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CLINICAL STUDY BRIEF REPORT

A randomized, parallel arm controlled clinical trial to assess safety and efficacy of weight management Gummies supplementation.

Protocol Number- MHC/CT/20-21/030

(Ver.1 dated 1st Feb 2021)

Sponsor's Signatory	CRO Signatory
Aesthetic Nutrition Pvt. Ltd.	***Mprex Healthcare Pvt. Ltd.***
Mr. Divij Bajaj **Director**	**Dr. Gayatri Ganu** **Director**

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INVESTIGATOR DECLARATION

A randomized, parallel arm controlled clinical trial to assess safety and efficacy of weight management Gummies supplementation.

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We hereby certify the authenticity of the Clinical Study Report and declare that the results are an accurate interpretation of the data; to the best of our knowledge. We also hereby provide assurance that this study was conducted in compliance to the protocol and as per applicable Good clinical Practices and Ethical Guidelines laid down.

Site Number	Name and Address	Investigator details	Signature & Date

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Chapter 1: BACKGROUND AND STUDY RATIONAL:

In both developed and developing countries, the proportion of people with excess body weight has risen in recent decades. It is a major public health problem that is becoming more prevalent in low- and middle-income countries. [1]

Overweight is one of the top 10 risk conditions in the world, according to the World Health Organization. Obesity is defined as having excess fat, especially around the waist. Obesity, which is caused by an imbalance in energy intake and expenditure, has emerged as a major health risk factor around the world, raising the risk of chronic diseases such as diabetes and heart disease.[2]

Obesity can be induced by excessive consumption of ultra-processed foods with low nutritional content, resulting in micronutrient deficiencies. [3] Obesity is linked to deficiencies in various micronutrients, such as vitamins and iron. Obese persons may have a higher mortality rate from COVID-19 disease, according to new research. [4]

Obesity affects a substantial percentage of people in most developed and developing countries. Understanding the nature of the association between chronic positive caloric imbalance and COVID-19 pathology may open up new paths for lowering the mortality toll caused by this dangerous new virus.[5] We could prevent weight gain in the majority of the population while dealing with this pandemic. Small changes in behavior, such as increasing physical exercise, eating a balanced diet, and supplementing with nutrients from nutraceutical goods, can help achieve this.

By incorporating nutraceuticals into one's diet, more people will be able to control their weight and lessen the physical, social, and psychological burden that obesity can impose. [6] Obesity is being treated using a multidisciplinary approach rather than a single treatment method. Diet, exercise, nutritional awareness, and a healthy psychological state of mind all contribute to a favorable environment in which this disease can be managed in the future. [7]

Given the link between vitamin deficiency and obesity, we hypothesize that combining the use of weight management gummies with moderate lifestyle changes such as a 2000-calorie diet and 30 minutes of mild exercise will have a synergistic impact that will help to effectively manage bodyweight. Weight management gummies also contains herbal extracts, such as green coffee seed extract, which are shown to help in weight loss. As a result, this product was employed as an exploratory product in the current study to confirm its safety and efficacy in weight management.

Chapter 2: INVESTIGATIONAL PRODUCT DESCRIPTION

The use of weight management gummies aids in body weight control. Modified amino acid (L-carnitine), Green coffee and ascorbic acid (vitamin C) are included in these gummies.

The possible beneficial effects of ascorbic acid in weight management are-

a. Modulating adipocyte lipolysis
b. Regulating the glucocorticoid release from adrenal glands
c. Inhibiting glucose metabolism and leptin secretion on isolated adipocytes
d. Leading to an improvement in hyperglycaemia and decrease glycosylation
e. Reducing inflammatory response, improving immunity, and active lifestyle.

Packagimg- 60 gummies in a transperant PET bottle with outer cartoon as a secondary packaging with instered consumer information leaflet.

Chapter 3: STUDY OBJECTIVE(S) AND PURPOSE:

Primary Objective:

The primary objective of the study was to evaluate-

1. Changes in Body Weight
2. Changes in BMI
3. Changes in Quality of life of subjects by IWQOL-Lite score (The Impact of Weight on Quality of Life Questionnaire) in social and emotional aspect

Secondary Objectives:

The secondary objective of the study was to evaluate-

1. Changes in digestive behavior (Bloating, Heartburn, Flatulence, Constipation, Post Prandial Fullness etc.) in subjects
2. Changes in insulin resistance calculated as HOMA-IR score
3. Changes in Lipid profile
4. Changes in anthropometric parameters such as Waste/Hip Ratio, Mid upper arm Circumference, Body Fat %, Visceral Fat level % etc.
5. Changes in general complaints like profuse sweating, irregular thirst, dyspnea and uncontrolled hunger on 0-10 VAS score.

Study groups:

Treatment Group: Healthy individuals on weight management gummies 1 BD for 90 days. Consultation regarding diet and lifestyle modification was provided to all subjects and asked to follow for 90 days.

Control Group: Healthy individuals on consultation regarding diet and lifestyle modification for 90 days.

Diabetic Group: Known cases of diabetes mellitus with uncomplicated nature and on stable proscription. Consumed weight management gummies 1 BD for 90 days. Consultation regarding diet and lifestyle modification was provided to all subjects and asked to follow for 90 days.

Allocation of subjects in study groups:

In a ratio of 1:1:1

Dosage and Treatment Duration:

2 weight management gummies a day

Inclusion Criteria:

Subjects who meet all of the following criteria were included in the study

1. Obese patients (male/female and aged between 20-45 yrs.)
2. BMI between 30 - 40 kg/m^2
3. Subjects with or without comorbidities, if comorbidity exists should be on stable prescription and with following criteria- Hypertension (140/90 mmHg on prescription), Type 2 DM (HbA1C ≤ 7.5 on prescription)
4. Willing to provide consent
5. Willing for follow up

Exclusion Criteria:

Subjects who meet any of the following criteria were excluded in the study:

1. Subjects with any acute illness requiring immediate medical care.
2. Subjects with Type I DM/Complicated cardiovascular diseases / HbA1C ≥ 7.5. / History of TIA, Cerebrovascular accident, stroke or any revascularization.
3. Known subjects of hepatic failure/inflammation.
4. Pregnant, breast feeding or planning to become pregnant during the study.
5. Any other condition which proves subject unfit for the study participation

Primary Efficacy Endpoint:

Assessment of primary end points will be performed on following time points:

1. Changes in Body Weight on baseline, day 30, 60 and 90 i.e. end of the study.
2. Changes in BMI on baseline, day 30, 60 and 90 i.e. end of the study.
3. Changes in Quality of life of subjects by IWQOL-Lite score (The Impact of Weight on Quality of Life Questionnaire) in social and emotional aspect on baseline, day 30, 60 and 90 i.e. end of the study.

