that neurotransmitter processing and stimulation, primarily occurring in the small intestines, can be harnessed to achieve weight management through the consumption of a single, unrestricted meal per circadian cycle. This approach necessitates a diet that is not only nutritionally diverse to support complex biological functions but also satisfies the psychological need for varied tastes and textures. For many patients, however, the transition to such a dietary regimen can be challenging yet significantly facilitated with a natural appetite suppressant that enhances perceived energy levels and, therefore, compliance that achieves results.

Stratification based on initial evaluations was used in a physician-guided, personalized approach to ensure that each participant received the serotonin stimulant in a regimen tailored to their physiological profile. The outcome metrics included individual basal metabolic rate (BMR), body mass index (BMI), physical activity level, and total daily energy expenditure (TDEE). Specifically, participants were accepted for enrollment to begin a regimen of serotonin stimulant capsules based on an initial evaluation that included specific assessments as well as a discussion with the clinical supervisor about individual goals and desired outcomes. The study flowchart is indicated below (Figure 1) and illustrates the structured approach adopted for participant selection, compliance assessment, and outcomes.

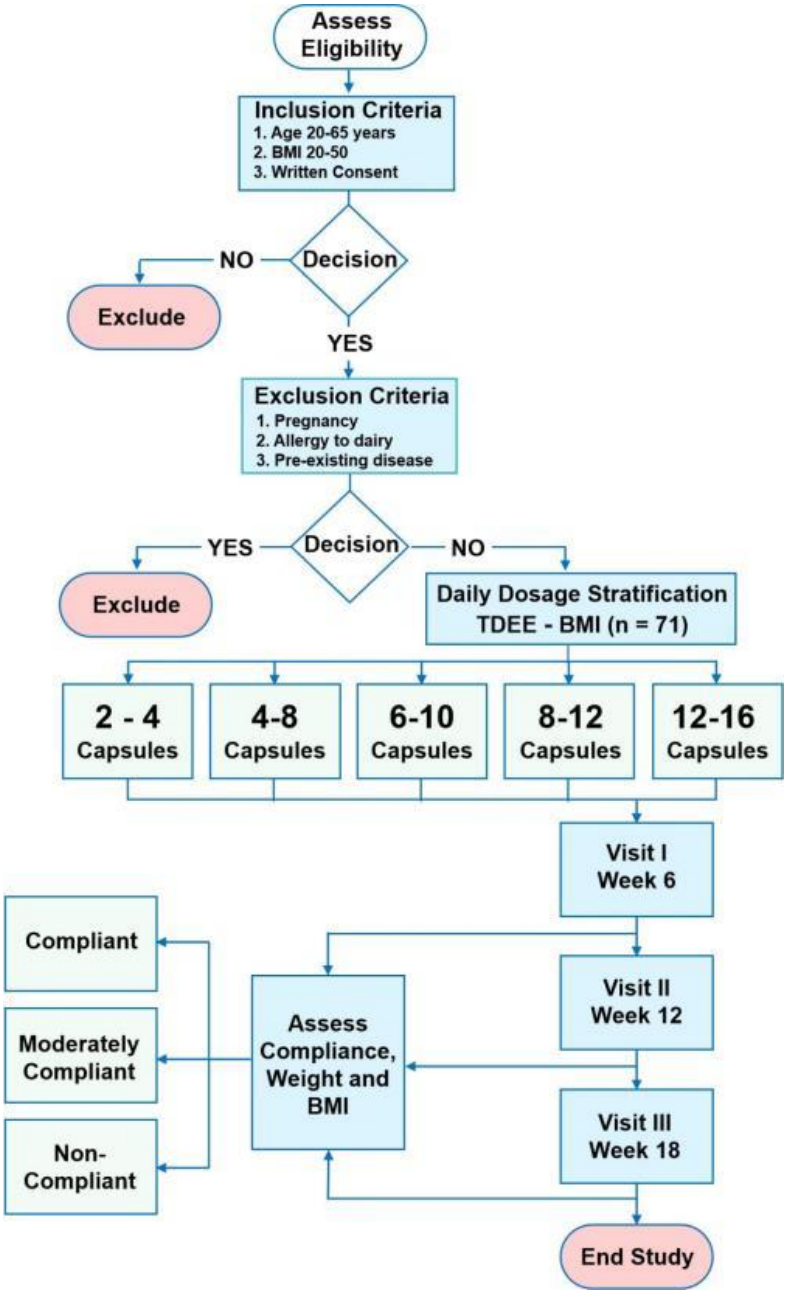

Figure 1 Participant Selection and Compliance Assessment Flowchart.

2.3 Participant Stratification

