STUDY OF THE GLYCEMIC INDEX OF THE MEDICAL FOOD NEO-MUNE

Supawan Buranapin

Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Thailand

Abstract

Objective: The study aimed to examine the glycemic index of the medical food Neo-Mune.

Methods: Ten healthy volunteers with normal pancreatic function were enrolled in this pilot study. All eligible subjects were asked to return to the research center a week later to consume 50 grams of glucose solution and their plasma glucose levels were measured at 0 (baseline), 30, 60, 90 and 120 minutes after glucose consumption. A week after that, the same cohort consumed 94.97 g Neo-Mune (advised carbohydrate provision of 50 grams) and again, their plasma glucose levels were recorded at 0, 30, 60, 90 and 120 minutes after consumption. The glycemic index (GI) was calculated from the area under the glucose response curve of Neo-Mune divided by the area under the glucose response curve of the glucose solution, multiplied by 100.

Results: The plasma glucose levels reached their highest levels at 30 minutes post-consumption and decreased gradually in both cases. However, the plasma glucose levels were lower at 30 and 60 minutes after Neo-Mune consumption compared with those after glucose solution consumption. The GI of Neo-Mune was identified as 42.12, which is classifies it as a low-GI food.

Conclusion: Neo-Mune, a low-GI food, is expected to show a low postprandial glycemic excursion after consumption.

Keywords : glycemic index; Neo-Mune; glycemic control

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Correspondence to:

Buranapin S, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Thailand

E-mail : supawan.b@cmu.ac.th

Introduction

Currently, diseases related to excess calorie intake or maintaining a high fat or high sugar diet are increasing. These include diabetes mellitus (DM), dyslipidemia and cardiovascular diseases. Therefore, consumers are being encouraged to focus on healthy diets and lifestyle modification. One of the strategies being used is to control carbohydrate consumption, a main source of energy, to lower postprandial glycemic response. Carbohydrates are classified in 2 main groups: simple and complex carbohydrates. They differ in terms of glucose absorption and postprandial glucose excursion. The consumption of appropriate levels of carbohydrates is effective in controlling both spikes and baseline levels of plasma glucose.

The classification of food based on glycemic response or "glycemic index" (GI) has been found to be useful for both patients and medical teams in maintaining plasma glucose levels. The GI is the area under the plasma glucose response curve for each food consumed expressed as a percentage of the area under the plasma glucose response curve after taking the same amount of carbohydrate as a reference food, which is typically glucose or white bread. A 50 gram (g) glucose intake typically has a glycemic index of 100.[1] Different carbohydrate sources raise blood glucose differently. The GI measurement was originally designed for patients with diabetes as a guide for food selection. Low-GI food has a low glycemic response following ingestion compared with high-GI food, therefore low-GI food is appropriate for diabetic control to prevent or delay long term diabetic complications.[2] The GI classification is categorized as low- GI (GI less than 55), medium-GI (GI from 55 to 69) and high-GI (GI more than 70).[2]

The amount of food consumed is also a major determinant in postprandial glucose excursion. The concept of glycemic load (GL) takes into account the GI of food and the amount consumed.[3] The present study was designed to examine the glycemic index of Neo-Mune, an immunonutrition product. Neo-Mune is aimed at supporting immunocompromised patients; however, its impact on the glycemic response among vulnerable patients is a concern. This study intended to investigate this impact.

Methods

Study subjects

This study was approved by the ethics committee of the Faculty of Medicine, Chiang Mai University and conducted at the Clinical Trial Unit, Faculty of Medicine, Chiang Mai University. Ten eligible subjects signed consent forms and fulfilled the following criteria: were 18 years or older, had a body mass index (BMI) 18.5-24.9 kg/m^2, had no underlying diseases, had no history of DM in their families or had no history of allergy to any of the ingredients in the formula (cow's milk protein, glutamine, arginine, fish oil etc.). These subjects also did not meet any of the following exclusion criteria: had underlying diseases (including DM, hypertension, cardiovascular diseases, renal or liver disease, metabolic disease, thyroid disease etc.), had taken any medication or food supplement or any vitamins within 7 days before commencement of the study, were pregnant or lactating, or did not comply with the study protocol.

Study product

Neo-Mune, an immuno-enhancing formula, provides a caloric distribution consisting of approximately 50% carbohydrate, 25% fat and 25% protein (**Table 1**).