Secondary Efficacy Endpoints:

Assessment of secondary end points will be performed on following time points:

1. Changes in digestive behavior (Bloating, Heartburn, Flatulence, Constipation, Post Prandial Fullness etc.) in subjects on baseline, day 30, 60 and 90 i.e. end of the study.

2. Changes in anthropometric parameters such as Waste/Hip Ratio, Mid upper arm Circumference, Body Fat %, Visceral Fat level % etc. on baseline, day 30, 60 and 90 i.e. end of the study.
3. Changes in general complaints like profuse sweating, irregular thirst, dyspnea and uncontrolled hunger on 0-10 VAS score on baseline, day 30, 60 and 90 i.e. end of the study.

Safety End Points:

Assessment of safety end points will be performed on following time points:

1. Tolerability of intervention by study subjects from baseline to end of study.
2. Safety of intervention evident by adverse events from baseline to end of study.
3. Changes in CBC, Lipid profile, Renal profile, HbA1c (only for diabetic subjects) at baseline and end of study

Visit Schedules:

Screening Day (-7 days), Baseline Day (Day 0), Day 30 (First assessment), Day 60 (Second assessment), Day 90 (Third assessment)

Chapter 4: STUDY OUTCOMES

Primary Outcomes:

1. Changes in Body Weight
2. Changes in BMI
3. Changes in Quality of life of subjects by
4. IWQOL-Lite score (The Impact of Weight on
5. Quality of Life Questionnaire) in social and emotional aspect

Secondary Outcomes:

1. Changes in digestive behavior (Bloating, Heartburn, Flatulence, Constipation, Post Prandial Fullness etc.) in subjects.
2. Changes in insulin resistance calculated as HOMA-IR score.
3. Changes in anthropometric parameters such as Waste/Hip Ratio, Mid upper arm Circumference, Body Fat %, Visceral Fat level % etc.
4. Changes in general complaints like profuse sweating, irregular thirst, dyspnea and uncontrolled hunger on 0-10 VAS score.

Safety Outcomes:

To assess safety of the test products by the investigator, Incidence of adverse event and biochemical parameters: Either self-reported by subject or assessed by Investigator.

Chapter 5: STUDY DESIGN

Parallel arm, randomized, controlled, prospective Clinical Trial.

Chapter 6: SELECTION AND WITHDRAWAL OF SUBJECTS

Recruitment Plan

We intent to complete 90 subjects at the end of the study. Additional subjects were recruited to complete the required number (90) of completed subjects for analysis. Subjects providing written informed consent and who were ready to provide regular follow ups till the completion of the study and meeting the inclusion and exclusion criteria were recruited in the study. Precautions were taken not to recruit the subjects belonging to possible vulnerable groups.

Withdrawal Criteria

Subject Withdrawal Criteria

Subjects should be withdrawn from the study (i.e. from any further study medication or study procedure) for the following reasons:

- At their own request i.e. withdrawal of consent at any time for personal reasons.
- If, in the investigator's opinion, continuation in the study would be detrimental to the subject's well-being.
- Protocol deviations that could invalidate interpretation of the results (i.e. intake of not permitted concomitant treatments etc.)

Subject Replacement Policy

Subjects who were recruited in the study should not be replaced.

Follow-up of Withdrawn Subjects

For subjects withdrawn from the investigational product and the study, the following procedures were performed:

In all cases, the reason for and date of withdrawal were recorded in the case record form and in the subject's medical records. The subject was followed up to establish whether the reason was an adverse event, and, if so this was reported. Investigators should follow subjects who have withdrawn from this study secondary to adverse event until the abnormality was resolved or stabilized, the subject had lost to follow up or event was otherwise explained.

As far as possible, all examination scheduled for the final study day were performed on the day subject was withdrawn. This applies to all randomized subjects who had received even one single dose of the investigational product. The investigator was making every effort to contact subjects lost to follow up. Attempts to contact such subjects were documented in the subject's records (e.g. times and dates of attempted telephone contact, receipt for sending a registered letter.)

Chapter 7: TREATMENT OF SUBJECTS

Treatment:

Dosage and Duration of the Treatment

As per A parallel arm clinical trial list, subject was allotted to either group. Subjects were advised to take given medication in the prescribed dosage.

The diet chart and exercise regime schedule which was followed by all subjects is enlisted as annexure 1.

Chapter 8: STUDY ASSESSMENT

Primary efficacy assessment:

1. Changes in Body Weight
2. Changes in BMI
3. Changes in Quality of life of subjects by
4. IWQOL-Lite score (The Impact of Weight on
5. Quality of Life Questionnaire) in social and emotional aspect

Secondary efficacy assessment:

1. Changes in digestive behavior (Bloating, Heartburn, Flatulence, Constipation, Post Prandial Fullness etc.) in subjects.
2. Changes in insulin resistance calculated as HOMA-IR score.
3. Changes in anthropometric parameters such as Waste/Hip Ratio, Mid upper arm Circumference, Body Fat %, Visceral Fat level % etc.
4. Changes in general complaints like profuse sweating, irregular thirst, dyspnea and uncontrolled hunger on 0-10 VAS score.

Subjects who continuously missed dosing for >3 consecutive days or total missed dose > 9 during the study period were treated as drop outs.
Palatability with dosage compliance of test product was assessed from the subjects at the baseline to end of the study.