Upon enrollment, participants underwent a comprehensive assessment to determine their TDEE and BMI. TDEE was calculated using predictive equations accounting for age, sex, weight, height, and physical activity level. BMI was determined by the weight in kilograms divided by the square of height in meters. The resulting data were plotted to create a stratification chart, guiding the allocation of dosages according to the intersection of TDEE and BMI values. These metrics served as the basis for five dosing categories, ranging from A to E (Figure 2 and Table 1). The stratification was intended to align the supplement dosage with individual physiological characteristics, hypothesizing that such alignment would optimize therapeutic outcomes. To establish eligibility parameters for participant selection and stratification, specific inclusion and exclusion criteria were delineated as follows:

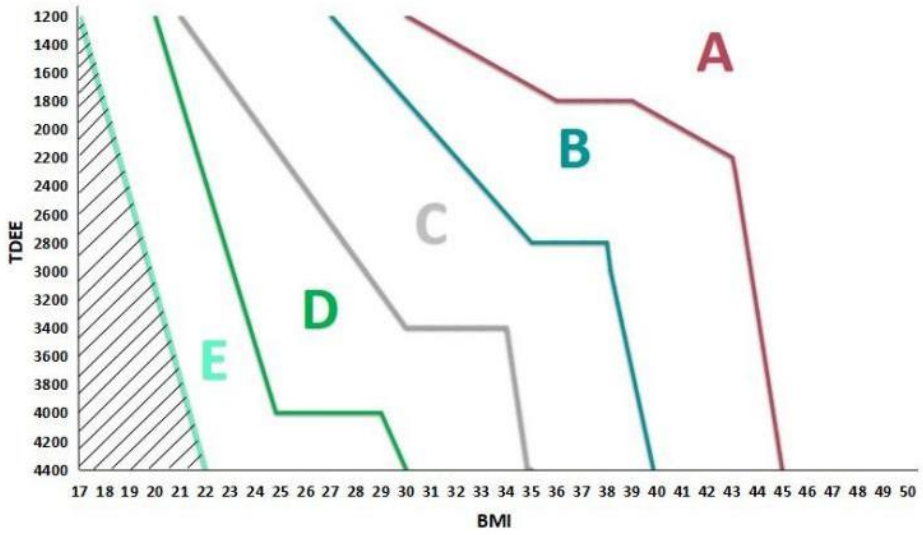

Figure 2 Patient Stratification Based on Total Daily Energy Expenditure (TDEE) and Body Mass Index. Eligible participants were separated into five categories (A-E) based on their TDEE in relation to BMI. Each category is represented by a different pattern and labeled with a corresponding letter. The shaded area to the left (Stripes) denotes the BMI range considered to be ineligible for participation.

Table 1 Stratification of dosage categories based on TDEE to BMI ratio.

Category	*Daily Capsules*	*Description*
Dosage A	12–16 Capsules	Assigned to individuals with the highest TDEE to BMI stratification ratio, reflecting a need for a higher dose due to significant body mass.
Dosage B	8–12 Capsules	Applicable to participants with a high but slightly less body mass compared to Dosage A.
Dosage C	6–10 Capsules	Targeted individuals with a moderate TDEE to BMI stratification ratio.
Dosage D	4–8 Capsules	Prescribed for those that fell lower on the TDEE to BMI stratification ratio, indicating a relatively lower body mass in comparison.
Dosage E	2–4 Capsules	The lowest dose, intended for participants with the lowest TDEE to BMI stratification ratio, representing the smallest body mass category in the study.

