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Glycemic Response to Oral Nutritional Supplements in Healthy Adults: A Single-Blind Crossover Study

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Abstract: **The relevance of glycaemic index (GI) to health is interconnected. A growing body of research over the last decades has shown that diets based on low GI can reduce the risk of developing diabetes and improve blood glucose control in people with diabetes. In this present study, the glycemic responses of 3 commercial oral nutritional supplements (Metabolic Energold (ME), Metabolic Gosure (MG) and Metabolic Basic (MB)) were assessed in 10 healthy individuals. The GI was determined based on the 50g of available carbohydrate portions in the test foods of the corresponding area following an equivalent amount of carbohydrates from the reference food (glucose). Postprandial plasma glucose was measured at intervals for two hours after intake of the test foods. The results showed that the area under the curve of ME, 228.47 ± 93.5 was greater than MG (190.54 ± 85.1) and MB (182.97 ± 102.97). Similarly, the glycemic index of ME, 65.33 ± 22.9 was greater than MG (53.1 ± 16.5) and MB (51.0 ± 20.8). As a conclusion, ME has an intermediate GI, whilst MG and MB have low GI, which are suitable for diabetic patients to better control of glucose levels.**

Keywords: **oral nutritional supplements, glycemic index, diabetes formula, postprandial blood glucose.**

I. INTRODUCTION

Diabetes is one of the major global public health problems, which the prevalence is estimated to set to escalate from 415 million to 642 million people by the year 2040 [1]. This current global estimation is linked to health, social and economic costs. Investment in modifiable factors including diet, physical activity and weight is suggested to improve or reverse the trend. Diet plays an important role in morbidity and mortality worldwide and thus, the importance of dietary management to prevent type 2 diabetes on weight and metabolic control is clear. Maintaining a proper nutritional status can be quite challenging due to acute disease, functional status or severe co-morbidities [2]. Oral nutritional supplements are encouraged when an individual's nutritional needs cannot be reached with usual dietary intake or meal modifications [3].

Oral nutritional supplements should provide sufficient macro and micronutrients, including energy, protein, vitamins and minerals to reduce the risk of malnutrition. However, some standard oral nutritional supplements may result in high postprandial glucose responses in patients with type 2 diabetes [4]. Hyperglycemia can result in glucosuria, leading to the increase risk of infections and urinary incontinence. Thus, preventing high blood glucose excursions can be a good target to improve patients' quality of life [5]. Dietary carbohydrates represent the largest contributor to dietary component that is influencing blood glucose levels, especially in the postprandial state. Thus, carbohydrate intake is extremely important in regulating blood glucose levels in people with diabetes [6]. Influence on carbohydrate-rich diets on glycemic control, plasma lipid levels have always been on debate. Controversies arise might due to their rate of digestion, absorption and metabolic effects [7]. Other important components, including fiber content, chemical composition of carbohydrates and physical structure of the food in the meal also contribute to the total effects of dietary carbohydrates. Thus, the concept of glycemic index (GI) was introduced by Jenkins et al. in year 1981 [8], giving a better quantification on the potency of carbohydrate food that raise blood glucose levels *in vivo*. GI values are generally divided into 3 categories: Low GI (1-55), Intermediate GI (56-69) and High GI (70 and higher) [9]. Most trials have demonstrated that low GI food is more effective on glycemic control [10]. Studies have shown that in nondiabetic populations, low GI diets have been associated with lower plasma levels of insulin and lipids, whilst in type 2 diabetes population, a better glycemic control has been observed [11]. A reduction of HbA1C by about 6% has been reported in the group of diabetic patients with low GI diets [12]. The reduction of glycated haemoglobin is very important as HbA1C contributes to the risk of diabetes complications as reported by United Kingdom Prospective Diabetes Study (UKPDS) [13].

Thus, carbohydrate consumption based on GI in the management and prevention of type 2 diabetes is important. American Diabetes Association and UK recommendations have recommended the utilization of GI in the diet for people with diabetes [14,15]. Our study aimed to evaluate the glycemic response of commercially available oral nutritional supplements, Metabolic Energold (ME), Metabolic Gosure (MG) and Metabolic Basic (MB).