0 = Not assessed	4 = No change
1 = Very much improved	5 = Minimally worse
2 = Much improved	6 = Much worse
3 = Minimally improved	7= Very much worse

Safety Assessment:
Safety was assessed by clinical review and safety laboratory parameters, including the following:

a. Adverse event reporting
b. Vital signs (Radial Pulse, Blood Pressure, Respiratory rate, Oral temperature).
c. Assessment of Overall Safety and Tolerability of the product by the physician and subject on global assessment scale by the investigator and by subject. The criterion for

the global assessment of overall safety was as follows:

1 = Excellent Overall safety (No adverse event/s reported)

2 = Good Overall safety (Mild adverse events (s) reported which subside with or without medication)

3 = Fair Overall safety (Moderate to severe adverse event(s) reported which subside with or without medication and do not necessitate stoppage of study treatment)

4 = Poor Overall safety (Severe or serious adverse event(s) which necessitate stoppage of study.)

Safety variables were listed individually for detailed clinical review, when needed. Additional tables were summarizing adverse events by severity and relationship to study product as well as leading to SAEs and withdrawal of the subjects from the study.

d. Laboratory testing i.e. CBC, LFT, RFT, lipid levels, blood sugar and serum insulin levels etc. test was done on screening visit and on day 90 of the study treatment. Change was these Laboratory parameters from baseline to 3 months were assessed.

Chapter 9: BRIEF STUDY METHODOLOGY:

After Ethics committee's approval, clinical study was registered on CTRI website. Subjects of age between 20 to 45 years of age (both inclusive) attending outpatient/consultation department of study site(s) were screened for eligibility criteria. On screening visit, a written informed consent was obtained from subjects confirming participation in the study. Their demographic details were taken. They were undergone clinical examination. Their medical, surgical and treatment history was taken. Their current medication if any was noted in the case record from (CRF). Their vitals were recorded. They were considered for further evaluation as per the inclusion and exclusion criteria.

During screening visit and the entire study duration subjects were advised to refrain from antioxidant agents, vitamins, anti-inflammatory drugs, hormones, Nutraceutical, Ayurvedic, Siddha, Unani, herbal /homeopathic medicines for maintenance of health.

A screening window of 7 days was kept, in case if there was requirement of any tests reports for confirming participation. On baseline visit, subject was recruited in the study if he or she meets all the inclusion criteria. They were then being randomized to the respective study groups as per the computer generated randomization list. They were asked for occurrence of any adverse event during screening period.

At baseline visit and at every follow up visit (except last follow up visit), they were provided with containers each containing 60 gummies for use if follow up was delayed maximum up to 5 days) of either group. They were advised to consume given supplement in a dose of 1 gummy twice a day after meal.

The consultation regarding diet of 2000 Kcal with light exercise routine of 30 min was advised to all subjects from three groups and asked to follow till end of the study i.e. 90 days.

They were advised to continue their concomitant medication other than antioxidant agents, weight loss management, vitamins, anti-inflammatory drugs, hormones, Nutraceutical, Ayurvedic, Siddha, Unani, herbal /homeopathic medicines etc. The record of concomitant medication was kept in the CRF. Investigational product compliance was assessed by the investigator on every follow up visit. If they continuously miss dosing for >3 consecutive days or total missed dose > 9 days during the study period, they were treated as drop outs.

They were allowed to come for follow up either 5 days prior or after the scheduled follow up visit, provided subject should continue the given treatment. On baseline and every visit the anthropometric parameters were assessed along with symptom grading and assessment of questionnaire for QoL.

On screening and day 90 visit all blood parameters were performed. After completion of 3 months of study treatment, they were asked to stop investigational product and take advice of investigator for further treatment.

Assessment of overall improvement was done by them and investigator on last follow up visit. Palatability with dosage compliance was assessed by the investigator and by them of investigational product from baseline to end of the study. They were closely monitored for any adverse event starting from baseline visit till the end of the study visit.

Chapter 10: ETHICAL CONSIDERATION

The study was initiated only after a written approval was obtained from Institutional Ethics Committee Lokmanya Medical Research centre, Chinchwad, Pune and subsequent registration of study on CTRI website. The study was conducted as per approved protocol and as per Good Clinical Practices guidelines. See Annexure 2 for EC approval.

Chapter 11: CTRI REGISTERATION:

After getting approval from the ethics committee, the study was registered on CTRI website. Patients were enrolled in the study only after registration of study on CTRI website.

The CTRI registration number is- CTRI/2021/03/032126 [Registered on: 18/03/2021] - Trial Registered Prospectively. See Annexure 3 for CTRI registration.

Chapter 12: STUDY MANAGEMENT AND ADMINISTRATION

Special Handling Requirements

The investigational product in their container was to be stored at room temperature away from heat, direct sunlight and out of reach of non-authorized personnel. A prolonged exposure of the container to a temperature above normal room temperature should be avoided. The investigational product was not to be stored near naked flame, heat or any incandescent material.

Prior and Concomitant Treatment

The illnesses present at the time of written informed consent was regarded as concomitant illnesses and would be documented in the case record form (CRF). Relevant past illnesses would also be documented in the CRF. All prior treatments taken by the subjects were recorded in the CRF. An accurate record of the use of any treatment other than the investigational product were kept in the case record form. The record was including name of the drug, the dose, and the date of administration and the indication for use. Illnesses first occurring or detected after recruitment

of the subject and worsening of a concomitant illness during the study was regarded as Adverse Events (AE's) and were documented in the CRF.

Not Permitted Concomitant Medication (Medication and Therapies)

Other than study drug, no other Allopathic, antioxidant agents, vitamins, health supplements, Nutraceutical, Ayurvedic, Homeopathic, Siddha, Unani drug(s) or any other traditional or folklore medicine or therapy were permitted for the said indications during study period. Acceptable concomitant medication may be allowed as per the investigator's discretion which would not have impact on study outcome.

Diet /Activity/Other

All the subjects were advised to continue their diet and exercise regimen advised by qualified dietician during the entire study.

Study Visits/ Follow Ups:

Study visits was consist of a screening visit (Within -07 Days prior to Day 0) and enrollment (Day 0), evaluation (Day 30 ± 5days and Day 60 ± 5days) and evaluation/end of study (Day 90 ± 2days).

Investigational Product Handling and Accountability:

Storage Requirement & Handling Description of Investigational Product

The Investigational product (IP) i.e. Study Drug provided was Gummies supplementation for weight management. The IP was stored at cool and dark place in room temperature away from heat, direct sunlight and out of reach of non-authorized personnel.