Inclusion Criteria: The study participant inclusion criteria were specifically designed to ensure a broad but relevant sample cohort. Adults between 20 and 65 years of age were considered eligible, covering a significant portion of the adult population likely to be affected by obesity-related issues. Additionally, individuals with a BMI of 20 to 39 kg/m^2 were included. This range represented body types from normal weight to obese, but not extremely obese, as the latter could require specialized medical intervention beyond the scope of this study. Finally, all participants were required to

provide written consent regarding their participation, ensuring that they received and understood all necessary information about the protocol, objectives, and limitations.

Exclusion Criteria: In addition to individuals falling outside the established TDEE and BMI ranges, indicated by the area with red hash marks on the stratification chart (Figure 2), participants with any of the following parameters were excluded: pregnancy; allergy towards dairy products; or pre-existing morbid disease (unless approved by study coordinator). These exclusion criteria were chosen to ensure safety and minimize the potential for extreme values to impact the final analysis.

After determining participant eligibility, the following calculations were used to determine dosage strategies:

Basal Metabolic Rate (BMR) Calculation:

- Men: $\mathrm{BMR} = 10(\text{Body weight; kg}) + 6.25(\text{Height; cm}) - 5(\text{Age; years}) + 5$
- Women: $\mathrm{BMR} = 10(\text{Body weight; kg}) + 6.25(\text{Height; cm}) - 5(\text{Age; years}) - 161$

Body Mass Index (BMI) Calculation:

- Men and Women: $\mathrm{BMI} = \text{Weight in kg}/[(\text{Height in cm}) \times 0.01]\text{^}2$

Activity Level Assessment:

- Sedentary ('Desk' employment, routine chores, minimal exercise); Modifier = 1.2
- Lightly Active (Routine chores, takes moderate walks and/or exercises 1 to 3 days a week); Modifier = 1.375
- Moderately Active (Physical activity throughout the day, takes moderate walks, and/or exercises 3 to 5 days a week); Modifier = 1.55
- Very Active (Physically demanding employment and exercises at a high intensity 5 to 7 days a week); Modifier = 1.725
- Extra Active (Intensely physically demanding employment and exercises at a high intensity nearly every day); Modifier = 1.9

Total Daily Energy Expenditure (TDEE) Calculation:

- Men and Women: $\mathrm{TDEE} = \mathrm{BMR} \times \text{Activity Modifier Lightly Active}$

This user study was thus designed to evaluate the efficacy and safety of an orally administered natural serotonin appetite appeasement aid across a spectrum of metabolic rates and body compositions. The study implemented a stratified dosing regimen, where dosages were allocated based on participants' TDEE (BMR × Activity Modifier) and BMI (Figure 2). Each of the dosage categories was defined as depicted in Table 1.

2.4 Considerations Regarding a Single Cohort

Given the certified, food-grade safety of the natural ingredients, the decision to proceed without a control arm was made with deliberation and a focus on 'real-world' scenarios. This approach provided actionable insights and contributed directly to potential results for participants who were highly motivated upon enrollment.

It would nonetheless follow that future studies would incorporate control groups as may be designed at the next phase toward commercialization. At this foundational stage, however, the primary objective was to essentially begin at the 'end' – where weight management succeeds or fails with 'real-world' patient compliance and the daily dietary choices they make, while enabling all participants to derive any potential benefits from this innovation and regimen.