II. MATERIALS AND METHODS

Study design and subjects

Study was conducted at the Head Quarter of Alpro Pharmacy Sdn. Bhd. in Malaysia. Healthy men and non-pregnant, non-lactating women aged 25 – 37 years were recruited from different departments of Alpro Pharmacy Sdn Bhd. and screened by height, weight and HbA1C. Exclusion criteria were: BMI > 23kg/m^2; HbA1C > 6%; those who suffer from diabetes. A total of 10 individuals took part (9 Chinese, 1 Malay; 3 men and 7 women), with the mean age 30.3 ± 4.11 years participated in this cross-sectional study through a convenient sampling. Informed consent was obtained from all subjects.

In vivo test and blood sample analysis

Subjects were studied on 4 different occasions in the morning after at least 8-hour overnight fasts. No restrictions were placed on the meal that was eaten prior to the test. Equal amount of available carbohydrate (50g/meal) of all oral nutritional supplements (ME, MG and MB) were served with a washout period of at least two days after the reference drink (glucose) was tested. Drink samples were served with 250mL of water. Each subject consumed the test food within 10 min period at a comfortable pace and remained seated throughout the duration of the study. Blood samples were collected at 15, 30, 45, 60, 90 and 120 min from when the subject first eating. Capillary blood samples were obtained using finger pricks with the used of the Microlet® lancet. The capillary blood samples were then analysed for glucose by GlucoDr. auto™ glucometer together with respective test trips for the device.

Data analysis

The incremental area under the glucose response curves (iAUC$_{120min}$) above baseline was calculated for each subject and respective oral nutritional supplement for 0-120 min 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. Significant differences among the AUCs were assessed with ANOVA, followed by Tukey's multiple comparison test. Differences resulting in P. values <0.05 were considered significant.

III. RESULTS

In this study, 10 healthy subjects were screened for participation into the study and all completed the study. A total of 7 female and 3 male participants were included in the analysis. Eligible subjects had the mean age of 30.3 ± 4.11 yrs and a normal BMI (20.65 ± 2.23 kg/m^2) with the mean of haemoglobin A1C (HbA1C) 5.56 ± 0.28 (**Table 1**). 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 1: Anthropometric characteristics of study participants (n = 10).

Characteristics	**Mean ± SD**	**Range**
Gender	Male 3 (30%) Female 7 (70%)	
Age (years)	30.3 ± 4.11	25 - 37
Height (cm)	164.7 ± 7.83	156 – 184
Body Weight (kg)	56.31 ± 10.18	48 – 82.6
BMI (kg/m^2)	20.65 ± 2.23	18.4 – 24.4
HbA1C	5.56 ± 0.28	5.1 - 6

Data presented as mean ± SD.

Glycemix index on oral nutritional supplements

Mean fasting plasma glucose levels at baseline for glucose, ME, MG and MB were comparable (5.12 ± 0.39, 5.11 ± 0.68, 5.08 ± 0.71 and 5.43 ± 0.63 respectively) (**Table 2**). Blood glucose levels increased significantly after consuming all the oral nutritional supplements at 15 min, with the reference food (glucose) having the highest peak (**Fig. 1**). The mean post-prandial blood glucose level for ME and MB reached its peak at 45 min after the start on the consumption of oral nutritional supplement whilst MG reaches its peak 15 min earlier, at the time point of 30 min. Blood glucose levels after consuming MG and MB were significantly lower than ME. At 120 min, only the mean post-prandial blood glucose level for MG return to pre-prandial levels (5.15 ± 0.39). Intriguingly, the mean post-prandial blood glucose for MB did not have a drastic decrease after reaching its peak at 45 min.

Table 2: Mean blood glucose responses of subjects at different time points after consuming oral nutritional supplements

Beverage	0 min	15 min	30 min	45 min	60 min	90 min	120 min
Glucose	5.12±0.39	7.5±0.95	9.58±0.89	9.86±1.23	9.35±1.83	7.57±1.03	5.86±1.22
ME	5.11±0.68	6.11±0.77	7.6±0.88	8.26±1.29	7.73±1.60	6.86±0.86	6.27±1.11
MG	5.08±0.71	6.45±0.88	7.91±0.70	7.58±1.02	7.45±1.10	6.1±0.58	5.15±0.83
MB	5.43±0.63	6.41±0.84	7.37±0.87	7.67±1.37	7.38±1.49	6.992±0.90	6.41±0.81