Table 1. Neo-Mune composition

Composition	In grams	Amount (g)	Calories (kcal)
Protein	Sodium caseinate	18.25	
	Glutamine	2.61	
	Arginine	5.21	
	Total	26.07	104.3
Carbohydrate	Maltodextrin	42.44	
	Trehalose	1.00	
	Fructose	5.21	
	Polydextrose	4.00	
	Total	52.65	210.6
Fat	MCT oil (52%)	6.28	
	Fish oil (19%)	2.32	
	Corn oil (29%)	3.48	
	Total	12.08	108.7
Total energy in 100.00 gram			423.6

Sample size calculation

Ten healthy subjects were enrolled in this pilot study. This was deemed to be the lowest sample size necessary to study the GI of the food.

Ethical aspects

The Research Ethics Committee, Faculty of Medicine, Chiang Mai University (No. 336/2016) approved the study design described below. All participants had to provide written informed consent before entering the study.

Study design and procedure

On screening days, the subjects had to abstain from consuming food and beverages for at least 10 hours. The subjects were informed about the study method and procedures before signing the consent form. The screening process involved a medical history check, a physical examination and laboratory tests for fasting plasma glucose, liver function, renal function, thyroid function, pancreatic function and a urine pregnancy test to confirm all inclusion and exclusion criteria. An oral glucose tolerance test (OGTT) was performed to evaluate pancreatic function. This was conducted by consuming a glucose solution which contained 75 g glucose dissolved in 250-300 mL of water within a 5-minute period. During OGTT, subjects were asked to remain still and not to smoke or drink any foods or beverages for 2 hours when their plasma glucose levels were measured. Those who had a 2-hour post-OGTT plasma glucose level of less than 140 mg/dL and other normal lab results were included in the study which was performed within 7±2 days.

At experimental visit 1 (Day 7±2), subjects had to abstain from consuming any food or beverages for at least 10 hours to evaluate their plasma glucose response after consuming a glucose solution containing 50 g of glucose dissolved in 400 mL of water within 5 minutes. Blood collection of 3 mL was drawn at 0, 30, 60, 90 and 120 minutes (on a normal saline solution (NSS) lock for convenience) after consumption.

At experimental visit 2 (Day 14±2), the subjects repeated the process of visit 1 (Day 7±2), the only difference being the consumption within 5 minutes of 94.97 g of Neo-Mune (providing 50 g of carbohydrate) dissolved in 400 mL

of water instead of the glucose solution. A second set of blood samples was used to measure plasma glucose levels. The plasma glucose levels after consuming the glucose solution and Neo-Mune were compared at each time interval. The GI of Neo-Mune was calculated as the area under the glucose response curve (AUC) within 2 hours after consuming Neo-Mune divided by the AUC within 2 hours after consuming the glucose solution and multiplied by 100. The GI recorded was the average GI from all 10 subjects.

Any adverse events that occurred during the study were addressed as open-ended questions and answers were recorded.

Statistical analysis

Results were expressed as mean ± standard deviation (SD) when data was continuous data. Categorical variables were expressed as proportions (percentages). To compare all the continuous parameters in each patient between baseline and at 30, 60, 90 and 120 minutes, statistical significance was tested using repeated measure ANOVA tests. Categorical variables were compared using Fisher's exact test. All statistical tests were two-tailed and statistical significance was set at a *p*-value less than 0.05.

Results

Ten healthy volunteers were included with a mean age of 33.4 ± 5.2 years, mean body weight of 56.5 ± 9.1 kg, mean BMI of 21.1±1.9 kg/m2, mean fasting plasma glucose of 84.7 ± 9.9 mg/dL, mean systolic blood pressure (SBP) of 115.78 ± 10 mmHg and mean diastolic blood pressure of 73.1 ±8.7 mmHg. (**Table 2**)

Table 2. Baseline characteristics of 10 subjects

Variables	**Mean±SD**
Age (years)	33.4 ± 5.2 (26-42)
Weight (kg.)	56.54 ± 9.07
BMI (kg/m^2)	21.12 ± 1.93
SBP (mmHg)	115.7 ± 10.0
DBP(mmHg)	73.1 ± 8.7
Laboratory blood tests	
Plasma glucose (mg/dL)	84.7 ± 9.9
Total bilirulin (mg/dL)	0.66 ± 0.35
Direct bilirulin (mg/dL)	0.23 ± 0.09
Albumin (g/dL)	4.64 ± 0.24
SGOT (IU/L)	18.2 ± 5.09
SGPT (IU/L)	18.6 ± 12.88
Creatinine (mg/dL)	0.87 ± 0.26
BUN (mg/dL)	11.2 ± 1.75
TSH (mU/L)	1.48 ± 0.92

All 10 subjects had normal pancreatic function confirmed by the OGTT with a mean plasma glucose level of 97.7 26.3 (ranging from 53-138) mg/dL.