2.5 Ethics Statement

The internal review of the study protocol was approved by a Board-Certified Plastic Surgeon, Dr. Lowell Hughes, and the staff at Hughes Medical Center, Lower South Hill, The Valley, Anguilla, on May 2, 2023. All participants were existing and active patients of the medical center and were closely monitored throughout the study. Informed consent was obtained from all participants prior to their inclusion in the study (a copy of the informed consent documentation is available upon request). The feasibility study was conducted on the island of Anguilla with Dr. Lowell Hughes. Dr. Hughes is one of the only medical caregivers residing on the island, who serves the entire community. All participants were current patients under Dr. Hughes' care. Although a formal Institutional Review Board (IRB) review was not obtained prior to the study, informed consent was provided by all participants to partake in the feasibility study and to use their anonymized data for research purposes. All data was provided to researchers outside of the medical center in such a manner that no identifying patient details were disclosed beyond the medical center staff. Participants remained under Dr. Hughes' care during and after the study. This study adhered to ethical guidelines by ensuring participant confidentiality, voluntary participation, and minimal risk. The small island of Anguilla lacks a dedicated ethics review organization, presenting certain challenges. The study outcomes and results revealed significant merit to share with the broader research community for numerous reasons, but notably the results represent a community that is often overlooked. Islands like Anguilla face unique challenges, including limited access to healthcare resources, higher rates of certain health conditions, and socioeconomic disparities. This study provides valuable insights into the health outcomes of this underrepresented population, which can be extrapolated more broadly.

3. Results

A total of 71 participants, distributed across age demographics, were enrolled in the study under the supervision of medical professionals. Despite the study predominantly involving female participants, a diverse age range was achieved, and initial findings reflected weight loss trends and/or improved BMI classifications among all compliant participants.

3.1 Baseline Demographics and Weight Outcomes

The user study cohort included a total of 71 participants (Figure 3), with a significant female majority (90.1%), reflecting a typical distribution in weight management studies [43]. This female predominance nonetheless offered insights into gender-specific weight loss challenges and outcomes [44]. The age distribution spanned from younger to older adults, providing a perspective on the efficacy of the intervention across different life stages. There was significant variation in baseline body weights, particularly between genders and across weight outcomes, which could

notably influence their experience and weight management results. Table 2 provides baseline demographic and body weight characteristics for the study participants, based on their weight outcomes.

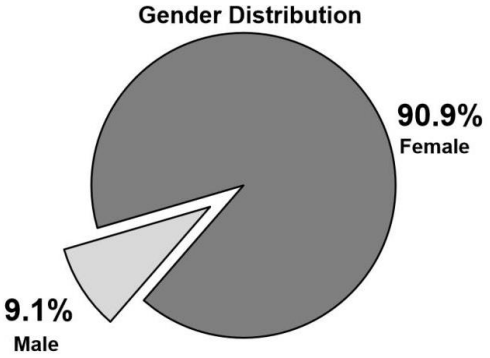

Figure 3 Gender Distribution.

Table 2 Baseline demographic and body weight characteristics of study participants categorized by weight outcomes.

Variable	Total	Weight Loss (WL)	Stable Weight (SW)	Weight Gain (WG)
Number	71	47	18	6
Total (%)	100%	66.2%	25.35%	8.45%
Female (%)	90.1%	91.49%	83.3%	100%
Male (%)	9.9%	8.51%	16.7%	-
Age (Years ± SD)	42.2 ± 10.9	43.3 ± 12.3	38.0 ± 7.3	45.6 ± 6.1
Baseline body weight; kg				
Females	103.4 ± 23.7	103.4 ± 23.3	104.1 ± 22.6	102.4 ± 31.6
Male	119.5 ± 30.4	107.7 ± 16.5	135.0 ± 41.5	-

The weight loss group (WL) comprised most of the participants (66.2%), with a 91.49% female participation (Figure 4). The stable weight group (SW) accounted for 25.35% of participants, with fewer females (83.3%), and all participants in the weight gain group (WG) were female. The average age of all participants was 42.2 years (±10.9). The WL subgroup had the highest average age of 43.3 years (±12.3), whereas the average age of the SW and WG groups were 38.0 years (±7.3) and 45.6 years (±6.1), respectively.

