

# Glycemic Index of a Diabetes-Specific Nutritional Powder: An Open-Label Study in Healthy Indian Adults

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## Abstract

**Background:** A balanced diet with a low glycemic index (GI) plays an important role in controlling and managing type 2 diabetes mellitus (T2DM). Here, we compared the GI of 2 flavors (vanilla and chocolate) of diabetes-specific nutritional (DSN) supplements to its comparator in healthy Indian adults under fasting conditions. **Methods:** This study was a 39-day open-label, non-comparative, single-center trial involving healthy adults aged between 18 to 45 years. The subjects received equal doses of 2 DSN powder (Treatments A and B), the comparator product (Treatment C), and dextrose monohydrate as a reference (Treatment R). Doses were administered as per the dosing schedule, after an overnight fast for 10 hours, with 2 intervening non-dosing days. Blood samples were collected on the dosing days to assess changes in capillary blood glucose levels. The primary endpoint of the study was the mean GI of Treatments A, B, and C (Defined as low:  $GI \leq 55$ ; medium:  $55 < GI \leq 70$ ; High:  $GI > 70$ ), generated using the incremental area under the curve ( $AUC_i$ ) methodology. Safety was assessed throughout the study. Values of all study parameters were represented in  $\pm$ SD or standard deviation. **Results:** Fourteen adult male subjects with a mean age of  $29.42 \pm 4.46$  years, and a body mass index of  $22.0 \pm 1.95$  Kg/m<sup>2</sup>, were enrolled in the study. The mean  $AUC_i$  for treatments A, B, and C were  $104 \pm 10$ ,  $111 \pm 12$ , and  $87 \pm 12$  mmol min/L, respectively and for Treatment R it was  $276 \pm 16$ ,  $319 \pm 28$  and  $338 \pm 25$  mmol min/L for Days 1, 6 and 8, respectively. The mean GI of Treatment A was  $33 \pm 3$ , Treatment B was  $35 \pm 3$  and Treatment C was  $29 \pm 5$ ; all GI means were  $\leq 55$ . Mild adverse events were reported in 2 (14.3%) subjects. No serious adverse events or deaths were reported in the study. All treatments were well tolerated by the subjects. **Conclusion:** The glycemic index of both

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test products and comparator was low (*i.e.*, GI < 55) as per ISO 26642:2010 standard.

## Keywords

Balanced Diet, Dietary Substitute, Glycemic Index, Healthy Subjects, India

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## 1. Introduction

Over the last few decades, the prevalence of diabetes has seen a marked increase in India, where, type 2 diabetes (T2DM) has been most prevalent with 74.2 million diagnosed cases in 2021 [1]. This upsurge is primarily due to rapid urbanization, a sedentary lifestyle, and unhealthy food habits leading to obesity among younger individuals [2] [3]. Furthermore, with the burden associated with undiagnosed cases (39.4 million), there's a risk of micro- and macro-vascular complications which demands immediate addressal of the situation to prevent a further rise in the disease burden of the country.

Management practices for patients with T2DM include lifestyle modifications that involve following a balanced diet before initiating pharmacotherapy [4]. However, managing T2DM with diet is challenging, as only 5% to 6% of patients are aware of the importance of diet in managing their condition [5]. This challenge is further compounded by the lack of physician training in nutritional interventions, thus, furthering the barrier to effective counselling of such patients [6] [7]. Moreover, patient access to registered dietitians/nutritionists/educators who could effectively guide dietary modifications for managing T2DM remains inadequate [8] [9] [10]. So, adequate dietary information and its importance in managing T2DM needs to be integrated into the diabetes care management guidelines.

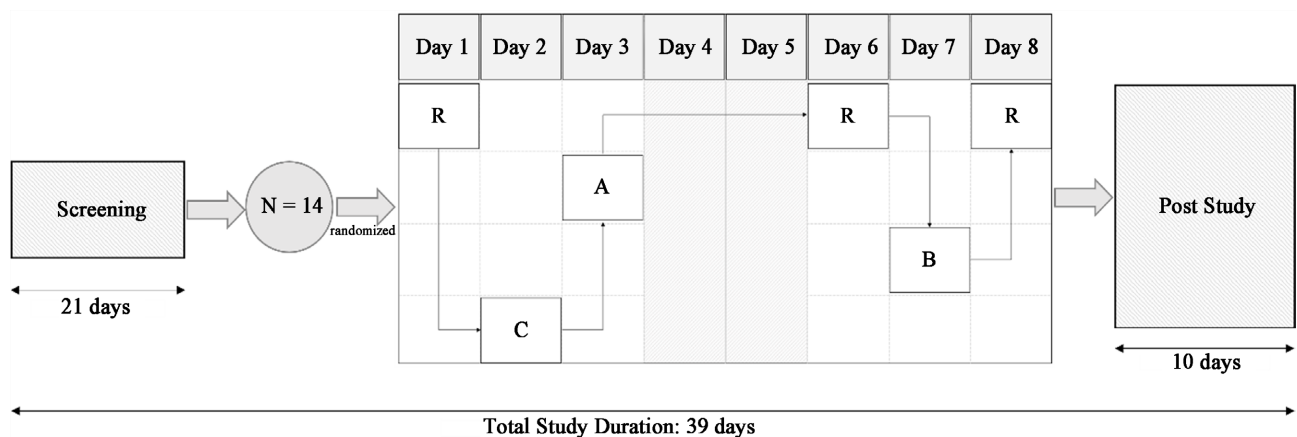
The current dietary guidelines for managing diabetes have evolved over the past few years [11]-[19]. However, in India, such comprehensive guidelines do not exist. It is well established that dietary components have a clinically significant impact on the modulation of blood glucose levels [20]. A diet balanced in carbohydrates, proteins, fats (low), micronutrients, vitamins, and minerals has been demonstrated to reduce excess body weight, thus, in turn, reducing the risk of developing T2DM [4] [16] [21]. The Glycemic index (GI) is used as a measure of carbohydrate quality and is recognized as a valid methodology for classifying carbohydrate foods according to their postprandial glycemic response [22]. Foods or dietary patterns with a low GI, help achieve effective control over blood glucose and reduce body weight. This is so because, such foods break down slowly and are absorbed gradually into the bloodstream, and hence have the potential to effectively control blood glucose levels [23]. A systematic review and meta-analysis of 54 randomized controlled studies in children or adults with impaired glucose tolerance, type 1 or 2 diabetes that demonstrated that low GI diets are beneficial over other diet types by reducing glycated haemoglobin (HbA1c), fasting blood glucose, body mass index (BMI), and blood lipids [24]. Another