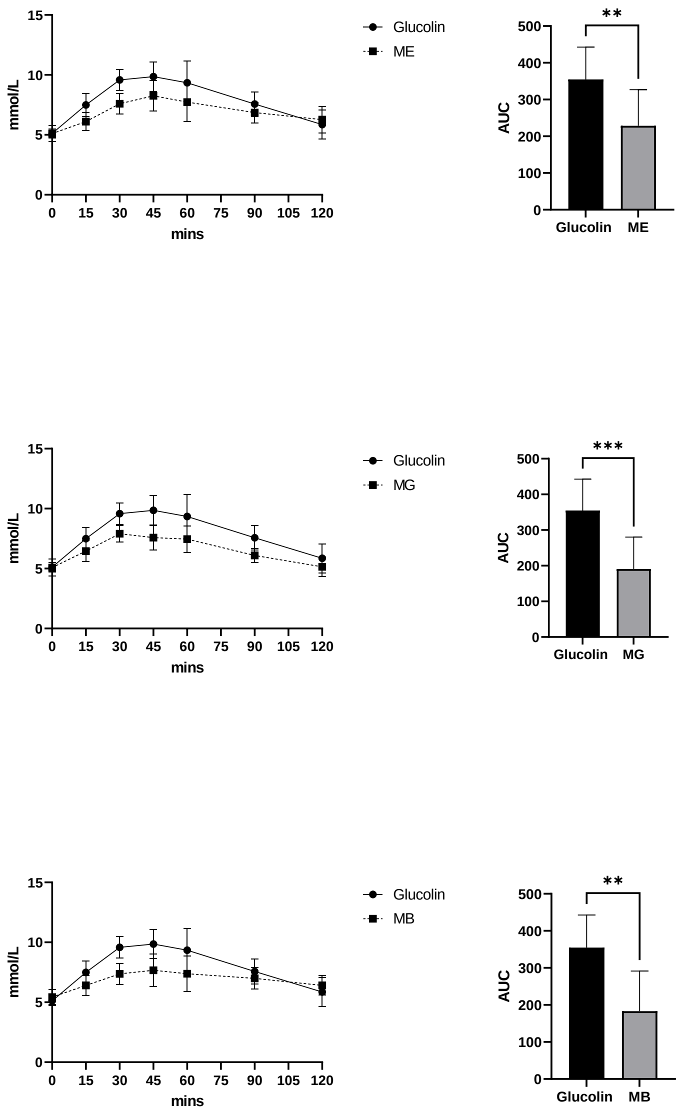

Figure 1: Comparison of glycemic response of glucose and respective tested oral nutritional supplements (ME, MG and MB) respectively.

Table 3: Incremental area under the curve (AUC) and glycemic index (GI) values of glucose and oral nutritional supplements (ME, MG and MB)

Beverage	Area Under the Curve (AUC) (mmol x min/L)	Glycemic Index
Glucose	354.84 ± 83.5	100 ± 0.0
ME	228.47 ± 93.5	65.33 ± 22.9
MG	190.54 ± 85.1	53.1 ± 16.5
MB	182.97 ± 90	51.0 ± 20.8

The iAUC of reference and oral nutritional supplements were calculated using trapezoidal method and the GI of each test food was calculated based on the assumption of Glucose (reference food) with GI of 100. The $iAUC_{120}$ reflects changes in blood glucose levels over the 2 hours after consuming different oral nutritional supplements. The mean AUC after glucose consumption was significantly greater than those after tested oral nutritional supplements. Within the oral nutritional supplements, ME has the highest $iAUC_{120}$ compared to MG and MB. The mean values of $GI_{measured}$ in descending order are ME (65.33 ± 22.9), MG (53.1 ± 16.5) and MB (51.0 ± 20.8), based on 50g available carbohydrates. These values were significantly lower than the reference food (GI = 100) (**Table 3**).

Table 4: Nutrition facts for each oral nutritional supplement per recommended serving size

Per serving	ME	MG	MB
Serving Size (g)	60.0	50.0	62.5
Energy (kcal)	259	215	276
Protein (g)	10.4	8.5	11.9
Fat (g)	8.4	7.9	10.3
Saturated fatty acid (g)	1.1	5.3	2.0
Monounsaturated fatty acid (g)	4.8	1.85	5.3
Polyunsaturated fatty acid (g)	2.1	0.3	2.6
Carbohydrate (g)	36.6	29.0	35.9
Fructooligosaccharides (g)	2.5	-	-
Isomaltulose (g)	-	2.5	-
Dietary Fiber (g)	-	3.0	4.0