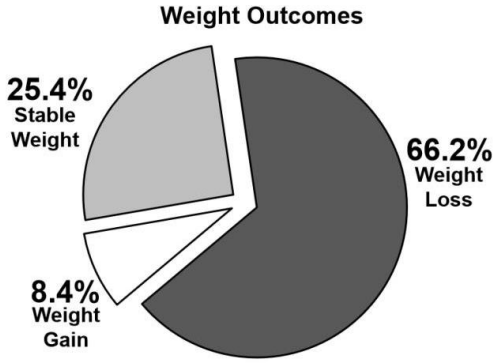

Figure 4 Weight Outcomes Distribution.

Baseline body weights varied between groups, with the females averaging 103.4 kg (±23.7). In the WL group, females had a nearly identical starting average of 103.4 kg (±23.3), while the SW group began with a slightly higher average (104.1 kg, ±22.6). The WG group had a slightly lower baseline (102.4 kg, ±31.6) compared to the other groups. Male participants, though fewer, started with a higher average weight of 119.5 kg (±30.4) than the females. The data indicate that, while females predominantly engaged in the study, their results varied, with different weight management outcomes across the groups.

3.2 Age-Related Outcomes

With respect to age-related responses, weight loss averages also varied across age groups. Age-related outcomes (Table 3 and Table 4) suggested a pattern where older participants, particularly those over 50, exhibited greater average weight loss compared to younger participants. This could indicate metabolic or lifestyle differences influencing the effectiveness of the supplement regimen and overall program design. In younger participants (<30), the weight loss was less pronounced, which might also reflect varying levels of control over their work and eating schedules, as well as time for exercise, metabolic rates, and capsule or dietary compliance.

Table 3 Age-related female participant data: Baseline characteristics, dosage stratification, and average weight outcomes.

Age	Participants	BMI	BMR	TDEE	Dosage	Weight Loss (kg)
<30	7	38.2 ± 8.5	1739.9 ± 226.9	2220.8 ± 349.9	29% A 14% B 14% C 29% D 14% E	2.77 ± 2.18
31-50	45	37.7 ± 8.3	1721.4 ± 287.3	2287.4 ± 412.8	15.5% A 15.5% B 20% C 29% D 20% E	2.95 ± 4.33
>50	12	40.8 ± 7.4	1663.7 ± 250.5	2267.9 ± 350.7	50% A 8.3% B 8.3% C 25% D 8.3% E	3.94 ± 3.37

BMI: Body mass index; BMR: Basal metabolic rate; TDEE: Total daily energy expenditure.

Table 4 Age-related male participant data: Baseline characteristics, dosage stratification, and average weight outcomes.

Age	Participants	BMI	BMR	TDEE	Dosage	Weight Loss (kg)
<30	1	40.9	2023.4	3136.3	100% B	-
31-50	3	43.2 ± 11.1	2308.1 ± 451.9	3196.0 ± 828.8	33.3% A 33.3% C 33.3% D	1.06 ± 1.83
>50	3	32.3 ± 2.8	1769.4 ± 128.0	2,222.7 ± 173.2	33.3% C 66.7% D	1.96 ± 1.46

BMI: Body mass index; BMR: Basal metabolic rate; TDEE: Total daily energy expenditure.

Among participants aged 31 to 50, moderate weight loss was observed, indicating an intermediate response that could reflect slightly more predictable work schedules, mid-life metabolic shifts and/or compliance variables. The dosage stratification aimed to address these age-specific responses by tailoring supplement intake to individual metabolic needs and activity levels, as well as a nuanced approach to weight management across different life stages.

The dosage stratification also led to a higher percentage of the oldest cohort in females assigned to the highest dosage (Dosage A), potentially contributing to their greater average weight loss. However, the oldest female cohort also had the highest baseline weight. Greater loss was thus consistent with anecdotal observations whereby heavier patients lose weight faster than those who literally have less to lose.