study that determined the long-term effects of changing the source and quantity of dietary carbohydrates on postprandial glucose in subjects with impaired glucose tolerance demonstrated that a low GI diet reduced the postprandial plasma glucose levels by 21% [25]. Similarly, a low-GI and low-fibre-rich cereal diet showed a significant difference in the absolute decrease in HbA1c level relative to the fibre-rich cereal diet group ( $-0.5\%$  vs.  $-0.18\%$ ) [26]. On the contrary, diets rich in carbohydrates have been linked to obesity, hyperinsulinemia, and insulin resistance, leading to an increased risk of T2DM [27] [28]. In India, food habits generally focus on refined carbohydrates and fat intake, with less consumption of cereals, fruits, and vegetables [29] [30]. Therefore, to effectively manage patients with T2DM in India, there is not only a need to focus on healthy dietary choices (foods with low GI, optimal consumer awareness and education) [31], but also integrate such guidance into the T2DM management plans. Studies on the effectiveness and impact of DSN on critically ill patients, hospitalized patients and T2DM patients are available in literature [32] [33] [34] [35]. Studies comparing the GI of DSN are rare in healthy subjects. Furthermore, data on the effect of nutrition with a low GI diet profile in an Indian setting remains limited. To our knowledge, there has been no study comparing the GI of DSNs with different flavors, against an active comparator during the study period. Hence, in this study, we determined the GI of our diabetes-specific nutritional (DSN) powders (Prohance D) with two different flavors (chocolate and vanilla) against an active comparator nutritional powder Glucerna SR, in healthy Indian adults in fasting conditions.

## 2. Methods

### 2.1. Study Design

The study was an open-label, single-dose, non-comparative study in healthy adults conducted at a clinical trial facility in India. The overall study duration was 39 days (February-March 2016) (Figure 1).



A, Treatment A (Diabetic Care Powder Chocolate Flavor 108 g); B, Treatment B (Diabetic Care Powder Vanilla Flavor 108 g); C, Treatment C (Glucerna SR Vanilla Flavored Powder 97 g); N, sample size; R, Reference product (Risidex/Dextrose monohydrate 55 g).

**Figure 1.** Study design flow chart.

The study was conducted in accordance with the Declaration of Helsinki and conformed to the local regulatory guidelines, Good Clinical Practice guidelines, and recommendations by the ISO 26642:2010 (E) [36]. Informed consent was obtained from all subjects prior to study entry. The study was reviewed and approved by the Institutional Ethics Committee of the participating site.

## 2.2. Study Population

Healthy adults aged between 18 to 45 years were included in the study if their body weight was at least 50 kg, BMI ranged between 18.5 to 25.0 Kg/m<sup>2</sup> (for males) or 17.0 to 25.0 Kg/m<sup>2</sup> (for females), had no evidence of any underlying disease during screening and whose physical examination was performed within 21 days before study initiation. The subjects should have had acceptable pre-study laboratory parameters, provided consent on their availability during the study and adhered to the protocol requirements of the trial. Females of childbearing potential had to follow an acceptable method of birth control for the study duration as suggested by the investigator.

Subjects were excluded from the study if they had a history of clinically significant disease in the last 12 months, allergy or significant history of hypersensitivity or idiosyncratic reactions or intolerance to any food or excipients. Patients who had positive outcomes in breath alcohol and/or urine drug screening test and had medical conditions that may jeopardize their health or confound the study results were also excluded from the study. A detailed list of additional exclusion criteria is provided in **Supplementary Table S1**.

## 2.3. Study Procedure, Treatment, and Administration

Post-screening, subjects were kept at the study facility for at least 12 hours prior to dosing on Day 1 and until 3 hours after dosing on Day 8. Lunch, snacks, and dinner were provided at 4-, 8-, and 12-hour post-dosing respectively, on all treatment days except on Day 8. On Days 4 and 5, no treatment was administered, and all 3 meals were provided at appropriate intervals. Water intake was prohibited for an hour before dosing until 2 hours post-dose and was allowed *ad libitum* 2 hours post-dose. Only standardized meals were allowed during the confinement period.

The study investigated the effect of 4 different nutritional supplements in healthy subjects under fasting conditions. On each dosing day (from Day 1 to Day 8), all subjects received a randomized treatment after a supervised overnight fast for at least 10 hours. This included 1 serving of the reference dextrose monohydrate (Risidex; Treatment R) with 250 mL of water on Days 1, 6, and 8, the comparator DSN powder (Glucerna SR powder; Treatment C) with 373 mL of water on Day 2; 2 flavors of investigating DSN powder (Prohance D) in chocolate and vanilla flavor (Treatment A and B, respectively) with 378 mL of water each on Day 3 and Day 7 respectively after reconstitution. No treatment was administered on Days 4 and 5 for the subject's convenience. The washout period

between consecutive dosing was at least 24 hours. Subjects were instructed to swallow the entire content of administered dose within 12 minutes. Treatment compliance was assessed through an examination of the oral cavity by a physician.

The 2 investigational DSN powders (Treatments A and B) were developed by Sun Pharmaceutical Industries Limited, Mumbai, India, [37] the comparator DSN powder (Treatment C) was developed by Abbott Healthcare Private Limited, India [38] and the reference food formulation (Treatment R) was developed by Roquette Riddhi Siddhi Private Limited, India. The nutritional information of the test (Treatment A and B) and comparator (Treatment C) products are presented in **Table 1**, and a detailed list of ingredients is presented in **Supplementary Table S2**.