Labeling

Sponsor supplied investigational products to CRO. The investigational products were supplied as bottles having information such as product code, Subject ID, date of mfg., and expiry date, and storage conditions. Study drug packs were also had a statement that the product was for clinical study use only. Additional statement(s) might be printed to meet all the local regulations.

Chapter 13: DATA RECORDING AND RETENTION OF STUDY DATA

Following guidelines were implemented- The CRO shall maintain adequate records for the study including CRFs, medical records, informed consent documents, drug disposition records, safety reports, information regarding participants who discontinued, and other pertinent data. The following documents are archived:

- Protocols (all Version s) & Amendments, if any
- Informed consent form (s) signed by subjects
- All correspondence with Investigators, regulatory authorities, and between CRO and Sponsor etc. relating to the clinical study
- All photocopies of the working papers correctly dated and signed on each page.
- CRFs
- IEC approval, Communications etc.

Chapter 14: STATISTICS

Sample size consideration:

Sample size calculation is derived taking considerations of primary and secondary outcomes by a qualified statistician. The software used for calculation of sample size is SPSS version 10.0

Analysis Sets:

Per protocol subset:

Patients without any major protocol violation were included in the per protocol population, including those patients who had good treatment compliance, who did not take any prohibited medications during the study period and whose CRF was complete as requested.

Safety analysis subset:

The safety population consisted of all patients enrolled into the study, who have received at least one dose of study products.

Methods of Analysis:

Primary Efficacy end points and secondary end points were analyzed using per protocol analysis.

Statistical methods:

Statistical interpretation regarding following were performed by qualified statistician.

- Descriptive methods
- Demographic and Baseline Information
- Analysis of Primary Efficacy Parameters

- Analysis of Secondary Efficacy Parameters
- Safety Analysis
- Incidence and rate of adverse events etc.

Software used for analysis:

SPSS Version 10.0/ Graphpad prism

Chapter 15: **OBSERVATIONS AND RESULTS**

Demographics and Baseline Characteristics:

Table 1: Demographic details of the subjects

Parameters	**Treatment**	**Control**	**DM**
Male	15	15	15
Female	15	15	15
Average Age (Yrs.)	30 (6.8)	37(7.5)	39.5 (4.7)

The gender described is expressed as number of subjects. The age is described as Mean yrs. (SD). There was equal destitution of subjects gender wise i.e. 45 females and 45 males. The average age difference between groups was not significant. It indicates homogenous sample size for consideration of this study.

Efficacy outcomes:

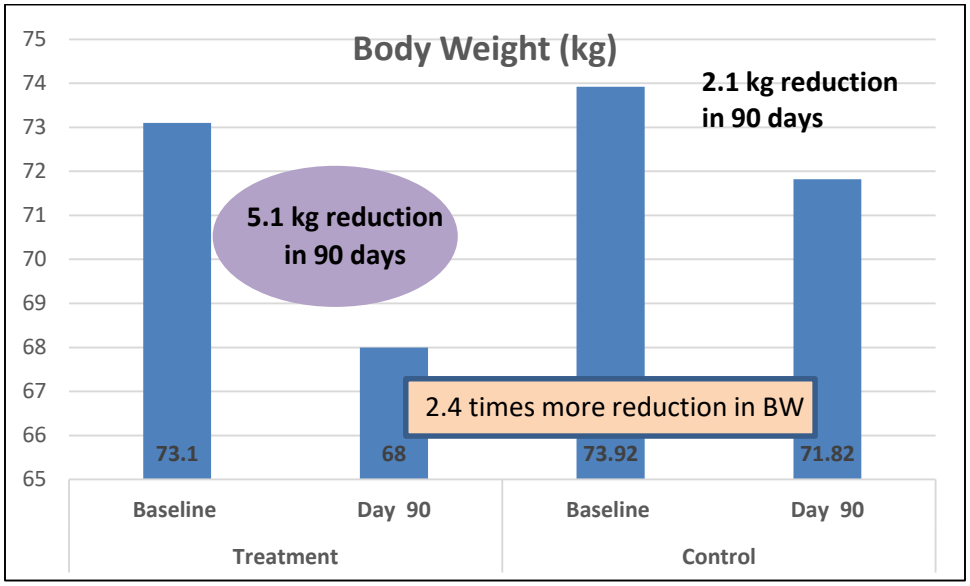
Table 2: Changes in body weight and BMI between groups (Treatment and control)

Parameter	**Baseline**		**Day 30**		**Day 60**		**Day 90**	
	Treatment	**Control**	**Treatment**	**Control**	**Treatment**	**Control**	**Treatment**	**Control**
Weight (kg)	73.10 (5.90)	73.92 (8.29)	70.95 (7.86)	73.24 (7.82)	70.10 (5.84)	72.44 (7.62)	68.00* (5.71)	71.82 (7.63)
BMI (kg/m^2)	29.09 (1.13)	30.68 (2.17)	28.18 (1.19)	30.40 (2.09)	28 (1.25)	29.97 (1.95)	26.43* (1.32)	29.79 (2.06)

Analyzed by student t test, *Significant $p<0.05$

There was gradual change in body weigh after treatment in healthy individuals receiving weight Management gummies supplementation. Subjects from treatment group shown 5.1 kg reduction in body weight with 9.2% decrease in BMI. In control group, subjects were only provided consultation regarding lifestyle modification were having 1.28 kg body weight reduction with marginal change in BMI. The reduction in body weight and BMI was statistically significant in treatment group versus control.