3.3 Gender Specific Outcomes

The user study enrollment was consistent with existing literature, where male participation in weight loss studies is generally lower than female participation and engagement in such interventions. Despite significantly fewer male participants, some insights were gleaned from their responses to the serotonin stimulant in contrast to findings among the female cohort.

Notably, female participants achieved varying levels of weight loss across different age groups, with those above 50 years of age showing the most significant average weight loss of 3.94 kg (Table 3). This group also had the highest baseline BMI, consistent with greater potential weight loss.

Comparatively, Table 4 highlights the male participants' outcomes. Although the sample was limited, it provided some initial insights. For males aged 31-50, a modest average weight loss of 1.06 kg was noted despite their high average baseline BMI and an equitable distribution among doses A, C, and D. In the over-50 group, a slightly better average weight loss of 1.96 kg was observed, with a notable shift towards higher doses, indicating a possible age-related metabolic response that merits further study. The under-30 male participant did not experience weight loss, which underscores the importance of larger studies for drawing further conclusions.

3.4 Correlation of Participant Compliance with Outcomes

The user study also revealed a clear correlation between compliance and weight loss as a critical component in this dietary intervention. Fully compliant participants, who adhered to the protocol and supplement regimen, experienced substantial weight loss, averaging 7.24 kg.

Conversely, non-compliant participants showed negligible weight loss. This apparent impact of compliance on outcomes suggests an efficacious approach when compliant, thereby emphasizing the importance of motivational strategies in weight management, given the ultimate participant behavioral impact (Table 5).

Table 5 Correlation of participant compliance with average age and weight loss outcomes.

Compliance	Ave. Compliance Rating	Percentage of Participants	Average Age (Years)	Average Weight Loss (kg)
Compliant	5	26.7%	44.3	7.24 kg
Moderately Compliant	3	30.9%	40.4	3.72 kg
Non-Compliant	0	42.3%	40.8	-0.05 kg

Compliant Participants = a rating of 5; Moderately Compliant participants = 3; and Non-Compliant participants = 0. A negative average weight loss indicates participant weight gain.

3.5 Specific Case Reports

Table 6 highlights individual participant findings among those with greater compliance that reflected significant weight reduction from the combined nutraceutical and protocol. One case in point was a 34-year-old female, who achieved a 21.7 kg weight loss, transitioning from Class II Obesity to a healthier weight category in approximately four months.

Table 6 Individual case outcomes: Weight loss and BMI reduction in compliant and non-compliant participants.

Females by Age (Years)	Compliance Rating	Dosage	Weight Loss (kg)	Starting BMI* by Obesity Class	Ending BMI by Obesity Class
34	Compliant	C	21.7 kg	35.9 (Class II)	28.0 (Mid-range Overweight)
43	Compliant	D	8.5 kg	32.6 (Class I)	29.3 (Upper-range Overweight)
52	Compliant	A	8.4 kg	49.2 (Class III)	46.3 (Class III)
60	Compliant	A	6.4 kg	45.8 (Class III)	43.1 (Class III)
29	Moderately Compliant†	B	3.6 kg	41.3 (Class III)	39.9 (Class II)
57	Non-Compliant‡	A	-4.1 kg	45.6 (Class III)	47.1 (Class III)

*CDC Obesity categories: Class I (BMI of 30 to 35); Class II (BMI of 35 to 40); and Class III (BMI > 40). †: Participant was initially compliant but became ineligible due to pregnancy. ‡: Participant was initially compliant but reported dyspepsia that precluded continued compliance.

Notably promising outcomes were also observed with other compliant participants. Another 43-year-old female lost 8.5 kg in a similar timeframe and transitioned from Class I Obesity to the upper range of the Overweight category. A third 52-year-old female experienced an 8.4 kg weight loss, and while remaining within Class III Obesity, lowered her BMI from 49.2 to 46.3.