**Table 1.** Nutritional information of Treatments A, B and C.

Nutrient (Units)	Treatments A and B (per 100g) [37]	Treatment C (per 100g) [38]
<b>Energy (kcal)</b>	454	435
<b>Protein (g)</b>	20.2	20.1
<b>Available Carbohydrate (g)*</b>	46.1	51.60
Sugar (g)	0	0
<b>Dietary Fiber (g)</b>	8.1	5.19
FOS (Fructo-oligosaccharides) (g)	3.5	3
<b>Fat (g)</b>	19.2	14.61
Saturated Fatty Acids (g)	2.3	1.17
Monounsaturated Fatty Acids (g)	11.2	12.02
Polyunsaturated Fatty Acids (g)	3.6	1.92
Linoleic acid (g)	3.0	
Alpha Linolenic acid (mg)	465	
Trans Fatty Acids (g)	0	<0.373
<b>Cholesterol (mg)</b>	0	<10
<b>Vitamins</b>		
Vitamin A (µgRE)	270.00 (from Acetate)	255 (from Palmitate)
Vitamin A (from Beta-carotene) (µgRE)	80.00	109
Vitamin D <sub>2</sub> (µg)	4.50	4
Vitamin E (mgTE)	5.60	10
Vitamin K <sub>1</sub> (µg)	24.00	30.6
Vitamin C (mg)	36.00	33.1
Vitamin B <sub>1</sub> (µg)	750.00	582
Vitamin B <sub>2</sub> (µg)	750.00	655
Vitamin B <sub>6</sub> (µg)	800.00	1529

**Continued**

Vitamin B <sub>12</sub> (µg)	1.10	1.48
Niacin (mg)	6.10	5.11
Folic acid (µg)	82.00	127
Pantothenic acid (mg)	3.00	2.91
Biotin (µg)	14.50	13.8
<b>Minerals</b>		
Sodium (mg)	320.00	324
Potassium (mg)	500.00	568
Chloride (mg)	305.00	480
Calcium (mg)	290.00	258
Phosphorus (mg)	200.00	258
Magnesium (mg)	50.00	91
Iron (mg)	4.20	4.73
Zinc (mg)	3.50	2.5
Copper (mg)	0.60	0.764
Manganese (µg)	980.00	1160
Iodine (µg)	50.00	58.2
Selenium (µg)	16.50	16.4
Chromium (µg)	27.00	25.5
Molybdenum (µg)	35.00	35.3
<b>Other Nutrients</b>		
Taurine (mg)	45.00	30.6
Carnitine (mg)	46.00	26.2
Choline (mg)	170.00	152.9
Inositol (mg)	350.00	305.7

\*Available Carbohydrate was calculated as (Total Carbohydrate – Dietary Fiber – FOS); g: grams; kcal: kilo calories; µg: microgram; mg: milligram; µgRE: microgram retinol equivalent; mgTE: milligram equivalent of d-tocopherol.

## 2.4. Blood Sampling

A total of ~24 mL of blood was collected from each subject. Of this, 10 mL was collected during screening to perform the routine haematology, biochemistry, and serological assays; 4 mL for pre-study laboratory investigations, ~4.8 mL (including ~2.4 mL discarded blood) for capillary blood glucose evaluation and 5 mL for post-study evaluation. On each dosing day, 8 blood samples were collected including the pre-dose blood samples using the finger prick method. An approximate volume of 0.05 mL blood was collected 5 minutes and 0 minutes before dosing followed by 15-, 30-, 45-, 60-, 90- and 120-minute post-dose.

## 2.5. Endpoints

The primary endpoint was the mean GI of Treatments A, B, and C in healthy adult subjects under fasting conditions for up to 120 minutes post-dosing. The secondary endpoint was the assessment of safety for all administered treatments in terms of reported adverse events (AEs) and serious adverse events (SAEs).

## 2.6. Assessments

Capillary blood glucose concentration was expressed as mmol/L using conversion factor 1 mg/dL = 0.0555 mmol/L. The mean GI of each treatment ( $I_{G,t}$ ) was generated using the incremental area under the curve (AUC<sub>i</sub>) method and was considered low if  $I_{G,t}$  was  $\leq 55$ , medium if  $I_{G,t}$  ranged between 56 to 70, and high if  $I_{G,t}$  was  $>70$ .

Safety was assessed by the investigator throughout the study. AEs were classified as mild, (defined as a transient event that did not interfere with daily activities); moderate (defined as an event that alleviated with simple therapeutic intervention, and which interfered with normal activities); or severe (defined as an event that required therapeutic intervention, and which interrupted daily activities). The relationship of AEs to the treatments was classified based on the causality assessment.

## 2.7. Statistical Analysis

A sample size of 14 healthy adults were deemed appropriate to achieve the study's primary objective as it met the standards of the ISO 26642:2010 food products recommendation to determine GI [36]. The analysis included capillary blood glucose data from subjects who received all the 3 doses of Treatment R and at least 1 dose of the study treatment.

All individual blood glucose concentration data along with the descriptive statistics (such as N, mean, standard error [SE], standard deviation [SD], minimum, and maximum) was presented for each subject. The AUC<sub>i</sub> of the blood glucose response curve was plotted as the blood glucose values vs. time for all subjects. Clinical and vital parameters were summarized and reported descriptively.

In each subject, the  $I_{G,t}$  (%) of treatments A, B and C were calculated by dividing the AUC<sub>i</sub> of the respective treatment by the average AUC<sub>i</sub> of Treatment R and multiplying by 100.

The GI of the treatment was calculated using the formulae:

$$I_{G,t} = \frac{A_t}{A_{ref}} \times 100$$

where:

$A_t$  was the AUC<sub>i</sub> of the Treatments A, B, C.

$A_{ref}$  was the mean AUC<sub>i</sub> of Treatment R of 3 days when Treatment R was administered.

The final GI of each treatment was expressed as

$$\text{where: } \bar{I}_G \pm s_{\bar{I}_G}$$

$\bar{I}_G$  was the mean GI value of subjects who completed the study.

$s_{\bar{I}_G}$  was the standard error of the mean.

All assessments were performed on the per-protocol (PP) population which included all enrolled subjects who completed the study as per the protocol without any major protocol deviations or violations. Safety was assessed throughout the study period and the safety population included all enrolled subjects who received the test treatments.

All analyses were performed using statistical analysis software version 9.2 or higher.

