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A Pilot Study Evaluating the Safety and Efficacy of Nutritional Formula for Enhancing Gastrointestinal Health

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ABSTRACT

The gut microbiota, a complex community of microorganisms in the digestive tract, is essential for maintaining immune, metabolic, and digestive health. Lifestyle and dietary habits significantly impact gut health, with poor dietary choices and sedentary behavior exacerbating gastrointestinal issues. To investigate the effectiveness and safety of a Supply6 360, a comprehensive nutritional formulation, in improving gastrointestinal health in adults. An open-label, single-arm clinical trial was conducted with 25 participants experiencing gastrointestinal symptoms. The supplement, containing a blend of vitamins, minerals, probiotics, and other nutrients, was administered for 60 days. Outcomes assessed included changes in gastrointestinal symptoms using the Gastrointestinal Symptom Rating Scale (GSRS), blood parameters, fatigue severity, and gut microbiota composition. Participants showed significant improvements in various health parameters. Blood analysis demonstrated increased levels of Vitamin B12 and D3, improved lipid profiles, and enhanced NAD+ levels. GSRS scores for abdominal pain, reflux syndrome, diarrhea, indigestion, and constipation decreased significantly, indicating symptom relief. Fatigue severity also decreased notably. Alpha diversity in gut microbiota improved, suggesting enhanced microbial balance. No significant adverse events were reported, confirming the safety and tolerability of Supply6 360. The nutritional formula demonstrated efficacy in improving multiple aspects of gastrointestinal health and overall well-being. The formulation, containing vitamins, minerals, probiotics, and various bioactive compounds, appears to support gut health and alleviate gastrointestinal symptoms. The observed benefits include improved vitamin and lipid profiles, reduced fatigue, and enhanced gut microbiome diversity. These findings highlight the potential of the supplement as a comprehensive approach to addressing gastrointestinal issues and promoting overall health.

Keywords: Gastrointestinal Health, Gut Microbiota, Clinical Trial, Prebiotics, Probiotics, Vitamins and Minerals

1. INTRODUCTION

The gut microbiota is a complex microbial community consisting of bacteria, viruses, fungi, and other microorganisms. A dynamic relationship of mutual benefits (symbiosis) has been formed between the microbiota and the human body. This helps keep the body's immune, metabolic, and motor functions normal, as well as ensuring proper digestion and absorption of nutrients [1]. The gut microbiota plays a

crucial role in various important functions within the human body. These include protecting against harmful pathogens by colonizing mucosal surfaces and producing antimicrobial substances [2], boosting the immune system, aiding in digestion and metabolism [3], regulating the growth and specialization of epithelial cells [4], impacting insulin resistance and secretion [5,6], influencing communication between the brain and gut, and ultimately affecting the mental and neurological functions of the host. Hence, the gut microbiota is essential for maintaining the normal functioning and health of the gut [7].

Our lifestyle and dietary habits, in particular, have a significant impact on whether or not we experience some digestive issues. Fast food dependency, compulsive overeating, excessive alcohol consumption, and smoking are only a few contributing factors in this context. These factors might exacerbate preexisting digestive issues, such as flatulence, abdominal discomfort, bowel irregularity, diarrhea, vomiting and heartburn. They impose a substantial burden on global public health [8]. Frequently prescribed drugs to treat gastrointestinal issues are analgesics, antacids, and antispasmodics. However, it is important to note that these medications simply provide relief from symptoms and do not address the underlying cause of the problem. However, adequate diet and lifestyle modifications are considered to be the most valuable aspects of the therapeutic procedure. Implementing modifications in these domains enhances the overall well-being of individuals with such gastrointestinal problems [9].

In today's fast-paced and modern world, people often find it challenging to engage in physical activity due to sedentary desk occupations. This lifestyle, paired with difficulties in accessing healthy meals, contributes to the ingestion of unhealthy (junk) food. As a result, these individuals may encounter gastrointestinal symptoms, such as pain in the upper abdomen, discomfort in the abdominal area, heartburn, nausea and bloating etc. In order to address this problem, a formulation that is enhanced with vitamins, minerals, and bioactive substances and intended to improve gastrointestinal health is needed.
The purpose of the study was to evaluate the effect of a Supply6 360, a comprehensive nutritional formulation, in adult participants with gastrointestinal symptoms. This supplement consists of multi-vitamins, multi-minerals, and a variety of ingredients that provide nutritious benefits to the gut microbiota, leading to improved gastrointestinal health and overall well-being. The investigational product was used as an exploratory treatment in the current trial.