A fourth compliant 60-year-old female achieved a 6.4 kg weight loss and lowered her BMI to 43.1 from 45.8. While remaining within the same obesity class, her improvement showed promise across the age distribution in the study.

Another notable participant was a 29-year-old female, who enrolled with dual goals: to reduce her weight from Class III Obesity status and to improve her fertility, as she had been unable to conceive prior to the study after a significant number of cycles. This participant lost 3.6 kg and achieved her initial BMI goal, transitioning from 41.3 (Class III Obesity) to 39.9 (Class II Obesity). During her participation, she also achieved her goal of conceiving, after which she discontinued her enrollment. Whether coincidental or a consequence, this outcome highlights the promise of enhanced well-being from a healthy weight (or shifting closer to achieving it) contributing to metabolic homeostasis.

However, a non-compliant 57-year-old female demonstrated the challenges and complexities inherent in weight management intervention. Her experience, including perceived dyspepsia (perhaps consistent with transient hypoglycemia), reflected the need to balance compliance and individual circumstances to achieve weight loss.

3.6 Participant Attrition and Feedback

During this user study, a subset of participants did not complete the intervention or were non-compliant, impacting the overall findings (Table 5 and Table 6). Their challenges may be attributed to personal constraints or dissatisfaction, while others may reflect biologically relevant factors, further emphasizing the need for robust engagement in weight management research. These observations will aid in refining future study designs for more conclusive findings and consistent participant acceptance of the approach.

Despite these obstacles, the design reflected a ‘real-world’ user study environment, assessing the nutraceutical supplement impact on appetite and weight loss. Overall participant feedback was predominantly positive with reported improvements in general well-being, ease of lifestyle integration, and psychological benefits. Nevertheless, constructive criticism offered further insights into refinements with respect to alternative embodiments and innovations.

4. Discussion

The present user study demonstrates the potential of a natural serotonin-stimulating nutraceutical combined with a single, unrestricted meal per day to achieve effective weight management. The findings reveal promising weight loss results, particularly among compliant participants, with significant variations observed across age groups and BMI categories.

These outcomes suggest that the nutraceutical approach not only facilitates appetite suppression but also aligns with circadian eating patterns, leading to improved compliance and weight outcomes. By leveraging natural, biologic hunger regulation, this approach offers a novel, non-invasive alternative to traditional pharmaceutical or surgical interventions, with implications for broader access and long-term sustainability in addressing the global obesity crisis.

By 2018, 39.8% of adults in the United States had BMIs consistent with obesity, while an additional 31.8% were classified as overweight, and 7.6% as severely obese [45]. The trends suggest that more than a billion adults around the world will be obese by 2030. The present study addresses this urgent crisis while offering a fresh perspective, by employing a patented, natural serotonin

stimulant with a novel composition and approach for obesity treatment. Whereby, enhancing serotonin production, pivotal in regulating appetite and mental acuity, can facilitate the transition to a circadian diet with a single, satisfying, and unrestricted daily meal. The natural composition of the supplement further minimizes risks compared to pharmaceutical interventions, presenting a viable option for a broad demographic.

The present work diverges from conventional weight management approaches, which often revolve around caloric and/or food group restrictions or drug therapies. With varying degrees of success, they face similar motivational challenges but may not provide requisite metabolic and hormonal support [46]. By contrast, the biologic underpinnings of this approach foster the most fundamental vitality of cellular homeostasis with optimal DNA up- and down-regulation throughout billions of cells when aligned with circadian cycles of optimal nutrient bioavailability – and its absence [47].

Participant attrition and compliance may have nonetheless been reflective of issues characteristic of obesity research. These factors likewise emphasize the opportunity for further validation and insights on the path to commercialization and potential global distribution. However, this study employed this 'real-world' design, as weight management begins and ends with the decisions made by the patient for every snack, beverage, and meal they consume. The nutraceutical approach was also developed for access across the spectrum of economic strata and cultural contexts to support compliance and treatment outcomes.