Graph 1: Changes in body weight between groups (Treatment and control)



Graph 1: Changes in BMI between groups (Treatment and control)

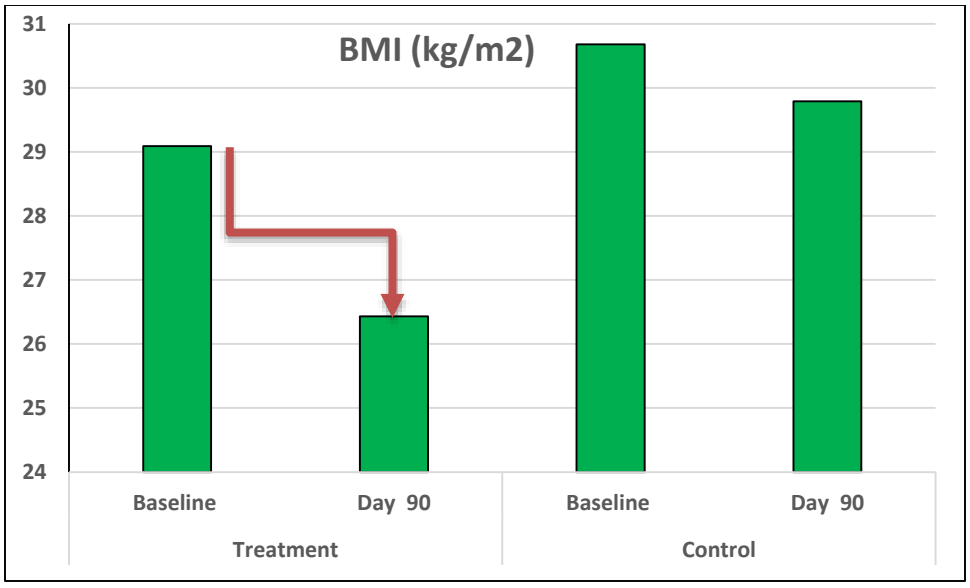


Table 3: Changes in body weight and BMI between groups (Group DM)

Parameters	Baseline	Day 30	Day 60	Day 90
Weight (kg)	76.35 (6.90)	75.98 (4.87)	74.95 (5.77)	73.36 (5.22)
BMI (kg/m^2)	29.41(1.26)	29.26(1.23)	28.76(1.07)	28.28(1.18)

Analyzed by ANOVA test, non-significant p>0.05

Changes in body weight (kg) and BMI of known case of DM patients on stable prescriptions were measured and depicted in table 3. There was almost 3 kg decrease in mean body weight. There was guidance regarding diet and lifestyle modification provided to all subjects. From baseline through day 30, day 60, and day 90, body weight decreased gradually. There was 1.13 kg/m^2 decrease i.e. almost 4% decrease in BMI of diabetic patients after 90 days of treatment.

Table 4: Changes in score of modified Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire between groups

Parameter	Baseline		Day 30		Day 60		Day 90	
	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control
IWQOL-Lite Score	124 (2.18)	125.03 (2.06)	114.79 (38.68)	118.69 (2.90)	103.25 (2.96)	110.47 (4.77)	80.20* (15.19)	108.16 (4.26)

Analyzed by student t test, *Significant p<0.05

Impact of weight on quality of life (QOL) score was significantly decreased in treatment group compared to control. There was around 35.33% reduction in the score.

The present study indicated enhanced quality of life as more the score there is much more distress, exhaustion and low self-esteem in following 5 domains of assessment. The questionnaire focuses on following domains as a measure of QoL and addressed following impact of increased weight in domains of social, physical and emotional wellbeing. The considerations are depicted in table 5.

Graph 3: Changes in score of modified Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire between groups

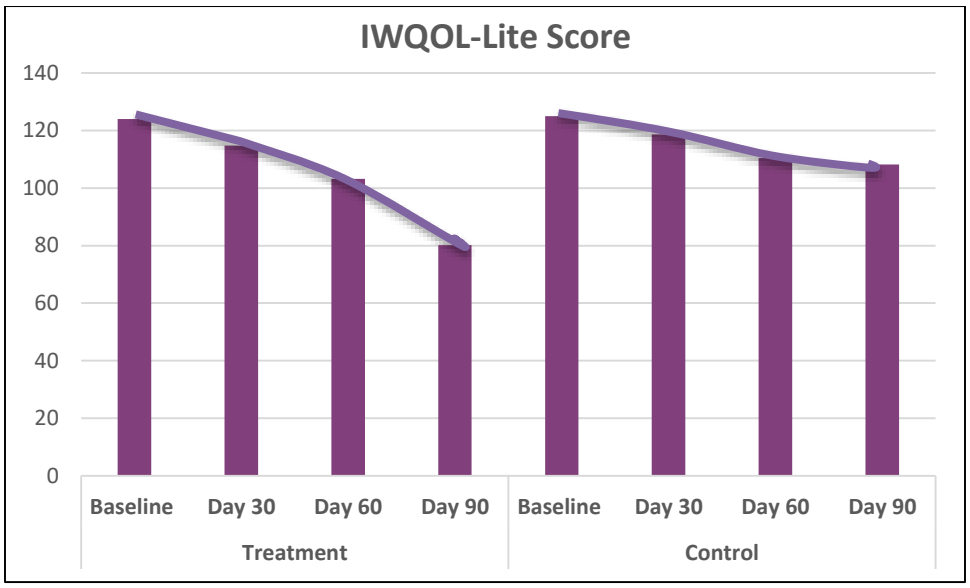


Table 5: Considerations addressed in the present modified IWQOL-Lite questionnaire

Domains	Concepts addressed in the present modified IWQOL-Lite questionnaire
Physical functions	Trouble bending over Tired or winded Unable to stand comfortably Lack energy Not physically active
Self esteem	Self-conscious eating in social settings Less confident Feel judged by others Viewed as less important or less worthy Decreased self-esteem
Sexual life	Less interest in sexual activity
Public distress	Frustrated shopping for clothes Feel bad or upset about pictures of self Experience discrimination
Work	Trouble accomplishing things Less productivity

Ref: Kolotkin RL, Ervin CM, Meincke HH, Højbjerre L, Fehnel SE. Development of a clinical trials version of the Impact of Weight on Quality of Life-Lite questionnaire (IWQOL-Lite Clinical Trials Version): results from two qualitative studies. Clin Obes. 2017 Oct;7(5):290-299. doi: 10.1111/cob.12197. Epub 2017 May 22. PMID: 28544443; PMCID: PMC5599949.

Table 6: Changes in score of modified Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire in subjects with DM

Parameters	Baseline	Day 30	Day 60	Day 90
IWQOL-Lite Score	124.90 (1.95)	118.60 (4.39)	103.47 (3.45)	93.53* (21.62)

Analyzed by ANOVA test, *Significant $p<0.05$

Impact of weight on quality of life (QOL) score was significantly decreased in diabetic patients group when compared to baseline. There was around 25.2% reduction in the score. It indicated enhanced QoL.