2. MATERIALS AND METHODS

Study Design

The study was an open-label, single-arm clinical trial that aimed to evaluate the safety and effectiveness of Supply6 360 in improving gastrointestinal health and wellness. In this study, 25 patients were enrolled, and Supply6 360 was given to the participants along with instructions about consumption. The treatment duration was 60 days. The patients were recruited after the Ethics Committee's approval and registration with the Clinical Trials Registry-India (CTRI) registration number CTRI/2024/03/063507. The study was conducted as per the approved protocol, Declaration of Helsinki and Good Clinical Practices (GCP) guidelines.

Inclusion Criteria:

Participants who met all of the following criteria were eligible for the study: those who were symptomatic males and females between 25 and 35 years of age, both inclusive, with a Body Mass Index (BMI) between

18.5 and 29.9 kg/m². Those who self-reported at least two gastrointestinal symptoms, such as epigastric discomfort, heartburn, bloating, nausea, fullness in the stomach, abdominal pain, or anorexia. Additionally, those who were not consuming probiotics, prebiotics, or similar substances. Lastly, participants demonstrated their willingness to participate in the study and comply with its procedures by signing a written informed consent.

Exclusion Criteria:

Participants who met any of the following criteria were not eligible for the study: those with a history of major abdominal surgery, inflammatory bowel disease, diverticular disease, celiac disease, allergic diseases including asthma, psychiatric disorders, or critical systemic illness, as assessed by medical history, appropriate consultations, and/or laboratory tests. Participants actively having a gut infection or with a history of or complications from malignant tumors were also excluded. Females who were pregnant, had a positive urine pregnancy test, were planning to become pregnant, were lactating, or were not using reliable methods of contraception were ineligible. Additionally, participants with heavy alcohol consumption or smoking/tobacco use were excluded. Any condition that, in the opinion of the investigator, could have precluded the participant's ability to complete the study or might have confounded study outcomes, were also excluded from the study.

Methodology

A total of 25 participants were enrolled in the study. The following parameters were assessed: Changes in the Gastrointestinal Symptom Rating Scale (GSRS) score from screening to end of the study. Changes in lipid profile, serum vitamin B12 and vitamin D3 levels, fatigue severity score, levels of Nicotinamide Adenine Dinucleotide (NAD+), gut microbiota at screening and end of the study. Blood samples for the assessment of blood parameters were collected at both the screening and the end of the study by a trained phlebotomist. These samples were then analyzed by a laboratory accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL). Additionally, stool samples were collected for microbiome assessment. Percent responders to a reduction in requirement of rescue medication from baseline to end of study (at least 50% reduction in doses or medication events in a month).

Treatment compliance and tolerability of the study intervention in terms of adverse events (AEs), serious adverse events (SAEs) were assessed from baseline to end of the study.

Sample size

As the study was a proof-of-concept study. The sample size was considered to be twenty- five completer participants based on the clinical and research judgment of the investigators.

Statistical analysis

Primary symptoms were evaluated for normality by ‘Kolmogorov-Smirnov Test’. Blood parameters, fatigue severity score data was analyzed by student t-test. GSRS score data was analyzed by student-t test

and Wilcoxon test. Fecal samples were extracted and sequenced using a shotgun metagenomics approach. Statistical analysis has been done by using Statistical Package for the Social Sciences (SPSS) software.

Investigational Product Composition
(Table 1)

RESULT

A total of 25 participants completed the study. The details are provided in the Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 1).

Assessment of demographics characteristics

Table 2 summarizes the demographic details of the participants. A total of 18 male and 07 female participants completed the study. The average age of study participants was 30.08 ± 2.97 years (Table 2).

Assessment of Blood Parameters

Vitamin B12 levels showed a substantial and significant increase by 91.79% by Day 60. Vitamin D3 levels also significantly increased by 66.57%. NAD+ levels also increased significantly after 60 days of treatment by 19.85% as compared to screening.