Plasma glucose reached its highest levels after 30 minutes in both postglucose solution and postNeo-Mune consumption before gradually decreasing. However, the plasma glucose levels at 30 and 60 minutes post Neo-Mune consumption were lower than the levels postglucose solution consumption; p = 0.004 and 0.005, respectively (**Table 3**). The incremental rise of plasma glucose levels from the baseline was also lower after Neo-Mune consumption than after glucose solution consumption at 30 and 60 minutes after consumption (**Figure 1**).

Table 3. Plasma glucose levels at each time after glucose and Neo-Mune consumption

Time after consumption (minutes)	Plasma glucose level (glucose solution) (mg/dL)	Plasma glucose level (Neo-Mune) (mg/dL)	Mean Difference (95%CI) (mg/dL)	p-value (mg/dL)
0	84.3 ± 8.27	77.4 ± 8.46	6.9 (-2.29, 16.09)	0.124
30	135.8 ± 29.64	110 ± 26.03	25.8 (10.71, 40.89)	0.004*
60	121.9 ± 28.12	89.3 ± 18.49	32.6 (12.76, 52.44)	0.005*
90	108.8 ± 25.75	94 ± 18.02	14.8 (-4.34, 33.94)	0.114
120	95.3 ± 25.51	83.4 ± 18.66	11.9 (-6.16, 29.96)	0.170

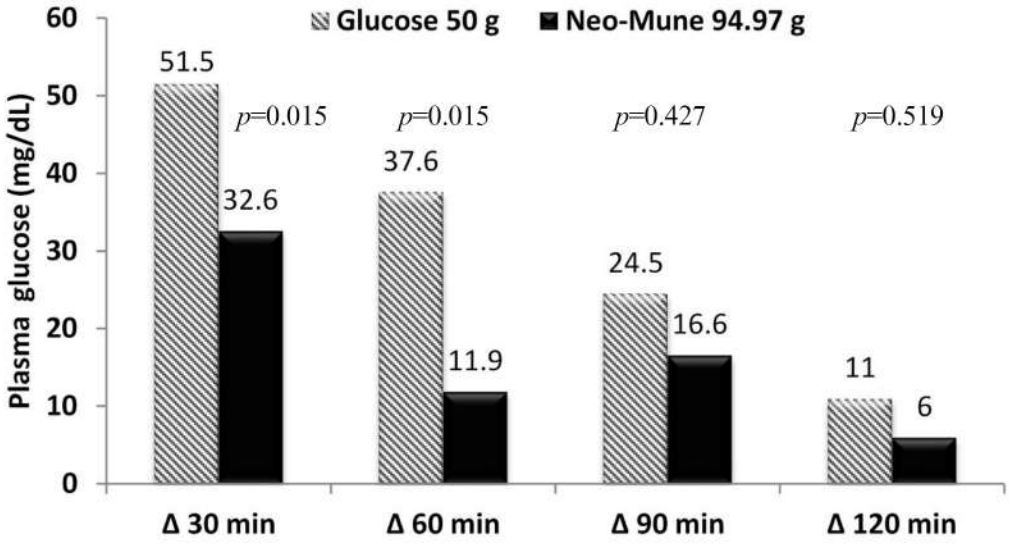
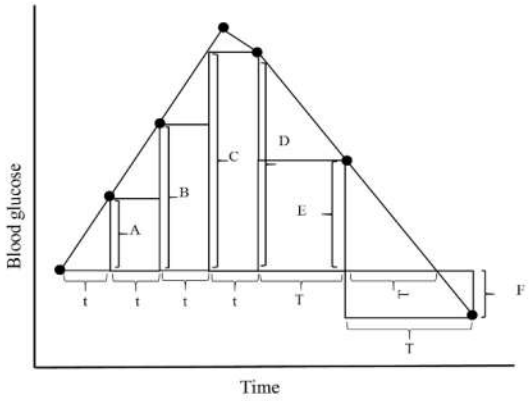


Fig 1. The incremental levels of plasma glucose from baseline at each time point after consuming glucose solution or Neo-Mune (mg/dL)