5. Conclusions

In conclusion, this user study to evaluate a patented, natural serotonin stimulant and an unrestricted daily meal calls for greater awareness of the complexities of obesity and the need for innovative, integrated approaches. While the number of male participants limited the broader generalization of these findings, the data suggest that age, BMI, compliance, and dose stratification play roles in the efficacy of this novel weight loss regimen for both genders. The observation that older males and females achieved greater average weight loss also suggested age-related factors influencing the efficacy of the dietary supplement and/or the need for adjustments in the timing and dosage for younger patients.

While a small, mostly female, cohort, these initial conclusions align with early findings from a recent trial conducted by Novo Nordisk, which investigated an oral GLP-1 agonist alternative, amycretin, involving 16 individuals [48]. Such preliminary research, although conducted on a limited cohort, can provide valuable insights into the potential efficacy and safety of new treatment paradigms. A notable limitation of this study is the timespan of 12 to 16 weeks, though this duration is patterned after numerous GLP-1 duration reports. While this period offers valuable preliminary insights into weight loss outcomes, it is insufficient to fully evaluate the long-term sustainability and maintenance of weight loss. Extended follow-up studies, ideally spanning at least one year, are necessary to assess longer-term results and to provide a clearer understanding of how the nutraceutical intervention may impact sustained weight management. Furthermore, future research should explore the effects of diverse dietary patterns, which may offer insights into how different eating strategies interact with the nutraceutical appetite regulation mechanism and enhance overall weight management outcomes.

Ultimately, these preliminary results with a patented nutraceutical and a single, satisfying unrestricted daily meal emphasize the interplay between lifestyle, diet, circadian rhythms, metabolism, and the evolutionary biology of the species. By leveraging safe, biologic mechanisms for successful weight management, this approach is clearly a promising alternative to surgical and pharmaceutical interventions in overweight and obesity management.

Abbreviations

BMI	Body Mass Index
IF	Intermittent Fasting
TRE	Time-Restricted Eating
GLP-1	Glucagon-like peptide-1
fMRI	Functional Magnetic Resonance Imaging
ATP	Adenosine triphosphate
BMR	Basal Metabolic Rate
TDEE	Total Daily Energy Expenditure
WL	The weight loss group
SW	The stable weight group
WG	The weight gain group

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Author Contributions

All authors have given approval to the final version of the manuscript. TB, AD, LH, AI, and MG: conceptualization, methodology, design and formal analysis, writing, reviewing, editing, and ongoing communications. LG and LH: data collection, design analysis assistance. AD and AI: manufactured the nutraceutical supplement utilized in the study. TB and MG: manuscript review and editing. MG: ongoing review and edits to the manuscript. TB, AD, LH, AI, LG and MG:

conceptualization, design analysis assistance, writing, reviewing, and editing. All authors contributed to the article and approved the submitted version.

Competing Interests

TB, AD, LH, and MKMG are listed as inventors of nutraceutical supplement, Lactova™, used in research: US Patent No. 11,771,125 – Concentrated Nutritional or Supplemental Compound for Intestinal, Gut-Brain Axis and Neurobiological Homeostasis through Calibrated Absorption Including Neurotransmitter or Any Equilibrating Compound Release to Treat or Mitigate Disease and Co-morbidities, Particularly Obesity and Malnourishment and US Patent No. 11,813,363 – Concentrated Nutritional or Supplemental Compound for Intestinal, Gut-Brain Axis and Neurobiological Homeostasis through Calibrated Absorption Including Neurotransmitter or Any Equilibrating Compound Release to Treat or Mitigate Disease and Co-morbidities, Particularly Obesity and Malnourishment.

Data Availability Statement

The original data presented in the study are held on file at Hughes Medical Center, and further inquiries can be directed to the corresponding author for anonymous raw data.

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