High-Density Lipoprotein (HDL) levels increased significantly from 42.62 ± 12.15 mg/dL to 49.68 ± 11.64 mg/dL. Total cholesterol levels decreased significantly from 210.88 ± 29.06 mg/dL at screening to 158.74 ± 22.10 mg/dL on Day 60. Low-Density Lipoprotein (LDL) levels also dropped from 131.81 ± 27.94 mg/dL to 81.83 ± 22.16 mg/dL. Very Low-Density Lipoprotein (VLDL) levels decreased significantly from 36.45 ± 11.32 mg/dL to 27.23 ± 10.37 mg/dL. Triglycerides level were significantly reduced by 25.28% from 182.25 ± 56.62 mg/dL at screening to 136.17 ± 51.86 mg/dL on Day 60.

Overall, the data indicates that the participants experienced an improvement in both vitamin levels and lipid profile parameters over the 60-day period (Table 3).

Assessment of Gastrointestinal Symptom Rating Scale (GSRS) questionnaire score

In this study, all five domains of GSRS—abdominal pain, reflux syndrome, diarrhea, indigestion, and constipation—showed a gradual yet significant reduction in scores from Day 15, with continued improvement through Day 60 (Table 4)**.**

Assessment of Fatigue Severity Scale (FSS) Score

A notable improvement in fatigue severity from the screening to Day 60 was noted in this study. The average FSS score decreased from 3.49 ± 0.47 at screening to 2.78 ± 0.38 on Day 60, representing a 20.25% significant reduction (Table 5).

Assessment of Vital Signs

No clinically significant changes in vital signs were observed throughout the study. All vital parameters remained within normal physiological ranges.

Assessment of cumulative number of participants requiring rescue medications and % responders

Responders were defined as participants demonstrating at least a 50% reduction in the frequency or dose of rescue medication use. Rescue medications were administered for symptoms such as hyperacidity, heartburn, and flatulence. At baseline, 11 of 25 participants were using rescue medication. By Day 15, 4

of 11 participants (36.36%) were classified as responders, achieving at least a 50% reduction in rescue medication use. By Day 30, and sustained through Day 60, all participants had completely discontinued rescue medication use, resulting in a cumulative responder rate of 100%.

Assessment of Gut microbiome

Fecal samples were extracted and sequenced using a shotgun metagenomics approach. Each sample was used to classify bacterial and fungal taxonomic composition. Alpha diversity indices (Shannon) of the microbiota (Figure 2 and 3) demonstrated a significant improvement in Shannon alpha diversity in the subjects between baseline and post treatment ($p = 0.002$).

Assessment of Tolerability and Compliance

No adverse event reported. All participants consistently reported excellent tolerability throughout the study period in response to the investigational product. There was around 100% investigational product consumption compliance observed on day 15 which was continued till day 60.

3. DISCUSSION

The present study evaluated the safety and effectiveness of Supply6 360 in improving gastrointestinal health and wellness over a 60-day period.

Significant improvements were observed across multiple domains. Blood parameter analyses demonstrated notable increases in Vitamin B12 and D3 levels, alongside favorable changes in lipid profiles including increase in HDL and decrease in LDL, total cholesterol, triglyceride levels. Moreover, gastrointestinal symptoms assessed through the GSRS questionnaire indicate improved gastrointestinal health from Day 15 onwards. Fatigue severity, as measured by the FSS, also showed a substantial reduction by Day 60. Additionally, improvements in NAD+ levels, suggests enhanced energy levels and gastrointestinal function. Overall, these findings underscore the potential of the intervention in improving multiple aspects of gastrointestinal health and wellbeing.

Supply6 360 is a distinct blend of various vitamins, minerals, adaptogens, probiotics, fruits and greens including detox blend, omega blend, adaptive blend, berry blend, greens juice powder, superfruit juice powder, probiotics, digestive enzyme blend, antioxidant blend, pea protein, brown rice protein, amaranth seeds powder, coconut milk powder, fructooligosaccharides (FOS), fruit powder, vegetable powder, vitamin mix, mineral mix & xanthan gum. These ingredients are proven to aid in balance the gut flora, digestion, support optimal nutrient absorption, increase immunity, support eye health, detoxify the body, improve bone strength, and improve energy and focus. Various clinical trials provide valuable insights into the efficacy of the individual ingredients used in Supply6 360.