### 3. Results

#### 3.1. Demographics

A total of 14 healthy adult males were screened and enrolled in the study. The mean  $\pm$  SD age of the subjects was  $29.42 \pm 4.46$  years (range: 23 to 37 years), mean  $\pm$  SD body weight was  $61.06 \pm 6.45$  kg (range: 51.94 to 69.77 kg), and mean  $\pm$  SD BMI was  $22.0 \pm 1.95$  kg/m<sup>2</sup> (range: 18.8 to 24.9 kg/m<sup>2</sup>). The baseline and demographic characteristics of all subjects were comparable. The demographic data is provided in **Supplementary Table S3**. The clinical and laboratory parameters were normal and were comparable among all subjects (**Supplementary Tables S4-S6**). No subject discontinued the study.

#### 3.2. Capillary Blood Glucose Concentrations and Glycemic Index

The peak mean capillary blood glucose concentration for Treatment A and B reached a value of 6.1010 mmol/L and 6.4498 mmol/L, respectively, at 45 minutes post-dose, while for Treatment C, it peaked at a value of 5.9214 mmol/L at 60 minutes post-dose. Alternatively, for Treatment R, it was 8.4994 mmol/L on Day 1, 9.1932 mmol/L on Day 6 and 9.8354 mmol/L on Day 8, 45 minutes post-dosing, respectively. The detailed results are provided in **Supplementary Tables S7-S12**.

The mean  $\pm$  SE GI of Treatment A was  $33 \pm 3$ , Treatment B was  $35 \pm 3$  and Treatment C was  $29 \pm 5$  respectively, **Supplementary Table S13**. All GI means were  $\leq 55$  and were considered low as per the ISO reference standard. The mean AUC<sub>i</sub> for all treatments and the reference is shown in **Table 2**.

**Table 2.** Incremental AUC (mmol min/L).

Subject No.	AUC (mmol min/L)					
	Day 1 Treatment (R)	Day 2 Treatment (C)	Day 3 Treatment (A)	Day 6 Treatment (R)	Day 7 Treatment (B)	Day 8 Treatment (R)
1	177	71	55	321	118	364
2	283	74	96	415	84	348
3	197	76	76	328	141	330
4	316	71	116	564	136	490

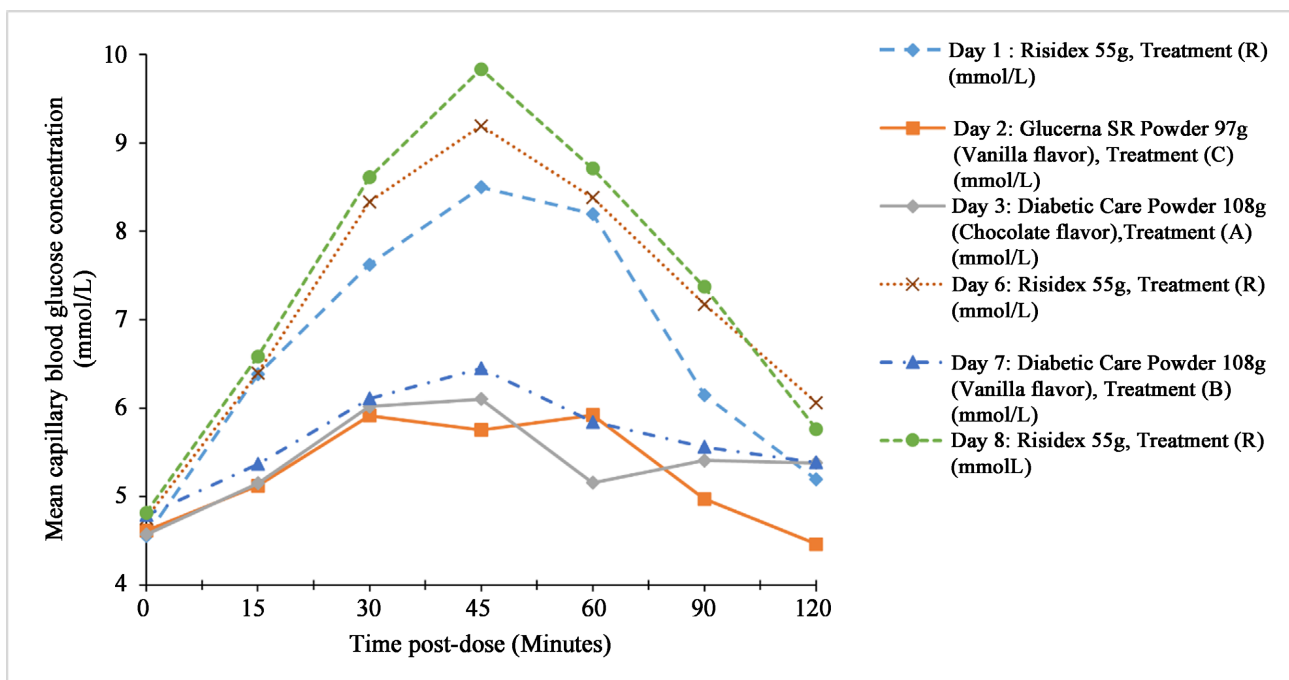


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5	248	*	133	275	75	244
6	264	71	150	385	156	416
7	257	38	98	303	178	440
8	237	51	66	236	33	234
9	275	205	128	296	110	342
10	337	64	83	311	102	180
11	203	152	78	183	71	351
12	367	94	171	427	175	450
13	329	98	154	280	108	339
14	369	60	52	144	62	205
<b>Mean (±SE)</b>						
-	<b>276 (±16)</b>	<b>87 (±12)</b>	<b>104 (±10)</b>	<b>319 (±28)</b>	<b>111 (±12)</b>	<b>338 (±25)</b>

\*Sample was not collected as the subject experienced vomiting after receiving Treatment C. AUC: Area under the curve; SE: Standard Error; Treatment A: Diabetic Care Powder 108 g (Chocolate flavor); Treatment B: Diabetic Care Powder 108 g (Vanilla flavor); Treatment C: Glucerna SR Powder 97 g (Vanilla flavor); Treatment R: Risidex (Dextrosemonohydrate) 55 g.

The mean AUC was lower for Treatments A, B, and C than Treatment R indicating less glycemc incursion in low GI products (Figure 2).



A, Treatment A (Diabetic Care Powder Chocolate Flavor 108 g); B, Treatment B (Diabetic Care Powder Vanilla Flavor 108 g); C, Treatment C (Glucerna SR Vanilla Flavored Powder 97 g); Treatment R, reference product (Risidex/Dextrose monohydrate 55 g).

