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Evaluation of Postprandial Glycemic Response on Diabetes-Specific Formula

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Abstract: **Diabetes-specific formulas have shown to be effective at improving glucose control with additional nutritional benefits. Furthermore, diabetes-specific formulas are commonly used for diabetic patients with insufficient oral intake. However, not much diabetes-specific formulas in the market shows the GI of these formulas, which is clinically useful on glycemic control in patients with diabetes. The aim of this study was to assess the GI of a newly developed diabetes-specific formula, Contro eazy NOW. The open labelled, single center study involved 11 individuals from a pool of 18 healthy subjects. After an overnight fast, volunteers were given Contro eazy NOW containing 50g of carbohydrate or the reference drink (glucolin) on different occasions in random order. Postprandial blood glucose levels were measured in finger pricked capillary blood for two hours after intake of the beverages and positive incremental area under the curve (AUC) was calculated for both Contro eazy NOW and reference drink. The GI of Contro eazy NOW was determined by dividing AUC (Contro eazy NOW) by the AUC (reference drink). The results show that the diabetes-specific formula has the GI of 38.4, which is categorized as low GI. Therefore, Contro eazy NOW with low GI can be the preferred option for nutritional management of diabetic patients in need of nutritional support.**

Keywords: **diabetes-specific formula, diabetes, low glycemic index, medical nutrition therapy.**

I. INTRODUCTION

A major nutritional treatment goal of diabetes is to normalize plasma glucose levels in both the fasting and the postprandial state. Besides fasting blood glucose, postprandial hyperglycemia is not only a risk indicator for micro and macrovascular complications in patients with type 2 diabetes, but also those with impaired glucose tolerance. Thus, treatment targeting postprandial blood glucose levels is expected to improve overall glycemic control and long-term outcomes, including reduction of cardiovascular disease and all-cause mortality [1]. Nutrition and diet have been used as an important tool in optimizing blood glucose levels by medical professionals and health care organizations. Nutrition plays an important role in blood glucose changes where the postprandial blood glucose response is strongly influenced by the specific composition of the diet [2]. The quantity, as well as the quality of the carbohydrates are some of the factors that can influence blood glucose response to a meal. The presence of fibre in the diet also can reduce postprandial hyperglycemia, as well as the amount of fat in a meal can play a role to influence the glycemic response to these meals [3].

To compare the effects of specific foods on blood glucose response, glycemic index (GI) has been introduced by Jenkins et al. [4] The GI is defined as the area under the glucose response curve after consumption of a food containing 50g of carbohydrates, which is expressed as percentage of the area under the blood glucose response curve after intake of 50g of carbohydrates in standard food such as glucose solution or white bread. The standard procedure is to assess the GI in healthy volunteers. Nonetheless, the concept of GI is a useful tool to improve glycemic control in diabetic patients as shown in several clinical trials [5].

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Generally, low-GI food has been clinically proven to be useful in glycemic control in patients with diabetes. A study has shown that a reduction of 7.4% of glycated proteins (HbA1C) in diabetic patients when a low GI diet is administered as compared to high GI diet [6]. Thus, GI is considered as an important tool as a dietary treatment of diabetic patients by several diabetic and healthcare organizations [7].

Worldwide prevalence of diabetes has increased over the last 40 years from 4.7% to 8.5% of the adult population [8], especially in the elderly population, the prevalence of diabetes is high, which is approximately 5-20% [9]. Elderly diabetic patients that are admitted to nursing or elderly homes are often malnourished and their nutritional status seems to decline after admission [10]. Thus, products with complete and balanced nutrition that could induce a delayed and limited rise in postprandial glucose levels is essential for this group of population. In this study, we will be assessing a diabetic oral nutrition supplement and GI of this product will be determined.

II. MATERIALS AND METHODS

Study design

This was an open labelled, single center study to evaluate the efficacy of a diabetes-specific formula, Contro eazy NOW (Ethos Healthcare, Malaysia) in maintenance of postprandial blood glucose level in healthy subjects. The macronutrient composition of the formula is shown in Table 1. This study was conducted at Alpro Academy.

Table 1: Nutrition information of Contro eazy NOW.