Moreover, the favorable changes in blood parameters, including increased levels of Vitamin B12 and D3, and improvements in lipid profiles with decreased LDL cholesterol, total cholesterol, and triglyceride levels, may suggest a potential role in cardiovascular health. These findings align with previous research

highlighting the cardioprotective effects of certain ingredients present in the formula, such as omega-3 fatty acids from flax seeds, antioxidants from berries, and soluble fiber from oats and chia seeds [10-14]. In today's fast-paced world, many are experiencing various digestive issues due to micronutrient deficiency, enzyme insufficiencies, and altered gut microflora. The lack of optimal digestive function associated with enzyme inadequacy may lead to malabsorption and related health issues. The observed reductions in gastrointestinal symptoms, including abdominal pain, reflux syndrome, diarrhea, indigestion, and constipation, suggest an improvement in gut health and digestive function. Ingredients like probiotics, ginger, and fiber-rich foods such as oats and flax seeds have been associated with enhanced gastrointestinal health and symptom relief in various studies [15-18].

Increased NAD+ levels and a decrease in fatigue severity scores suggest that the formula may contribute to improved energy levels and overall vitality. This could be attributed to ingredients such as ginseng, maca root extract, and vitamin B12, which are known for their adaptogenic and energizing properties [19-21].

The impairment of gut microbiota can worsen or cause alterations in digestive functions, so the restoration of microbial homeostasis represents a reliable therapeutic option for the management of several digestive disorders [22].

Treatment with Supply6 360 for 60 days significantly improved alpha diversity of bacterial taxa of all the subjects ($p<0.002$). An increase in alpha diversity assessed via shotgun metagenomics analysis suggests that the investigational product may have positively influenced the gut microbial ecosystem by promoting microbial richness and evenness. This finding indicates that the probiotic component of the investigational product may have successfully integrated into the existing gut microbiota and supported the growth of other beneficial microorganisms, thereby fostering a more balanced and diverse microbial community. The enhanced microbial diversity may reflect the ability of the probiotic to create a favorable intestinal environment through modulation of microbial interactions, suppression of potentially harmful bacteria, and support of beneficial taxa. Restoration of microbial homeostasis during dysbiosis is generally related to improved gut health, increased resilience of the microbiome, and potential overall health benefits. Thus, the investigational product demonstrated a significant effect on modulating gut microbiota. An increase in alpha diversity suggests that the probiotic effectively enhances the diversity of the gut microbiome, which is often linked to improved gut health and overall well-being.

The human colon contains trillions of microorganisms constituting the gut microbiota responsible for maintaining host homeostasis. Any changes in the composition of these microorganisms lead to metabolic shifts, altering the host phenotype. The gut microbiome keeps changing throughout the lifetime due to environmental stressors and triggers. Intestinal homeostasis maintenance is essential. Probiotics such as B. coagulans, L. acidophilus, and Lactobacillus rhamnosus can help restore microbial balance during dysbiosis [24].

B. coagulans are non-toxic and efficacious for managing gastrointestinal complications like inflammatory bowel diseases and also for preventive treatments to maintain overall wellness [25]. L. acidophilus regulates the intestinal microflora by lowering the acidity of the environment as well as preventing

pathogenic bacteria. This microorganism also competes for adhesion and lowers serum cholesterol levels [26]. L. rhamnosus GG microorganism has been observed to have an excellent capability for proliferation, adherence, bile tolerance, and protection [27].

The vital signs remained stable throughout the study period. No adverse events were reported, and the intervention was found to be safe and well tolerated. This is consistent with previous research indicating the safety of the individual ingredients used in the formula [23].

This pilot study has several limitations, including its open-label design, lack of a placebo-controlled comparator, relatively small sample size, and limited age range (25–35 years), which may affect the generalizability of the findings. Therefore, the results should be interpreted with caution. Further investigation through larger, randomized, placebo-controlled clinical trials is warranted to validate these findings and better elucidate the underlying mechanisms of action. Nevertheless, the findings of this study suggest that the nutritional formula may hold promise as a comprehensive nutritional approach for supporting gastrointestinal health and overall well-being.

4. CONCLUSION

The present 60-day clinical evaluation of Supply6 360 demonstrated statistically and clinically meaningful improvements across a broad range of biochemical, metabolic, gastrointestinal, microbiome, and wellbeing-related parameters in both male and female participants. Collectively, the findings indicate that daily supplementation with Supply6 360 was associated with favorable modulation of nutritional biomarkers, lipid metabolism, gastrointestinal function, gut microbial diversity, cellular energy metabolism, and fatigue severity, while maintaining an excellent safety and tolerability profile.