Figure 2. Mean blood glucose concentration vs. time curve.

### 3.3. Safety

AEs were reported in 2 (14.3%) subjects. On Day 2, 1 subject vomited 20 minutes post-dose (Treatment C) and the event resolved in 48 minutes. High alanine aminotransferase and aspartate aminotransferase values were reported in the other subject beyond the follow-up period on Day 8 (Treatment R). The event was followed up and resolved within 9 days post the last dose. Both AEs were mild in intensity and considered unlikely by the investigator to be related to the treatments. No SAEs and deaths were reported in the study.

## 4. Discussion

Our study demonstrated that the DSN powders, when administered as a breakfast meal under fasting conditions in healthy Indian adults, had low GI. The  $AUC_i$  of all 3 treatments was low with respect to the reference product, indicating appropriate glucose tolerance. The treatments did not alter the clinical parameters or laboratory profiles of the subjects and were well tolerated with only 2 reports of mild AEs that resolved without intervention. Hence, these findings suggest that the diabetes-specific nutritional powder could be used as a nutritional meal option in pre-diabetics and T2DM patients requiring management of blood glucose and body weight.

Globally, GI has been established as a measure of carbohydrate quality [22] and is classified as low ( $\leq 55$ ), intermediate ( $>55$  and  $<70$ ) or high ( $\geq 70$ ) as per the Food and Agriculture Organization and World Health Organization, 1998 [39]. With established evidence of the benefits associated with low GI diets in T2DM patients, considering the GI of food is an important parameter of dietary advice in such patients. Low GI diets have been implicated in the management of HbA1c levels, decrease in lipids and weight loss in obese individuals [40]. Additionally, a low GI diet has also been shown to improve postprandial glucose concentration and insulin in diabetic patients [41] [42]. The International Carbohydrate Quality Consortium (ICQC) recommends a low GI diet in the context of a healthy diet plan [43]. In India, dietary advice from the Indian Council of Medical Research (ICMR) for the management of T2DM recommends diets consisting of carbohydrates (55% - 60%) including cereals, mixed coarse grains, whole pulses, salads and soybeans; proteins (10% - 15%) and fats (20% - 25%) comprising  $< 7\%$  of saturated fats, monounsaturated and polyunsaturated fatty acids (considered as healthy fats) [44]. The Indian Consensus Group for Prevention of Diabetes specifies a carbohydrate diet which provides 65% of daily energy. It includes 400 g of fruits, vegetables, and legumes, and 400 g of cereals, in conjunction with 25 g of soya bean or mustard or canola oils with moderate physical activity for the effective prevention of T2DM and the associated cardiovascular complications [45]. Although guidelines for dietary standards and management of T2DM exist, patient load, inaccessibility to registered dietitians/educators, and lack of robust education and awareness serve as barriers to the implementation of these strategies [46]. As a result, there is a need to address

the existing challenges for uniform understanding and implementation of dietary guidelines for the management of T2DM.

In India, regional dietary variations, and the lack of awareness of the impact of diet on the management of T2DM, combined with a reluctance to adhere to dietary regimens due to sociocultural preferences, remain common [4]. As part of organized primary care facilities in India focusing on the quality of diabetes care, physicians and registered dietitians can counsel and sensitize patients with dietary measures for the prevention and management of T2DM by utilizing a shared decision-making approach [8]. Clinical evidence suggests that sustained counselling on diet management to patients has an impact on HbA1c, triglycerides, and body weight [47]. Medical nutrition therapy is a promising approach that provides evidence-based knowledge to assist clinicians and registered dietitians in customizing appropriate meal plans for diabetics [48]. Likewise, the effectiveness of low GI diets in improving glycemic control or HbA1c is well documented [49] [50] [51] [52]. Thus, as part of balanced meal planning for effective blood glucose control, the DSN powder used in our study with a low GI (<55), which consists of a balanced mix of maltodextrin, isomaltulose, whey protein, soy protein, minerals, and vitamins, could be of potential benefit in Indian patients with T2DM.

In view of increasing prevalence of T2DM world-wide, dietary intake plays crucial role in glucose control. From an intervention study, it was found that taking a low GI multi-nutrient supplement as replacement of breakfast by T2DM patients reduced glycated serum protein, HbA1c, increased their total plasma proteins, and helped maintain their fasting blood glucose (FBG), homeostatic model assessment for insulin resistance (HOMA-IR), blood pressure and body weight [53]. In a meta-analysis low GI/glycemic load (GL) dietary patterns result in improvement of glycemic control and cardiometabolic risk factors beyond concurrent treatment in adults with Type 1 and 2 diabetes [54]. Thus, it seems that there are measurable health advantages associated with a low GI supplement in individuals with diabetes.

Our study design was aligned with the ISO 26642:2010 food products recommendation to determine GI in at least 10 subjects [36]. The main objective of the study was to determine the GI of diabetes-specific nutritional powder as per ISO 26642:2010E recommendations and thus, further studies are required to understand the effect and impact of this nutritional supplement in managing T2DM.

Our study had some limitations: the sample size of the study was small and limited to male subjects. Furthermore, the long-term effects of the low GI DSN on HbA1c should be assessed in future studies. Hence, the study rationale should be kept in mind while trying to interpret or generalize the study findings to a broader patient population in a real-life scenario.

## 5. Conclusion

A low GI and a low AUC<sub>i</sub> were observed for all the products administered in this

study compared to the reference. The investigational DSN powders with their low GI could potentially function as diet replacements or supplements to achieve optimal blood glucose levels and body weight control in patients with T2DM who are unable to achieve optimal levels under a normal diet. Future long-term studies in India are needed to add to the growing evidence of the importance of low GI diets in maintaining blood glucose and managing body weight.

### Data availability

Any additional declassified datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request and satisfactory justification.

### Author Information

Kirti Patel is a full-time employee of Sun Pharmaceutical Industries Limited and Suyog Mehta, Deepak Bachani and Vinay Kudrigikar are full-time employees of Sun Pharma Laboratories Ltd.