Per Serving	Amount
Serving size	50g
Energy (kcal)	215
Total fat (g)	8.9
Saturated fat (g)	2.3
Monounsaturated fat (g)	4.2
Total carbohydrates (g)	26.5
Dietary fiber (g)	5.5
Protein (g)	10.0

Informed consent was obtained from all participants before the start of the study. A total of 18 healthy volunteers (15 Chinese, 2 Malays, 1 Indian; 7 men and 11 women) aged 22 – 41 were recruited from different departments of Alpro Pharmacy Sdn Bhd and screened by height, weight and HbA1C. Cobas b 101 system (Roche, Switzerland) was used to assess HbA1C. BMI is calculated based on the formula: weight in kilograms divided by height in meters squared. Exclusion criteria were: Pregnant and Lactating mothers, BMI > 24.9; HbA1C > 5.7 and those who suffer from diabetes.

In vivo test and blood sample analysis

Volunteers reported at Alpro Academy after an overnight fast of at least 8 hours. Equal amount of available carbohydrate (50g/meal) of the diabetes specific formula (Contro eazy NOW) was served with a washout period of two days after the consumption of reference drink (glucolin). The diabetes specific formula was served with 250 mL of warm water. The volunteers were instructed to consume the drink within a 10-min period at a comfortable pace and were requested to remain seated and not consuming any food or beverage throughout the duration of the study. Capillary blood obtained by finger-prick using Microlet® lancet. Blood samples were collected for estimation of blood glucose at stipulated time points (Baseline at 0 min and post-meal at 15, 30, 45, 60, 90 and 120 min) as per schedule of assessment. Blood glucose was assessed using Contour® Plus blood glucose monitoring system (Ascensia, Switzerland), which has been shown to be precise and reliable [11].

Data analysis

The area under curve (AUC) of blood glucose from baseline, the incremental area under response curve was calculated for each subject by using GraphPad PRISM (version 9; GraphPad Software Inc, San Diego). All AUCs below the baseline were excluded from calculations. The AUCs were expressed as means ± s.e.m.'s. The average AUC for the diabetes specific formula and glucose was compared using ANOVA, followed by Tukey's multiple comparison test. Differences resulting in P values <0.05 were considered significant.

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III. RESULTS

Subject characteristics

The subjects' baseline characteristics are presented in Table 2. Of the 18 subjects enrolled, one subject had incomplete data, 3 did not meet eligibility criteria and another 3 withdrew consent, leaving 11 subjects with complete data for analysis. Eligible subjects had the mean age of 30 ± 5.6 and a normal BMI 20.1 ± 2.2 with the mean of haemoglobin A1C (HbA1C) 5.2 ± 0.2 (Table 2). There was no day-to-day variation on the subjects' usual daily diet intake and physical activity throughout the study period. Everyone attended all the experiment days and the timing of the blood samples taken was strictly followed by the same person in charge that obtained the blood samples.

Table 2: Anthropometric characteristics of study participants (n = 11)

Characteristics	Mean ± SD	Range
Gender	Male 4 (36.4%) Female 7 (63.6%)	
Age (years)	30 ± 5.6	22 - 41
Height (m)	1.6 ± 5.6	1.53 – 1.81
Body Weight (kg)	54 ± 5.9	46 – 69
BMI (kg/m^2)	20.1 ± 2.2	16.2 – 23.9
HbA1C	5.2 ± 0.2	4.8 – 5.4

Blood glucose response to diabetes-specific formula

The change in glucose concentrations from baseline over 120 min for the tested diabetes-specific formula (Contro eazy NOW) is illustrated in Figure 1. The mean blood glucose concentrations for the diabetes-specific formula and control were 6.87 ± 0.82 and 5.74 ± 0.82 mmol/l respectively and were comparable at baseline (Table 3). Compared to the baseline (0 min), there was a significant increase in blood glucose concentrations within 10 min in response to a dietary challenge with the control (glucolin), which lasted until 30 min. In contrast, only moderate increases in blood glucose concentrations occurred until 30 min with diabetes-specific formula, with no further increase in blood glucose across time. Comparing to glucolin, the increase in diabetes-specific formula was significantly lower when the subjects were given diabetes-specific formula compared to glucolin across 6 time points from 15 to 120 min. Blood glucose returned to almost baseline level at 60 min for diabetes-specific formula and no longer significantly different between glucolin and diabetes-specific formula at 90 min. The maximum of the mean glucose concentrations (mmol/l) for the diabetes-specific formula were smaller than those of the glucolin over the course of the study [6.6 ± 0.74 and 8.5 ± 0.8 respectively].