5. ACKNOWLEDGMENT

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6. DECLARATION OF CONFLICT OF INTERESTS

Mr. Vaibhav Bhandari and Mr. Rahul Jacob are directors of Kanari Nutrition Pvt. Ltd. Other author declares no conflict of interest.

7. DATA AVAILABILITY

The datasets generated and/or analysed during the current study are not publicly available due to Intellectual property constraints but are available from the corresponding author on reasonable request.

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Tables

Table 1 Active Ingredients of Supply6 360:

Name of the Ingredient	**Scientific Name**	**Name of the Ingredient**	**Scientific Name**
Detox Blend		Garlic Juice Powder	Allium sativum
Chlorophyll	Chlorophyll	Ginger Juice Powder	Zingiber officinale
Spirulina	Arthrospira platensis	Green Onion Juice Powder	Allium fistulosum
Omega Blend		Cauliflower Juice Powder	Brassica oleracea var. Botrytis
Oats Powder	Avena sativa	Mint	Mentha
Flax Seed Powder	Linum usitatissimum	Asparagus Juice Powder	Asparagus officinalis
Chia Seed Powder	Salvia hispanica	**Superfruit Juice Powder**	
Adaptogen Blend		Custardapple Powder	Annona squamosa
Maca Root Extract	Lepidium meyenii	Pineapple Powder	Ananas comosus
Shiitake Mushroom	Lentinula edodes	Banana Powder	Musa
Maitake Mushroom	Grifola frondosa	Pomegranate Juice Powder	Punica granatum
Panax Ginseng	Panax ginseng	**Prebiotics**	
Green Coffee Bean Extract	Coffea canephora	Sunfiber Powder	Partially hydrolyzed guar gum
Berry Blend		**Probiotics**	
Acai Berry Powder	Euterpe oleracea	Bacillus coagulans, L. Rhamnosus, L. acidophilus	-

Maqui Berry Powder	Aristotelia chilensis	**Digestive Enzyme Blend**	
Tart Cherry Powder	Prunus cerasus	Amylase, Protease, Cellulase, Lipase, lactase	-
Strawberry Powder	Fragaria	**Antioxidant Blend**	
Blackberry Powder	Rubus	Lutein/ Zeaxanthin Complex Powder	-
Blueberry Powder	Vaccinium sect. Cyanococcus	Beta Carotene Powder	β-Carotene
Raspberry Powder	Rubus idaeus	Astaxanthin Powder	Haematococcus pluvialis
Greens Juice Powder		**Other Ingredients**	
Beetroot Juice Powder	Beta vulgaris	Pea Protein Powder	Pisum sativum
Carrot Juice Powder	Daucus carota	Brown Rice Protein	Oryza sativa
Spinach Juice Powder	Spinacia oleracea	Coconut Milk Powder	Cocos nucifera
Broccoli Juice Powder	Brassica oleracea var. italica	Inulin	Beta (2-1) fructans
Tomato Juice Powder	Solanum lycopersicum	FOS-95	Fructo-oligosaccharide
Kale Juice Powder	Brassica oleracea	Vitamin Premix	Blended Vitamins – FSSAI
Cabbage Juice Powder	Brassica oleracea var. capitata	Mineral Premix	Blended Minerals – FSSAI
Cucumber	Cucumis sativus	Amaranth Seed Powder	Amaranthus spp
		Xanthan Gum	Xanthomonas campestris

Table 2 Assessment of Demographic Characteristics

Demographic Details		
Gender	Male (n = 18)	Female (n =07)
Age (years)	29.83 ± 3.37	30.71 ± 1.60
P Value	0.517	
Average age (years)	30.08 ± 2.97	

Data is represented as mean ± SD. The data was analyzed using Student T-test for independent means, significant at p-value < 0.05.

Table 3 Assessment of Blood Parameters

Parameter	**Screening**	**Day 60**	**P Value**	**Percentage Change**
Vitamin B12 (pg/mL)	231.16 ± 103.39	443.34 ± 133.74	<0.001*	91.79 %
Vitamin D3 (ng/mL)	25.19 ± 12.39	41.95 ± 9.86	<0.001*	66.57 %
Lipid Profile				
Total Cholesterol (mg/dL)	210.88 ± 29.06	158.74 ± 22.10	<0.001*	24.72 %
Low-Density Lipoprotein (LDL) (mg/dL)	131.81 ± 27.94	81.83 ± 22.16	<0.001*	37.92 %
High-Density Lipoprotein (HDL) (mg/dL)	42.62 ± 12.15	49.68 ± 11.64	<0.001*	16.56 %
Very low-density lipoprotein (VLDL) (mg/dL)	36.45 ± 11.32	27.23 ± 10.37	0.001*	25.28 %
Triglycerides (mg/dL)	182.25 ± 56.62	136.17 ± 51.86	0.001*	25.28 %
NAD+ (umol/L) (by Elisa)	32.84 ± 7.49	39.36 ± 7.58	<0.001*	19.85 %

Data is represented as Mean ± S.D. The data was analyzed using Student T-test for dependent means and Student T-test for independent means, significant at p-value < 0.05.