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### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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## Online Supplementary Material

**Table S1.** Exclusion criteria.

Exclusion Criteria
<ul style="list-style-type: none"> <li>• Subject with a history of clinically significant cardiovascular, pulmonary, hepatic, renal, hematological, gastrointestinal, endocrinal, immunologic, dermatologic, musculoskeletal, neurological, or psychiatric disease in the last 12 months</li> <li>• Allergy or significant history of hypersensitivity or idiosyncratic reactions or intolerance to any food or excipients</li> <li>• Subjects who showed positive result in breath alcohol and/or urine drug screening test</li> <li>• Subjects determined by the study physician to have any medical condition that could jeopardize their health or prejudice the results (e.g., history of surgery of the gastrointestinal tract, which may interfere with digestion and absorption of nutrients, except for appendectomy)</li> <li>• History of gastroenteritis in previous six months</li> <li>• Subjects taking an unusual or special diet (for e.g., high protein diet, low sodium diet, any form of dieting, etc.)</li> <li>• A known history of diabetes mellitus or the use of antihyperglycemic drugs or insulin to treat diabetes and related conditions</li> <li>• First and/or second order family history of diabetes</li> <li>• A major medical or surgical event requiring hospitalization within the preceding three months</li> <li>• The use of steroids, protease inhibitors or antipsychotics (all of which have major effects on glucose metabolism and body fat distribution)</li> <li>• Subjects with a history of alcohol, drug or substance abuse in the past 12 months</li> <li>• Subjects who had used drugs known to affect glucose tolerance</li> <li>• Subjects who had used enzyme-modifying drugs (like phenytoin, carbamazepine, barbiturates, griseofulvin etc.) within 30 days of Day 1 dosing</li> <li>• Subjects deemed uncooperative or noncompliant</li> <li>• Subjects who smoked (<math>\geq 10</math> cigarettes/day or equivalent) or consumed tobacco products (<math>\geq 4</math> chews of any form/day)</li> <li>• Female subjects who are pregnant, lactating or likely to become pregnant or had a positive pregnancy test at screening or during check-in</li> <li>• Subjects who had participated in another clinical study for at least 90 days prior to first dosing.</li> <li>• Subjects who had: <ul style="list-style-type: none"> <li>○ Systolic blood pressure <math>&lt; 90</math> mmHg or <math>&gt; 140</math> mmHg Diastolic blood pressure <math>&lt; 60</math> mmHg or <math>&gt; 90</math> mmHg</li> <li>○ Minor deviations (2 - 4 mmHg) at check-in were acceptable at the discretion of the investigator</li> <li>○ Radial pulse rate <math>&lt; 60</math>/min or <math>&gt; 100</math>/min</li> </ul> </li> </ul>

**Table S2.** Summary of product ingredients (Treatments A, B, C and R).

Treatment	Ingredient
<b>A and B</b>	Maltodextrin, vegetable oil (Sunflower high oleic oil, rapeseed low erucic oil, sunflower oil), calcium caseinate, whey protein isolate, soya protein isolate, isomaltulose, fructose, acacia gum, fructooligosaccharides (FOS), inulin, soya lecithin, tribasic sodium citrate, dibasic potassium phosphate, potassium chloride, calcium carbonate, inositol, tribasic potassium citrate, choline bitartrate, sodium chloride, premix of vitamins and minerals, magnesium oxide, L-carnitine, L-ascorbic acid and flavor.
<b>C</b>	Maltodextrin, calcium caseinate, vegetable oils (high oleic sunflower oil, soy oil), fructose, FOS, minerals, soy polysaccharide, flavor, m-inositol, vitamins, taurine, l-carnitine, mixed tocopherols (antioxidants)
<b>R</b>	Dextrose monohydrate as 99.92% dry glucose.

A, Diabetic Care Powder 108 g (Chocolate flavor); B, Diabetic Care Powder 108 g (Vanilla flavor); C, Glucerna SR Powder 97 g (Vanilla flavor); R: Risidex powder.

**Table S3.** Demographic characteristic.

Category	Age (Years)	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )
Mean	29.42	166.64	61.06	22
SD (±)	4.46	4.28	6.45	1.95
Range (Minimum)	23	160	51.94	18.8
Range (Maximum)	37	177	69.77	24.9
CV%	15.17	2.574	10.57	8.88

N: Total number of subject enrolled; all enrolled subjects were male; SD: Standard deviation; CV%: Coefficient of variation.

**Table S4.** Summary of vital signs by day and time points.

Day	Time Point	Parameter	Mean ± SD	Range (Min-Max)
Day-1	Pre-dose (-2.00 to 0.00)	Systolic BP	111.43 ± 3.368	106 - 118
		Diastolic BP	70.57 ± 3.877	66 - 80
		Temperature	97.57 ± 0.233	97.2 - 97.8
		Radial pulse	71.00 ± 1.617	68 - 73
Day-1	1.0 hrs	Systolic BP	113.86 ± 4.185	108 - 124
		Diastolic BP	71.57 ± 2.954	68 - 80
		Temperature	97.31 ± 0.244	97 - 97.8
		Radial pulse	71.86 ± 2.413	67 - 76
Day-1	2.0 hrs	Systolic BP	113.43 ± 2.980	110 - 120
		Diastolic BP	71.71 ± 1.541	70 - 76
		Radial pulse	71.21 ± 2.225	66 - 76
Day-2	Pre-dose (-2.00 to 0.00)	Systolic BP	113.14 ± 4.130	106 - 120
		Diastolic BP	72.29 ± 2.585	68 - 76
		Temperature	97.47 ± 0.389	97 - 98.2
		Radial pulse	70.93 ± 1.492	68 - 73
Day-2	1.0 hrs	Systolic BP	112.14 ± 2.983	108 - 118
		Diastolic BP	71.43 ± 2.766	68 - 78
		Temperature	97.77 ± 0.436	97 - 98.4
		Radial pulse	70.29 ± 1.383	68 - 72
Day-2	2.0 hrs	Systolic BP	112.29 ± 3.750	108 - 120
		Diastolic BP	71.71 ± 2.920	68 - 80
		Radial pulse	72.00 ± 1.881	70 - 76
Day-3	Pre-dose (-2.00 to 0.00)	Systolic BP	111.86 ± 1.834	110 - 116
		Diastolic BP	74.07 ± 2.495	70 - 78
		Temperature	97.39 ± 0.166	97.2 - 97.6
		Radial pulse	74.21 ± 2.293	70 - 78