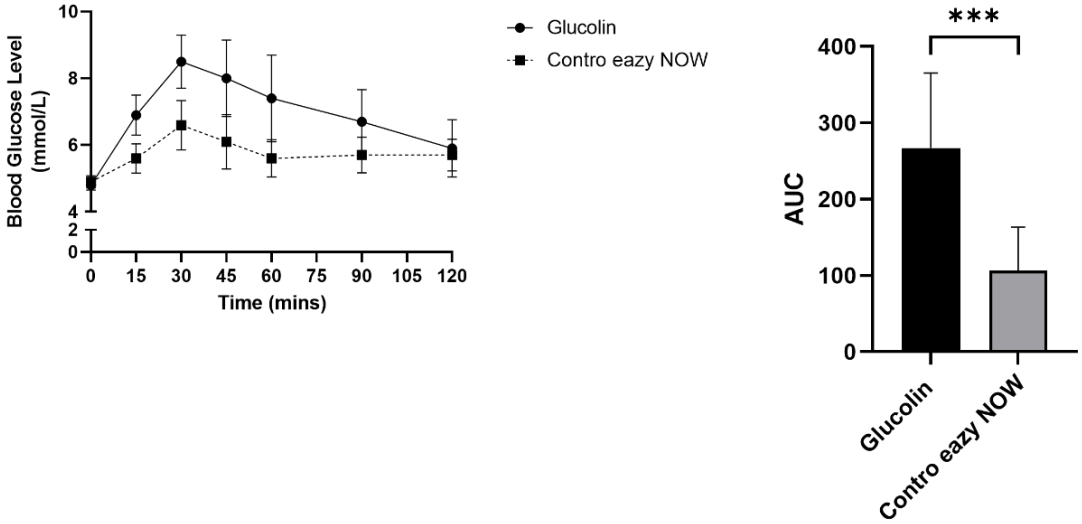

Figure 1: Mean blood glucose responses of subjects at different time points after consuming Contro eazy NOW.

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Table 3: Mean blood glucose responses of subjects at different time points after consuming Contro eazy NOW

Beverage	0 min	15 min	30 min	45 min	60 min	90 min	120 min
Glucolin	4.8 ± 0.15	6.9 ± 0.60	8.5 ± 0.8	8.0 ± 1.15	7.4 ± 1.3	6.7 ± 0.96	5.9 ± 0.86
Contro eazy NOW	4.9 ± 0.18	5.6 ± 0.44[a]	6.6 ± 0.74[b]	6.1 ± 0.82[b]	5.6 ± 0.56[c]	5.7 ± 0.54	5.7 ± 0.48
[a]Significantly difference than the reference drink ($p<0.05$)							
[b]Significantly difference than the reference drink ($p<0.0001$)							
[c]Significantly difference than the reference drink ($p<0.001$)							

Glycaemic index (GI) value of Contro eazy NOW

GI of Contro eazy NOW is calculated as the incremental area under the curve (iAUC) for blood glucose after consumption of Contro eazy NOW divided by the iAUC of glucolin containing the same amount of carbohydrate, which is 50g. The iAUC for blood glucose was calculated by using the trapezoidal method. GI of Contro eazy NOW was calculated based on the assumption of Glucolin (reference food) with GI of 100. The $iAUC_{120}$ reflects changes in blood glucose levels over the 2 hours after consuming Contro eazy NOW. The mean value of GI measured in Contro eazy NOW is 38.4, based on 50g available carbohydrates (Table 4). The AUCs for glucose are shown for each subject in Table 5.

Table 4: AUC and GI of Glucolin and Contro eazy NOW.

Beverage with 50g available carbohydrate	AUC ± Mean SD	GI Index
Glucolin	267.3 ± 93.3	100 ± 0.00
Contro eazy NOW	106.5 ± 54.4	38.4 ± 10.2

Table 5: Area under the curve (AUC), Maximum value (C_{max}), and time of maximum value (T_{max}) for glucose values in individual subject receiving diabetes specific formula.

Subject	AUC: Contro eazy NOW	AUC: Glucolin	C_{max}: Contro eazy NOW	C_{max}: Glucolin	T_{max}: Contro eazy NOW	T_{max}: Glucolin
101	91.50	273.8	6.8	8.5	45	30
102	91.50	178.5	6.7	7.8	45	30
103	98.25	335.3	6.9	9.4	30	30
104	156.00	307.5	6.3	9.3	45	45
105	222.00	428.3	7.7	10.3	45	60
106	94.50	258.8	6.8	8.2	30	30
107	66.00	172.2	5.8	7.7	30	30
108	33.00	173.3	5.7	7.4	15	30
109	43.50	159.8	5.9	7.9	30	30
110	98.25	228.00	7.4	8.1	30	30
111	177.0	424.5	8.0	10.0	30	30