Table 1 Assessment of GSRS Score

GSRS Score				
Parameter	**Screening**	**Day 15**	**Day 30**	**Day 60**
Abdominal Pain (P value)	3.11 ± 0.39	2.19 ± 0.37 (<0.001*)	1.57 ± 0.28 (<0.001*)	1.31 ± 0.27 (<0.001*)
Percentage Change		29.61 %	49.36	57.94
Reflux syndrome (P value)	3.08 ± 0.61	2.22 ± 0.76 (<0.001*)	1.62 ± 0.70 (<0.001*)	1.30 ± 0.46 (<0.001*)
Percentage Change		27.92 %	47.40 %	57.79 %
Diarrhea syndrome (P value)	3.12 ± 1.39	2.20 ± 1.17 (<0.001*)	1.59 ± 0.74 (<0.001*)	1.09 ± 0.23 (<0.001*)
Percentage Change		29.49 %	49.15 %	64.96 %
Indigestion syndrome (P value)	3.58 ± 0.30	2.59 ± 0.26 (<0.001*)	1.88 ± 0.27 (<0.001*)	1.41 ± 0.26 (<0.001*)
Percentage Change		27.65 %	47.49 %	60.61 %
Constipation syndrome (P value)	4.88 ± 1.19	3.51 ± 0.97 (<0.001*)	2.37 ± 0.68 (<0.001*)	1.47 ± 0.37 (<0.001*)
Percentage Change		28.14 %	51.37 %	69.95 %

Data is represented as Mean ± S.D. The data was analyzed using Wilcoxon Test and Student T-Test for dependent means, significant at p-value < 0.05.

Table 2 Assessment of changes in Fatigue Severity

Fatigue Severity Scale Score				
Parameter	**Screening**	**Day 60**	**P Value**	**Percentage Change**
FSS Score	3.49 ± 0.47	2.78 ± 0.38	<0.001*	20.25 %

Data is represented as Mean ± S.D. The data was analyzed using Student T-test for dependent means, significant at p-value < 0.05.