**Continued**

Day-3	1.0 hrs	Systolic BP	114.00 ± 3.328	110 - 118
		Diastolic BP	74.00 ± 1.569	70 - 76
		Temperature	97.37 ± 0.281	97 - 97.8
		Radial pulse	72.57 ± 2.027	70 - 76
Day-3	2.0 hrs	Systolic BP	114.71 ± 2.164	112 - 118
		Diastolic BP	73.86 ± 1.657	70 - 76
		Radial pulse	72.36 ± 0.929	70 - 73
Day-4	At 9:00:00 AM	Systolic BP	113.57 ± 2.102	110 - 116
		Diastolic BP	73.86 ± 2.538	70 - 78
		Temperature	97.40 ± 0.157	97.2 - 97.6
		Radial pulse	75.21 ± 2.293	72 - 78
Day-5	At 9:00:00 AM	Systolic BP	114.71 ± 3.474	110 - 120
		Diastolic BP	73.43 ± 1.828	70 - 76
		Temperature	97.50 ± 0.340	97 - 98
		Radial pulse	73.29 ± 1.773	70 - 76
Day-6	Pre-dose (-2.00 to 0.00)	Systolic BP	114.29 ± 4.890	106 - 122
		Diastolic BP	72.57 ± 3.081	68 - 78
		Temperature	97.61 ± 0.396	97 - 98.2
		Radial pulse	71.29 ± 2.301	67 - 75
Day-6	1.0 hrs	Systolic BP	114.43 ± 4.380	106 - 122
		Diastolic BP	73.29 ± 2.164	70 - 76
		Temperature	97.66 ± 0.403	97 - 98.2
		Radial pulse	71.50 ± 1.990	69 - 76
Day-6	2.0 hrs	Systolic BP	114.57 ± 4.033	110 - 122
		Diastolic BP	73.00 ± 1.710	70 - 76
		Radial pulse	72.21 ± 1.805	70 - 75
Day-7	Pre-dose (-2.00 to 0.00)	Systolic BP	115.00 ± 4.946	106 - 124
		Diastolic BP	73.14 ± 3.207	68 - 78
		Temperature	97.73 ± 0.338	97 - 98.2
		Radial pulse	72.29 ± 2.758	68 - 77
Day-7	1.0 hrs	Systolic BP	114.57 ± 3.458	110 - 122
		Diastolic BP	72.43 ± 1.785	70 - 76
		Temperature	97.50 ± 0.291	97.2 - 98
		Radial pulse	71.86 ± 1.460	70 - 74
Day-7	2.0 hrs	Systolic BP	113.86 ± 3.718	110 - 120

**Continued**

		Diastolic BP	72.43 ± 2.102	70 - 76
		Radial pulse	71.50 ± 1.605	69 - 74
Day-8	Pre-dose (-2.00 to 0.00)	Systolic BP	111.50 ± 3.391	105 - 118
		Diastolic BP	71.21 ± 3.142	65 - 78
		Temperature	97.81 ± 0.372	97 - 98.4
		Radial pulse	71.79 ± 1.477	70 - 76
Day-8	1.0 hrs	Systolic BP	113.86 ± 2.878	108 - 118
		Diastolic BP	72.00 ± 1.569	70 - 74
		Temperature	97.66 ± 0.298	97.2 - 98.2
		Radial pulse	72.43 ± 1.910	70 - 76
Day-8	2.0 hrs	Systolic BP	115.00 ± 2.572	110 - 120
		Diastolic BP	71.71 ± 1.326	70 - 74
		Radial pulse	72.21 ± 1.578	70 - 74

BP, blood pressure; SD, standard deviation.

**Table S5.** Summary of vital parameters

Clinical Exam Period	Test	Mean ± SD
Check-in	Temperature	97.5 ± 0.23
	Systolic BP	115.4 ± 3.96
	Diastolic BP	74 ± 3.59
	Radial pulse	70.6 ± 1.83
Check-out	Temperature	97.7 ± 0.33
	Systolic BP	113.1 ± 3.11
	Diastolic BP	71 ± 1.3
	Radial pulse	71.9 ± 1.61

BP, blood pressure; SD, standard deviation.

**Table S6.** Summary of tests

General				
Clinical Exam Period	Test	Results	N	n (%)
Check-in	Well/Unwell	Well	14	14 (100)
		Unwell	14	0
Check-out		Well	14	14 (100)
		Unwell	14	0
<b>Respiratory system functioning</b>				
Check-in	AEBE	Clear	14	14 (100)
Check-out		Clear	14	14 (100)

**Continued****Cardiovascular test**

Check-in	1 <sup>st</sup> heart sound	Normal	14	14 (100)
Check-out		Normal	14	13 (93)
		Not reported	14	1 (7)
Check-in	2 <sup>nd</sup> heart sound	Normal	14	14 (100)
Check-out		Normal	14	13 (93)
		Not reported	14	1 (7)
Check-in	Murmur	No	14	14 (100)
Check-out		No	14	14 (100)

**Alimentary system**

Check-in	Per abdomen	Soft	14	14 (100)
Check-out		Soft	14	14 (100)
Check-in	Liver and Spleen	Non palpable	14	14 (100)
Check-out		Non palpable	14	14 (100)
Check-in	Bowel Sounds	Normal	14	14 (100)
Check-out		Normal	14	14 (100)

**Central nervous system**

Check-in	Consciousness	Yes	14	14 (100)
Check-out		Yes	14	14 (100)
Check-in	Well Oriented	Yes	14	14 (100)
Check-out		Yes	14	14 (100)
Check-in	Motor Deficit	No	14	14 (100)
Check-out		No	14	14 (100)
Check-in	PL—Both Limbs	Yes	14	14 (100)
Check-out		Yes	14	14 (100)

**Infection inflammation and safety**

Check-in	Infection and	No	14	14 (100)
Check-out	Inflammation at local site	No	14	13 (93)
		Not reported	14	1 (7)
Check-in	Fit/Unfit	Fit	14	14 (100)
Check-out		Fit	14	13 (93)
		Not reported	14	1 (7)
Check-in	Qualify for enrolment?	Yes	14	14 (100)
Check-out	Safety assessment	Significant	14	1 (7)
		Insignificant	14	13 (93)

AEBE: Air entry bilaterally equal; N: Total number of subjects in each category; n (%): number (percentage) of subjects in each category; PL: Plantar flexor.