Peak blood glucose concentration (C_{max}) and time of C_{max} (T_{max}) are also shown in Table 5. The peak glucose concentrations of diabetes specific formula were consistently lower than the reference drink, glucolin for all subjects. The time to achieve the highest glucose value (T_{max}) varied between subjects with some achieving their highest values 15 min and others up to 45 min. Interestingly, the diabetes specific formula also influenced the T_{max} with some subjects by delaying the peak time. Although overall T_{max} for diabetes specific formula and glucolin is 34.1 ± 9.25 min, but the AUC for diabetes specific formula is significantly lower than glucolin, which is 106.5 ± 54.4 and 267.3 ± 93.3 respectively.

IV. DISCUSSION

The results of the present study show that diabetes specific formula, Contro eazy NOW is leading to a lower spike of post-meal blood glucose level as compared to the reference drink, glucolin in healthy subjects.

Postprandial glucose response is an important contributor to overall glycemic control, and therefore can be a major treatment target in patients with diabetes. Besides that, there is mounting evidence that postprandial glucose is associated with cardiovascular disease [12]. The International Diabetes Federation (IDF) has addressed the importance of harmful

effects on post-meal hyperglycemia including oxidative stress, inflammation, endothelial dysfunction, carotid intima-media thickness, and micro-vascular complications [13]. Some studies have shown that individuals with diabetes had a two-fold increase in the risk of death from cardiovascular disease [14].

The postprandial glycemia depends on the amount of carbohydrates ingested as well as on the type of the carbohydrates in the diet (glycemic index). The glycemic index (GI) of the diabetes specific formula, Contro eazy NOW is 38.4 (as compared with glucolin reference drink), which is lower than the recommended GI value (55 or less) by international diabetes organizations. Intake of low GI diets is associated with improvement in HbA1C reduction. Low GI diets were beneficial in patients with type 2 diabetes as it can lead to a significant reduction in HbA1C and total cholesterol levels compared with high GI diets [15]. Low GI diets also help in maintaining post-meal hyperglycemia. The diabetes-specific formula administered in the present study has a property of slower absorption that do not cause a spike in blood glucose. The diabetes specific formula is consistent with the dietary recommendations of American Diabetes Association (ADA) [16] (Table 1).

A meta-analysis to assess the effects of carbohydrate and fiber intake on glycemic control studies have reported that moderate carbohydrate-high fiber diets significantly reduced postprandial plasma glucose values by 21% when compared with moderate carbohydrate low fiber diet [17]. The diabetes specific formula consumed in this study provides 44.2% of total calories as complex carbohydrate. The protein content of this diabetes specific formula is 18.6% of total calories and the high quality of protein blend made up of whey protein concentrate that can fulfil patient's essential amino acid requirements. Whey is an ideal protein source during metabolic stress and also helps to maintain glutamine levels and enhances gut integrity. Moreover, whey is a fast-acting protein and spikes amino acid levels before dropping [18]. The diabetes specific formula also has a specific fat blend (4.6% of the total calories from saturated fatty acid, 8.4% of the total calories from MUFA, 3.8% of the total calories from polyunsaturated fatty acids (PUFA) and provides 11.0g fiber. Of the 3.8% polyunsaturated fatty acids, 2.7% is Omega-6 and 1.2% is Omega-3, giving the optimal ratio of omega-6 to omega-3 (2:1) that could bring health benefits [19]. Both omega 3 & omega 6 are beneficial for improving lipid profiles in type 2 diabetic patients by lowering triglycerides and VLDL-cholesterol [20]. Besides that, Contro eazy NOW is formulated with medium chain triglycerides (MCT) that could improve thermogenesis and weight management, as well as reducing risk for heart disease [21].

Dietary fiber also plays an important role in postprandial glycemic response. Contro eazy NOW contains viscous, soluble fibers that can diminish postprandial glucose excursions by their effects on intestinal motility and gastrointestinal hormones and enzymes. Overall, this diabetes specific formula has a well-balanced energy distribution between carbohydrates and fats designed for low GI to help manage the glycemic response. Moreover, this diabetes specific formula contains 28 essential vitamins, minerals and trace elements that allow the product to be used as sole source of nutrition.

V. CONCLUSION

This study shows that the newly developed diabetes-specific formula, Contro eazy NOW is characterized by low GI, with the glycemic index value 38.4. As diets with low GI have been shown to improve glycemic control, thus, Contro eazy NOW can be a preferred option to be used as nutritional management of diabetic patients in need of nutritional support.

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