Table 7: Changes in digestive behavior between groups

Parameters	Number of events per month Mean (SD)			
	Baseline		Day 90	
	Treatment	Control	Treatment	Control
Bloating	13.31 (1.44)	13.39 (1.39)	6.53 (0.84)	7.46 (0.98)
Heartburn	7.31 (1.25)	7.60 (0.87)	4.21 (0.94)	6.15 (0.95)
Flatulence	6.03 (0.86)	7.10 (0.99)	2.93 (0.71)	4.75 (1.04)
Constipation	7.46 (1.19)	7.22 (1.09)	3.09 (0.73)	5.62 (0.87)
Post Prandial Fullness	13.15 (1.48)	13.78 (1.18)	6.50 (1.13)	8.34 (1.09)

Analyzed by student t test. Non-significant $p>0.05$

As per the results of number of events per month for the digestive complaints depicted in table 7, it can be concluded that there is reduction in the digestive complain events by the treatment of weight management gummies than the control but statistically non-significant.

Table 8: Changes in digestive behavior in diabetic group

Parameters	Number of events per month Mean (SD)	
	Baseline	Day 90
Bloating	13.28 (1.49)	9.88 (1.38)
Heartburn	7.47 (1.36)	6.39 (0.83)
Flatulence	7.39 (0.29)	5.39 (0.34)
Constipation	10.29 (1.49)	6.39 (1.38)
Post Prandial Fullness	18.39 (2.49)	14.38 (1.24)

Analyzed by student t test. Non-significant $p>0.05$

As per the results of number of events per month for the digestive complaints depicted in table 8, it can be concluded that there is reduction in the digestive complain events in diabetic group after treatment of weight management gummies though not statistically significant.

Table 9: Changes in anthropometric parameters between groups

Parameters	Mean (SD)			
	Baseline		Day 90	
	Treatment	Control	Treatment	Control
Anthropometric Indices				
Waist Circumference (cm)	96.00 (2.98)	95.84 (3.13)	87.78* (3.21)	94.30 (3.12)
Hip Circumference (cm)	103.66 (1.89)	102.62 (2.26)	97.97 (1.86)	100.7 (2.15)
Bioelectrical Impedance				
Body Fat (%)	28.93 (0.93)	28.78 (0.98)	24.18* (0.80)	27.18 (0.72)
Visceral Fat level (%)	21.88 (1.26)	21.70 (1.35)	18.63 (1.01)	19.89 (0.68)

Analyzed by student t test. Significant $p<0.05$

As per the results of anthropometric and bio-impedance indices there was gradual reduction in waist and hip circumferences in treatment group as well as control group but magnitude wise there was more decrease in treatment group than control. The results are not statistically significant but show the reducing trend. Body fat% and visceral fat % was also reduced more in treatment group than in control.

Table 10: Changes in anthropometric parameters in diabetic groups

Parameters	Mean (SD)	
	Baseline	Day 90
Anthropometric Indices		
Waist Circumference (cm)	96.09 (3.29)	94.01 (3.28)
Hip Circumference (cm)	103.56 (1.60)	99.46.04)
Bioelectrical Impedance		
Body Fat (%)	28.81 (1.20)	26.35 (1.26)
Visceral Fat level (%)	22.11 (1.01)	20.35 (0.96)

Analyzed by student t test. Non-significant $p>0.05$

As per the results of anthropometric and bio-impedance indices there was gradual reduction in waist and hip circumferences in diabetes group after treatment with weight management gummies. The results are not statistically significant but show the reducing trend. Body fat% and visceral fat % was also reduced at day 90 compared to baseline.

Table 11: Changes in symptoms related to increased body weight between groups (Treatment and control)

Parameter	Baseline		Day 30		Day 60		Day 90	
	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control
Profuse Sweating	7.69 (1.00)	7.66 (0.87)	5.25* (0.62)	7.69 (0.90)	5.03* (0.97)	6.34 (1.04)	2.91 * (0.82)	5.94 (0.91)
Irregular thirst	7.59 (0.80)	7.72 (0.92)	4.44* (0.91)	7.78 (0.94)	4.47* (1.02)	6.13 (1.04)	2.91 * (0.89)	5.88 (1.34)
Dyspnea	7.59 (0.04)	7.81 (0.93)	5.16* (0.72)	7.84 (0.92)	4.81* (0.86)	6.22 (1.04)	2.69 * (0.82)	5.40 (1.41)
Uncontrolled hunger	7.81 (7.78)	8.00 (0.72)	5.25* (0.62)	8.06 (0.76)	4.91* (0.78)	6.44 (1.29)	2.63 * (0.79)	5.29 (0.87)

Analyzed by student ANOVA test, *Significant $p<0.05$

In the present study, there were comparable symptoms related to increased body weight at baseline in both treatment and control groups. Gradually from day 30 to 90 the symptom severity declined. The score mentioned is expressed as mean score of VAS (0-10) zero being no symptom and 10 is severe which can interfere the daily activities most. The score between 0-5 represents milder symptoms not interfering daily activities. There is reduction in severity of symptoms evident as significantly reduced score after treatment of 90 days. From 30 days the treatment group started showing significant reduction in severity of symptoms and continued till day 90. Ij control group though there was slight decrease in the score but not significant compared to treatment group.

Table 12: Changes in anthropometric parameters in diabetic groups

Parameters	Baseline	Day 30	Day 60	Day 90
Profuse Sweating	7.80 (0.96)	7.60 (0.93)	6.27 (1.01)	5.83* (0.91)
Irregular thirst	7.87 (1.04)	7.73 (0.01)	6.30 (1.24)	5.27* (1.34)
Dyspnea	7.63 (0.93)	6.97 (0.89)	6.50 (1.20)	5.13* (1.50)
Uncontrolled hunger	7.80 (0.76)	7.50 (0.94)	6.63 (1.40)	4.70* (1.15)

Analyzed by student ANOVA test, *Significant $p<0.05$

In the present study, in diabetic subjects there was gradual decrease in the symptom score from baseline to day 90. The reduction in symptoms is statistically significant.