**Table S7.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 1) Risidex (Dextrose monohydrate) 55 g, Treatment R (N = 14).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.57479	4.53118	4.55301	6.38250	7.62332	8.49943	8.19814	6.14861	5.19321
SD (±)	0.468772	0.395216	0.399246	1.203802	1.071907	1.247845	1.359716	1.051277	1.187495
Range (Min)	3.6075	3.7740	3.8018	4.2735	5.5500	6.1050	5.4945	3.2745	3.4410
Range (Max)	5.2725	5.0505	5.0783	8.9910	9.1575	10.4895	10.3785	7.9920	7.3815
CV%	10.2	8.7	8.8	18.9	14.1	14.7	16.6	17.1	22.9

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Min: minimum; Max: maximum; CV%: Coefficient of variation.

**Table S8.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 2) Glucerna SR Powder 97 g (Vanilla flavor), Treatment C (N = 13).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.55954	4.67054	4.61507	5.12308	5.91715	5.75492	5.92142	4.97365	4.46135
SD (±)	0.347223	0.321107	0.294860	0.597918	0.688192	0.989807	0.866755	0.670049	0.506916
Range (Min)	3.7740	4.1070	3.9683	4.2180	4.8285	4.8285	4.8285	3.9405	3.8295
Range (Max)	5.1615	5.2725	4.9673	6.1605	6.8265	8.3250	7.4925	6.4380	5.4390
CV%	7.6	6.9	6.4	11.7	11.6	17.2	14.6	13.5	11.4

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Min: minimum; Max: maximum; CV%: Coefficient of variation.

**Table S9.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 3) Diabetic Care Powder 108 g (Chocolate flavor), Treatment A (N = 14).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.45982	4.68579	4.57283	5.14961	6.01779	6.10104	5.15754	5.40729	5.37954
SD (±)	0.358101	0.343310	0.301877	0.590647	0.712317	1.224771	0.447436	0.532655	0.724111
Range (Max)	3.9960	4.0515	4.1348	4.1625	4.6065	4.6065	4.1070	4.6620	4.4955
Range (Min)	5.4390	5.4390	5.1893	5.9940	7.2150	8.5470	5.6610	6.7155	7.5480
CV%	8.0	7.3	6.6	11.5	11.8	20.1	8.7	9.9	13.5

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Max: maximum; Min: minimum; CV%: Coefficient of variation.

**Table S10.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 6) Risidex (Dextrose monohydrate) 55 g, Treatment R (N = 14).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.72939	4.78093	4.75519	6.39836	8.33293	9.19318	8.38050	7.17536	6.06139
SD (±)	0.426681	0.525103	0.419952	0.866508	1.451490	1.788047	1.485557	1.639391	1.175959
Range (Min)	3.9405	3.8850	3.9128	5.0505	6.5490	6.6600	5.9385	5.3280	3.9960
Range (Max)	5.2725	5.9385	5.4668	7.7145	10.4340	12.6540	10.5450	11.3775	8.1585
CV%	9.0	11.0	8.8	13.5	17.4	19.4	17.7	22.8	19.4

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Min: minimum; Max: maximum; CV%: Coefficient of variation.

**Table S11.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 7) Diabetic Care Powder 108 g (Vanilla flavor), Treatment B (N = 14).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.74921	4.82850	4.78888	5.36764	6.10896	6.44989	5.84336	5.56189	5.38746
SD (±)	0.465729	0.408421	0.412855	0.435067	0.760499	0.918477	0.844630	0.693256	0.901627
Range (Min)	4.2180	4.1625	4.2180	4.6620	4.9395	4.9395	4.7175	4.4955	3.9960
Range (Max)	5.7720	5.5500	5.5500	5.9940	8.1030	8.1585	7.3260	7.2150	7.1040
CV%	9.8	8.5	8.6	8.1	12.4	14.2	14.5	12.5	16.7

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Min: minimum; Max: maximum; CV%: Coefficient of variation.

**Table S12.** Summary statistics—capillary blood glucose concentration (mmol/L); (Day 8) Risidex (Dextrose monohydrate) 55 g, Treatment R (N = 14).

Category	Time (minutes)								
	-0.083	0.000	0.000*	15.000	30.000	45.000	60.000	90.000	120.000
Mean	4.78489	4.85229	4.81861	6.58468	8.61043	9.83539	8.70954	7.37357	5.76407
SD (±)	0.419399	0.549730	0.425273	0.951778	1.224267	1.577032	1.555138	1.230637	1.226587
Range (Min)	4.1070	4.1070	4.1070	5.2170	7.1040	7.0485	6.4935	5.5500	3.4410
Range (Max)	5.6610	6.3270	5.5500	8.7135	11.4330	12.9870	11.5440	9.4350	7.3260
CV%	8.8	11.3	8.8	14.5	14.2	16.0	17.9	16.7	21.3

N: total number of subjects included in the analysis; \*Average value of two pre-dose concentrations at -0.083 hr & 0.000 hr; SD: standard deviation; Min: minimum; Max: maximum; CV%: Coefficient of variation.



**Table S13.** Determination of GI as percentage ratio.

Subject No.	Ratio A/R	Ratio B/R	Ratio C/R
1	19	41	25
2	28	24	21
3	27	49	27
4	25	30	16
5	52	29	*
6	42	44	20
7	29	53	11
8	28	14	22
9	42	36	67
10	30	37	23
11	32	29	62
12	41	42	23
13	49	34	31
14	22	26	25
	Mean ( $\pm$ SE)		
-	33 $\pm$ 3	35 $\pm$ 3	29 $\pm$ 5

\*Sample was not collected as subject experienced vomiting after receiving Treatment C. Ratio (%): Dividing the  $AUC_i$  of either Treatments A, B or C by the average  $AUC_i$  of Treatment R and multiplying by 100. Note: Average value of three administration of reference treatment (R) is used for ratio calculation. A: Diabetic Care Powder 108 g (Chocolate flavor) B: Diabetic Care Powder 108 g (Vanilla flavor) C: Glucerna SR Powder 97 g (Vanilla flavor); AUC: Area under curve; SE: Standard error.