The GI was calculated based on the area under the plasma glucose response curve above the fasting levels only. The formula is shown in **Figure 2**[4] and the calculation was based on the data of the increments of plasma glucose values from baseline at each time point after consumption of the 50g glucose solution and 94.97g of Neo-Mune (**Table 4**)



$$Area = (A + B + C + \frac{D}{2})t + \frac{(D+E)T}{2} + \frac{E^2T}{2(E+F)}$$

Fig 2: Formulation and graph to calculate the area under the glucose curve4

Table 4. Calculations of incremental area under the plasma glucose response curve

Time (minutes)	Plasma glucose (glucose solution) (mg/dL)	Increment of plasma glucose level from baseline (glucose solution) (mg/dL)	Plasma glucose (Neo-Mune) (mg/dL)	Increment of plasma glucose level from baseline (Neo-Mune) (mg/dL)
0	84.3	-	77.4	-
30	135.8	51.5	110.0	32.6
60	121.9	37.6	89.3	11.9
90	108.8	24.5	94.0	16.6
120	95.3	11.0	83.4	6.0

Therefore the area under the glucose response curve for 50 g glucose solution (AUCg) was equal to: (51.5 + 37.6/2) × 30 + (37.6+ 24.5) × 30/2 + (24.5 + 11) × 30/2 = 4762.75 mg/minute/dL The AUC for Neo-Mune (AUCn) was equal to: (32.6 + 11.9/2) × 30 + (11.9+16.6 + 6.0/2) × 30 = 2101.5 mg/ /dL The AUC ratio is equal to: AUCn/AUCg x 100 = (2101.5/4762.75) × 100 = 42.12. This means that consuming Neo-Mune raises plasma glucose 57.88% less than consuming the glucose solution. Therefore, the GI of Neo-Mune is 42.12 falling in the category of a low-GI food according to advisory guidelines. No adverse events occurred during the study.

Discussion

Assuming that Neo-Mune would have a low-GI was reasonable because of its composition. It contains fructose, instead of sucrose or polydextrose. Fructose helps to facilitate glucose clearance from plasma by forming fructose-1-phosphate by the liver. Fructose-1-phosphate activates glucokinase in the liver which catalyzes the phosphorylation of glucose into glucose-6-phosphate and subsequently enables it to be stored as glycogen in the liver, thus blunting the postprandial increment in plasma glucose levels.[5]

The presence of polydextrose may also play a role in

decreasing glucose response.[6] Polydextrose is a functional fiber which is not hydrolyzed by human digestive enzymes in the small intestine but partially fermented by endogenous microbiota in the colon to produce short chain fatty acids. Therefore, it has an energy contribution of only 1 kcal/g.[7]

Although polydextrose is not sweet, it can replace sugar, fat and calories. Not only has it been used as a low calorie bulking agent in a variety of foods including baked foods, dairy products and functional beverages, but also as a fiber content increment in processed food. Due to its laxative and satiety effects,[8] polydextrose functions as both a stabilizer and bulking agent, and helps to maintain moisture in food.[9] The glycemic index of polydextrose is only 7[10] and clinical trials have demonstrated that polydextrose has beneficial effects on appetite, satiety and energy intake.[11,12]

Regular consumption of high GI meals compared with isoenergetic and nutrient-controlled low GI meals, results in higher average 24-hour plasma glucose and insulin levels, higher C-peptide excursion and higher HbA1c in both diabetic and nondiabetic subjects.[13] Hyperinsulinemia may cause insulin resistance and consequently β-cell failure.[14] Salmeron J, et al.[15] conducted a cohort study surveying 65,173 women in the US aged 40-65 years old who had no cardiovascular disease, cancer or DM, and 42,759 men aged 40-75 years old who had no DM or cardiovascular disease.[16]

Subjects were asked to complete a dietary questionnaire over a 6-year period. The results revealed that dietary GI was positively associated with the risk of developing DM after adjusting for other confounding factors. The relative risk (RR) of developing DM in women was 1.37 (p=0.005) and in men was 1.37 (p = 0.03).