Table 13: Changes in lipid profile

	Mean levels (SD)			
	Treatment		Control	
	Baseline	Day 90	Baseline	Day 90
Total Cholesterol	185.10 (53.71)	160.49* (26.39)	189.16 (39.25)	186.12 (28.44)
Cholesterol HDL Direct	43.33 (12.11)	46.32(8.39)	44.49 (10.28)	45.88 (10.66)
Triglycerides	148.48(45.29)	130.62* (49.55)	165.49 (98.33)	160.48 (87.46)
LDL Cholesterol	108.38 (37.38)	94.35 (11.33)	120.20 (34.29)	115.48 (12.66)
VLDL Cholesterol	29.49 (21.48)	28.49 (9.33)	35.52 (29.36)	33.92 (17.56)

Analyzed by student t test. Significant $p<0.05$

At the end of 90 days of treatment, mean total cholesterol and triglycerides showed a significant reduction of around 14% and 12.45% respectively compared to control.

Safety assessment:

Assessment of tolerability of investigational product by investigator:

It was observed that 100% of subjects excellently tolerated weight management gummies with 100% compliance. There were no adverse events related or possibly related to the investigational; product. There were total 08 adverse events of menstrual pain, headache, cramps, and minor cut. The adverse events were mild in nature and required no rescue medication nor requirement to stop investigational product.

Changes in biochemical parameters:

There was no significant difference in the parameters like complete hemogram and biochemical parameter like liver and kidney function test at baseline and day 90 in all groups. This suggests that there are no systemic adverse events evident by abnormal laboratory values due to weight management gummies for long term use of 90 days. It suggests safety of the investigational product. There was no difference in blood sugar and serum insulin levels before and after treatment in diabetic group suggesting safety of consumption of weight management gummies in diabetic individuals.

Chapter 16: DISCUSSION

In the present study, weight management gummies were clinically evaluated for safety and efficacy in overweight- obese patients. It was observed from the present study that administration of weight management gummies for 90 days along with the lifestyle modification led to synergistic action and achieved more weight loss along with improvement in quality of life and symptom etc. compared to only lifestyle modification as control.
In the present study obese diabetic patients were also administered with weight management gummies for 90 days along with their concomitant medication and same lifestyle changes that of the healthy group. It is observed that there is weight loss and reduction in symptoms in these patients along with improvement in quality of life but was not statistically significant, we can conclude that the underlying comorbidity and metabolic changes must be the reason for the same.
Obesity and overweight continue to negatively impact society, overwhelming health, and healthcare services globally. Despite a real need, relatively few nutraceutical products are clinically proven to be safe and effective in the weight management.

The present study shows 12-week supplementation of weight management gummies reduces body weight, BMI, body fat, waist and hip circumference in overweight to obese participants with an average BMI of 29-30 kg/m^2. In addition, biochemical, hematological parameters and subject compliance demonstrate that weight management gummies are tolerable and safe for human consumption.

The primary outcome of the present study was reduction of baseline body weight compared with control. Body weight reductions of >5% have been associated with improvements in metabolic and cardiovascular health (8). Our data show that an average of 7% of the baseline body weight was lost in the treatment group after 12 weeks of intervention. Further analysis reveals that 22 out of 30 participants in the treatment group lost more than 5% of their baseline body weight at the end of the trial (Table 2).

BMI is a marker of adiposity globally and is also a reliable marker of visceral adiposity. Visceral adipose tissue increases in a quasi-linear manner with BMI in both sexes (9). Waist circumference (WC) and waist-hip ratio (WHR) are commonly used as surrogate markers of visceral adiposity (10). Visceral obesity is a significant risk factor for cardiovascular morbidity and mortality; therefore, increased WC is considered as one of the vital diagnostic criteria for Metabolic Syndrome (11). In the present study, weight management gummies supplementation conferred significant reduction of WC and a reduction in WHR, compared to the control. The reduction of

visceral adiposity in the treatment group is supported by the observation of a significant reduction of 4.75% total body fat achieved at the end of the study. Together, these data suggest that weight management gummies is an effective option for reducing body weight and fat in overweight participants (Table 9).

Weight management gummies supplemented participant experienced significant improvements in serum markers of lipid metabolism related to overweight and obesity. Hyperlipidemia is generally associated with overweight and obesity, which is known as a risk factor for CVD including atherosclerosis (12, 13). The study showed a reduction in serum LDL, VLDL, total cholesterol, triglyceride and LDL/HDL ratio following a similar pattern to weight loss over the 12-week trial period. There was significant reduction in triglyceride levels in treatment group compared to the control. Concomitantly, serum HDL level was also improved in the treatment group. The reduced level of harmful lipids in circulation i.e. LDL triglycerides reflected an improved status of fat metabolism and reduced stored fat in the body. Overall, the improvements in serum lipid profile in the treatment group imply possible preventive approach and can get the cardiovascular benefits for overweight participants (Table 13).

Obesity is related to the social stigma and leads to the low self-esteem with many social and emotional complications in overweight and obese subjects. In the present study we have assessed changes in score of modified Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire between groups (14). It was observed that due to the improved metabolism, reduced body weight and digestion overall quality of life of subjects was significantly improved as soon as 4 weeks in treatment group compared to control. There was great improvement in following domains as per subject reported questionnaire physical functions, self-esteem, sexual life, public distress and work. This presents overall improvement in wellbeing for an overweight subject as a result of consumption of weight management gummies for 90 days.

The health implications by obesity include a wide spectrum of benign digestive diseases and disorders ranging wide from bloating, constipation and post prandial fullness to gastro esophageal reflux disease (GERD), Barrett's esophagus (BE), nonalcoholic fatty liver disease (NAFLD), gallstones, and pancreatitis and digestive organ cancers. An effective and safe nutraceutical product managing body weight along with providing benefits to certain digestive complains can be a boon for overweight subjects (15). In the present study there is significant reduction in digestive complaints evident by reduced events of bloating, heartburn, flatulence, constipation and post prandial fullness compared to the control arm. This further adds to improved quality of life of subjects.