Figures

Figure 1 CONSORT Diagram for the Study

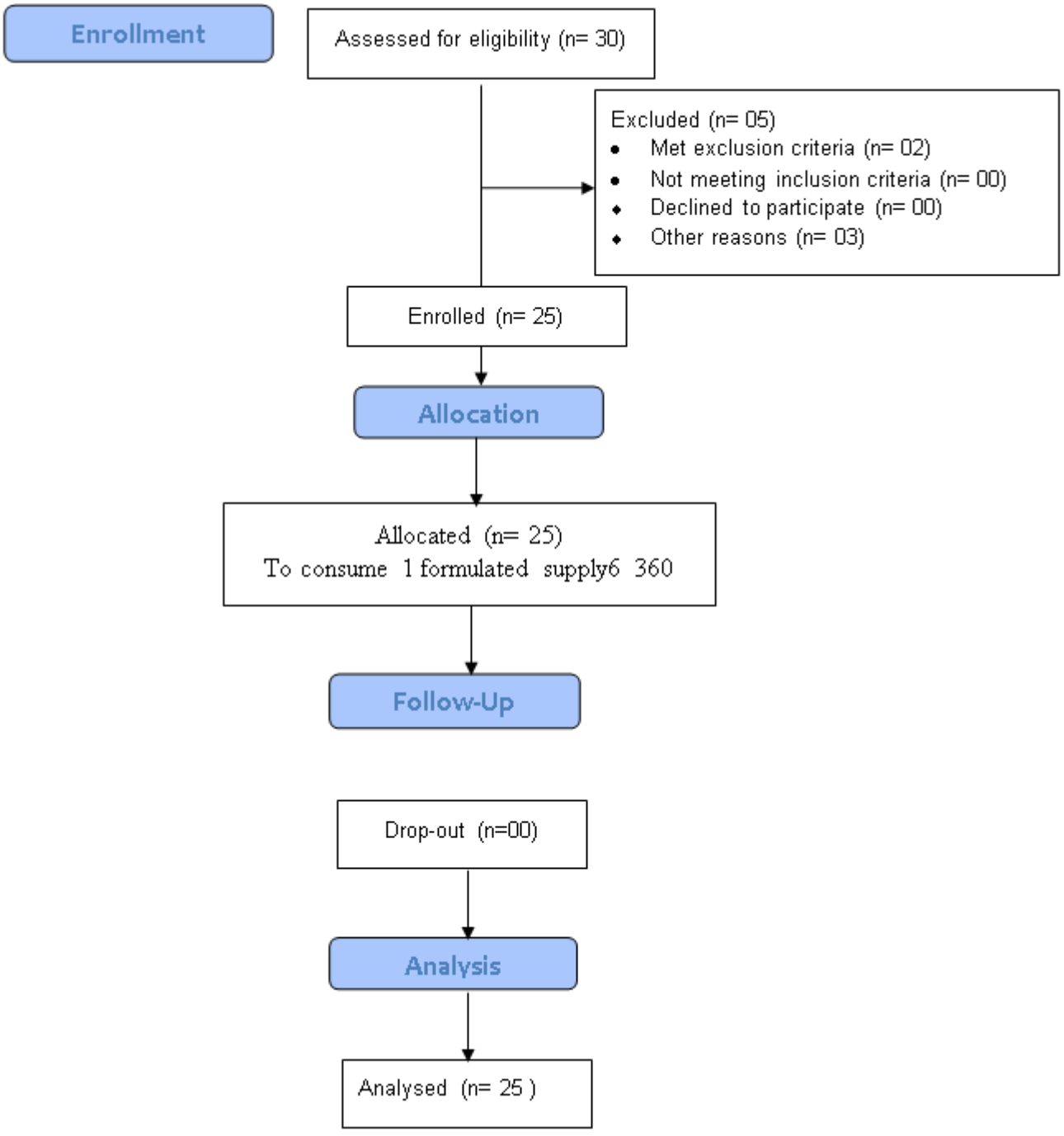

Figure 2 Alpha Diversity of Each Subject at Baseline and Day 60

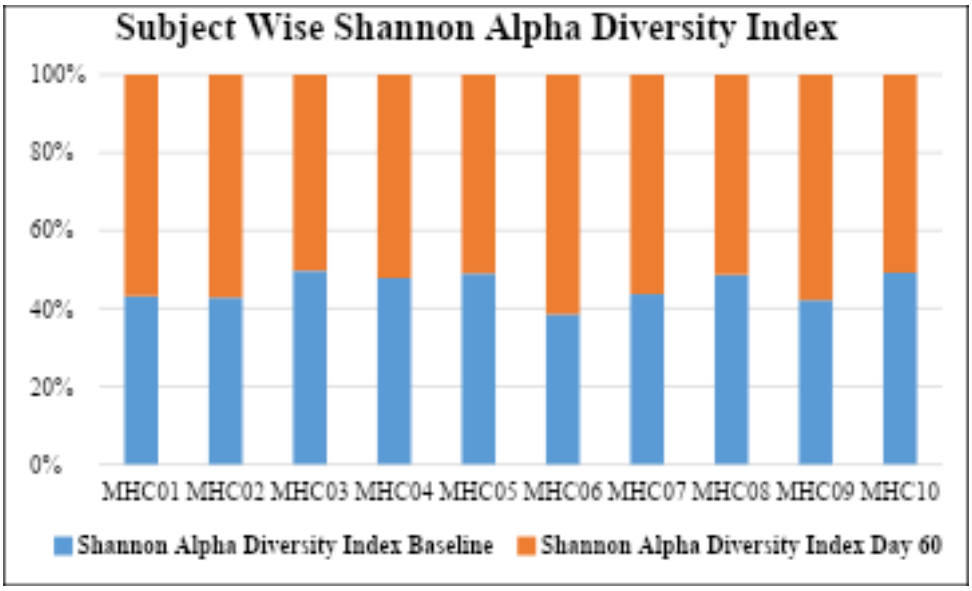

Figure 3 Comparative Alpha Diversity of Each Subject at Baseline and Day 60