Jarvi AE, et al.[17] conducted a randomized crossover study of 20 subjects with type 2 DM by providing different GI diets during 2 consecutive 24-day periods. Both diets had the same macronutrient composition and the same type and quantity of dietary fiber. The results showed that peripheral insulin sensitivity increased significantly and fasting plasma glucose decreased during both periods.The incremental area under the curve for both glucose and insulin was 30% lower in low GI diets compared with high GI diets. LDL-C was significantly lower in both diets; however, low-GI diets were significantly lower. Brand JC, et al.[18] conducted a crossover study to evaluate the effects of low GI and high GI diets on long term glycemic control over two 12-week periods among patients with type 2 DM and found that glycemic control was improved among those on the low GI diets compared with the high GI diets ($p < 0.05$). Mean HbA1c at the end of the low GI diets was 11% lower (7.0 ± 0.3%) than at the end of the high GI diets (7.9 ± 0.5%). However, mean fasting plasma glucose, total cholesterol, triglycerides, HDL-C and LDL-C did not significantly differ between groups. Willett W, et al.[19] reviewed metabolic and epidemiologic studies and found that replacing high GI with low GI carbohydrate diets reduced the risk of type 2 DM. Among patients with DM, replacing high GI with low GI carbohydrates improved glycemic control and reduced hypoglycemic episodes among those treated with insulin. Luscombe ND, et al.[20] examined the effects of high and low GI carbohydrate diets, and monounsaturated fats (MUFA) in 14 subjects with type 2 DM in a random crossover design study for 4 weeks. They demonstrated that HDL-C levels were significantly higher in the subjects on the low GI and high MUFA diets compared with the high GI diet. No significant difference was observed in metabolic control between the diets, even after adjusting BMI, glucose control and sex. Bouch´e C, et al.[21] evaluated whether 5 weeks on a low GI diet versus a high GI diet could affect glucose and lipid metabolism as well as total fat mass among 11 nondiabetic men using a crossover design with a 5-week washout period. They confirmed that the low GI diet resulted in lower postprandial plasma glucose levels, insulin profiles and areas under the glucose curve (AUC) than the high GI diet (p <0.05). The low GI diet was associated with a decrease in the total fat mass (p <0.05) and a tendency to increase lean body mass (p <0.07) without any change in body weight and a reduction in leptin, lipoprotein lipase and hormone-sensitive lipase mRNA in subcutaneous abdominal adipose tissue. Therefore, low GI diets might play a role in preventing metabolic diseases and cardiovascular complications. Yanai H, et al.[22] assessed the effects of carbohydrate and dietary fiber intake, glycemic index (GI) and glycemic load (GL)on HDL-C metabolism by reviewing meta-analyses and clinical studies in an Asian population. They concluded that low carbohydrate intake, GI and GL, as well as high dietary fiber might be beneficially associated with HDL-C metabolism in Asian populations.

Barclay WA, et al.[23] evaluated the association between GI, GL and chronic disease risk by performing a meta-analysis including 37 prospective cohort studies resulting in a total of 40,129 subjects. They illustrated that low GI and/or low GL diets were independently associated with reduced risk of certain chronic diseases including DM, coronary heart disease, gall bladder disease and breast cancer.

Therefore, maintaining low GI diets in the long term should confer greater benefits than high GI diets in many ways, including decreasing the glucose-insulin response, increasing insulin sensitivity, improving lipid profiles (higher HDL-C and lower LDL-C), decreasing fat mass and reducing the risk of developing diabetes, certain cancers and cardiovascular disease.

The present study enrolled a small sample size with limitations regarding statistical validity. It would be useful to repeat the exercise with a larger sample, possibly over a larger age group to obtain more detailed transferrable information, in particular, for patients with diabetes. It comprised a cross-sectional study, not a long term study. Further study of Neo-Mune concerning long term metabolic outcomes is warranted.

Conclusion

The present study showed that Neo-Mune has a low GI food. Neo-Mune has been recommended to cancer or critically ill patients to enhance their immune function. These groups of patients might also have underlying conditions including DM or stress-induced or medication-induced hyperglycemia. Therefore, confirming that Neo-Mune consumption would not have a negative impact on their glycemic control was necessary and indeed might actually help patients with diabetes control their plasma glucose more easily than those consuming standard oral or enteral nutrition. However, further study of Neo-Mune on long term metabolic outcomes is warranted.

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Declaration of conflicting interests

The author declares that no potential conflicts of interest exist with respect to the research, authorship and/or publication of this article.

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Availability of data and materials

All data generated or analysed during this study are included in this published article.

Supplementary Materials

Data on the subjects has been kept safely with the principle investigator. The case record forms included only patients' initials and surname and number, not their full name.

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