Obesity presents typical clinical symptomatology as profuse sweating, irregular thirst, dyspnea and uncontrolled hunger. In the present study, all symptoms were mild to moderately present in all subjects at baseline but gradually as treatment with weight management gummies progressed, the above mentioned symptoms were reduced in almost 70-75% subjects remarkably (Table 11) compared to the control group.

In case of the diabetic individuals, there was 3kg (3.92%) reduction in body weight along with 1.13kg/m^2 reduction in BMI. There was improved lipid profile though was not statistically significant difference compared to baseline. There was improvement in symptomatology ie symptoms related to digestive system as well as obesity related symptoms were reduced after treatment with the weight management gummies. There was reduction in WC, hip circumference and body and visceral fat % after treatment with weight management gummies to diabetic individuals on stable antidiabtic prescription.

For diabetic subjects blood sugar and serum insulin levels were measured at baseline and day 90 of treatment; it was observed that there were no significant changes indicating that the consumption of weight management gummies is safe in diabetic subjects as well.

It was observed that 100% of subjects excellently tolerated weight management gummies with 100% compliance. There were no adverse events related or possibly related to the investigational; product.

There was no significant difference in the parameters like complete hemogram and biochemical parameter like liver and kidney function test at baseline and day 90 in all groups. This suggests that there are no systemic adverse events evident by abnormal laboratory values due to weight management gummies for long term use of 90 days. It suggests safety of the investigational product. There was no difference in blood sugar and serum insulin levels before and after treatment in diabetic group suggesting safety of consumption of weight management gummies in diabetic individuals.

The possible beneficial activities obtained through the treatment of weight management gummies is possibly by virtue of the vitamin blend with L- carnitine and green coffee phytoconstituents.
L-carnitine present in the gummies aids in fatty acid oxidation in skeletal and cardiac muscle. Carnitine also helps with lipid metabolism. L-carnitine is a substance that aids in weight management by increasing energy expenditure and lipid metabolism. Several studies confirm the effectiveness of L-carnitine to improve body composition thus the anthropometric parameter and body impedance indices (16).

Green coffee consumption has been demonstrated to boost metabolism and give antioxidant effects, as well as aid in weight loss in previous studies. Green coffee may stimulate fatty acid oxidation and inhibit lipogenesis and body fat accumulation through the down-regulation of adipogenesis-related genes.

Green coffee extract has been reported to reduce the postprandial glucose and blood lipid levels. Reduction in the absorption of glucose in the intestine; by promoting diffusion of the Na+ electrochemical gradient is thought to be the mechanism of action. It is also reported in earlier studies to inhibit the enzymatic activity of hepatic glucose-6-phosphatase, involved in the homeostasis of glucose. Animals studies earlier performed confirm antiobesity effect of green coffee extract possibly by suppressing the accumulation of hepatic triglycerides and shifting the metabolism towards fat burning mode (17).

Future scope of the study is to plan a bigger sample size with more biochemical markers like leptin, adiponectin and for longer duration of time can give deeper insight for the activity of the weight management gummies.

Chapter 17: CONCLUSION:

- In the present study, weight management gummies were clinically evaluated for safety and efficacy in overweight- obese patients. It was observed from the present study that administration of weight management gummies for 90 days along with the lifestyle modification led to synergistic action and achieved more weight loss along with improvement in quality of life and symptom etc. compared to only lifestyle modification as control.
- There was average of 7% of the baseline body weight was lost in the treatment group after 12 weeks of intervention around 5.1 in 90 days.
- Twenty two out of 30 participants in the treatment group lost more than 5% of their baseline body weight at the end of the trial.
- There was significant reduction in BMI after treatment of weight management gummies.
- There was reduction of waist circumference by 8.22 cm i.e. around 3.5 inches after treatment of weight management gummies for 90 days.
- There was reduction of waist circumference by 5.70 cm i.e. around 2.5 inches after treatment of weight management gummies for 90 days.
- The reduction of visceral adiposity in the treatment group is supported by the observation of a significant reduction of 4.75% total body fat achieved at the end of the study.
- Together, these data suggest that weight management gummies is an effective option for reducing body weight and fat in overweight participants.
- There is around 12-14% decrease in total cholesterol and serum triglyceride levels after treatment of weight management gummies for 90 days.
- In the present study there is significant reduction in digestive complaints evident by reduced events of bloating, heartburn, flatulence, constipation and post prandial fullness compared to the control arm. This further adds to improved quality of life of subjects.
- Obesity presents typical clinical symptomatology as profuse sweating, irregular thirst, dyspnea and uncontrolled hunger. In the present study, all symptoms were mild to moderately present in all subjects at baseline but gradually as treatment with weight management gummies progressed, the above mentioned symptoms were reduced in almost 70-75% subjects remarkably compared to the control group.
- It was observed that due to the improved metabolism, reduced body weight and digestion overall quality of life of subjects was significantly improved as soon as 4 weeks in treatment group compared to control.

- There was great improvement in following domains as per subject reported questionnaire physical functions, self-esteem, sexual life, public distress and work indicating overall wellbeing enhancement.
- In case of the diabetic individuals, there was 3kg (3.92%) reduction in body weight along with 1.13kg/m^2 reduction in BMI. There was improvement in symptomatology ie symptoms related to digestive system as well as obesity related symptoms were reduced after treatment with the weight management gummies. There was reduction in WC, hip circumference and body and visceral fat % after treatment with weight management gummies to diabetic individuals on stable antidiabtic prescription. For diabetic subjects blood sugar and serum insulin levels were measured at baseline and day 90 of treatment; it was observed that there were no significant changes indicating that the consumption of weight management gummies is safe in diabetic subjects as well.
- It was observed that 100% of subjects excellently tolerated weight management gummies with 100% compliance.
- There were no adverse events related or possibly related to the investigational; product.
- There was no significant difference in the parameters like complete hemogram and biochemical parameter like liver and kidney function test at baseline and day 90 in all groups. This suggests that there are no systemic adverse events evident by abnormal laboratory values due to weight management gummies for long term use of 90 days.
- It suggests safety of the investigational product. There was no difference in blood sugar and serum insulin levels before and after treatment in diabetic group suggesting safety of consumption of weight management gummies in diabetic individuals.

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