IV. DISCUSSION

This study aimed to evaluate the glycemic response of 3 different oral nutritional supplements. The GI is a classification of the blood glucose-raising potential of carbohydrate foods. It is defined as the incremental blood glucose area under the curve (AUC) elicited by a 50 g available carbohydrate of the oral nutritional supplements expressed as a percentage of the response elicited by 50 g glucose in the same subject [16]. The concept of GI is mainly in relation to people with diabetes, providing helpful additional indicator regarding the appropriate carbohydrate containing foods for inclusion in the diet [17]. Our study has shown that GI value for ME, 65.33, is classified as intermediate GI, which is significantly higher than the other two oral nutritional supplements, MG and MB, having the range of low GI of 53.1 and 51.0 respectively. The relatively low AUC of MB may be due to the presence of fiber and protein found in portion size used in this study (**Table 4**). Proteins and fibers are reported to reduce postprandial blood glucose level by slowing gastric emptying rate and fiber can bind to glucose, reducing the availability of carbohydrates absorption [18]. The higher AUC values of ME are comparatively higher than MG and MB, which its carbohydrate may contribute to this factor.

Our results also showed a stable and lower postprandial blood glucose levels for MB, which has the lowest GI (51.0) as compared to the other two oral nutritional supplements. Albeit MG is classified as low GI (53.1), a spike of postprandial blood glucose was observed, however, there was a steady decrease of the blood glucose level before returning to the baseline. But not ME which has the intermediate GI (65.33), contributing the highest postprandial blood glucose levels. There is substantial evidence suggesting that consumption of low GI food minimize blood glucose fluctuations, which could help in prevention and management of diabetes and prediabetes. Our results suggested that MB can minimize the postprandial blood glucose spike and may improve glycemic control.

A number of studies have suggested that low GI diets reduce blood sugar levels in people with diabetes. Low GI diets were effective at reducing glycated haemoglobin (HbA1c), fasting glucose and body weight in people with prediabetes or diabetes. Low GI diet can reduce hepatic triacylglycerol production or increase peripheral clearance, thus lowering the concentrations of triacylglycerol and PAI-1 (plasminogen activator inhibitor-1; a marker of fibrinolytic capacity), reducing cardiovascular events [19]. While high GI diets are linked with greater risk in developing type 2 diabetes [20]. A recent study has reported that those with highest GI diets had up to 33% greater risk of developing type 2 diabetes than those with lowest GI diets [21]. Intriguingly, a systematic review has reported that an increased by 8% in developing type 2 diabetes for every 5 GI points [22].

The rate of hydrolysis of food in the gastrointestinal tract and the rate of gastric emptying determine the absorption rate which determines the extent and duration of the glucose rise after a meal. The dietary GI provides an indication of the rate at which carbohydrates foods are digested. The GI does not just measure the carbohydrate absorption in the small intestine directly but also indicates the effect of other factors in the food tested that can influence the rate of carbohydrate absorption in the small intestine. Adding protein or fiber to carbohydrate-containing food has the potential to reduce the glycemic response and lower the overall GI. Studies have reported that indigestible carbohydrates could reduce post prandial glucose levels and inclusion of fibre in food could also additionally help in reducing postprandial glucose level by slowing its digestion rate or by reducing glucose absorption from the intestine [23], which was reflected by MB, where low GI could significantly lower postprandial glucose level. High GI food are usually rapidly digested and thus contributing to significant fluctuations in blood sugar levels. This could result in counter-regulatory response with the release of free fatty acids, creating an insulin-resistant environment and reduced glucose tolerance [24]. Long term consumption of high GI food has been associated with higher risk of cardiovascular disease, type 2 diabetes, chronic kidney disease, but not with low GI food intake, which is associated with lower risk of diseases [25]. Low GI food tend to delay glucose absorption, resulting in reduced peak insulin concentrations and overall insulin demand. Low GI diets have been shown to improve insulin sensitivity in coronary heart disease patients as lower insulin requirements is needed to handle a standard glucose load and by the enhanced insulin-induced glucose uptake in adipocytes [26]. In healthy subjects, reduced blood glucose level and urinary C peptide output as a measure of insulin secretion have been observed [27]. Several health organizations throughout the world now recommend low GI food in the management of type 2 diabetes and as part of healthy diet recommended to the general population [28].

Our study has demonstrated that MG and MB with low GI is suitable for diabetics whilst for those who do not require strict blood glucose control, ME can be used.

V. CONCLUSION

In the assessment of the nutrient composition and GI value of oral nutritional supplements, the present study concluded that MG and MB have a low GI of 53.1 and 51.0 respectively, whilst ME has an intermediate GI of 65.33. As low GI diet leads to better control of blood sugar levels, thus the formula of MG and MB can be provided as reference opinions for diabetic population.

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