

## Original Article

# The Glycemic Index of standard and diabetes-specific enteral formulas

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A recent meta-analysis showed that foods with a low Glycemic Index (GI) have a clinically useful effect on glycemic control in patients with diabetes. Although diabetes-specific enteral formulas are commonly used for diabetic patients with insufficient oral intake, not much is known about the GI of these formulas. Therefore the purpose of this study was to assess the GI of several diabetes-specific formulas and to compare them with standard formulas. The randomised, double blinded, crossover study included twelve products which were tested in 7 – 10 individuals from a pool of 14 healthy volunteers. After an overnight fast, volunteers were given a portion of a product containing 25 grams of carbohydrate or the reference feed (200 ml containing 25 gram glucose) on different occasions in random order. Postprandial blood glucose levels were measured in venous whole blood for two hours after intake of the products and positive incremental area under the curve (AUC) was calculated for both the products and the reference feed. The GI of the test products was determined by dividing AUC (test products) by the AUC (reference feed). Enteral formulas varied widely in their GI values with the diabetes-specific enteral formulas being characterized by a significant ( $P=0.004$ ) lower GI (average  $\pm$ SEM:  $19.4 \pm 1.8$ ) than standard formulas ( $42.1 \pm 5.9$ ). However, there was an overlap between the two types of formulas. Three of the diabetes-specific formulas had significantly lower GI than 3 of the standard products. Although there is some overlap with the GI of diabetes-specific and standard formulas, certain diabetes-specific formulas had very low GI values, which may be clinically beneficial due to better glycemic control. Therefore the use of diabetes-specific formulas with a low GI should be the preferred option for the nutritional management of diabetic patients in need of nutritional support.

**Key Words:** diabetes, hyperglycemia, clinical nutrition, glycemic index, nutritional treatment.

## Introduction

A major nutritional treatment goal of diabetes is to normalize plasma glucose levels in both the fasting and the postprandial state.<sup>1</sup> Recently, a review by diabetes experts concluded that besides fasting blood glucose, postprandial hyperglycemia is a risk indicator for micro- and macrovascular complications, not only in patients with type 2 diabetes but also in those with impaired glucose tolerance.<sup>2</sup> In addition, several studies documenting postprandial hyperglycemia and the risk for increased mortality suggest that lowering postprandial blood glucose levels might be even more beneficial than lowering of fasting blood glucose levels.<sup>3-5</sup> Therefore, treatment targeting post-prandial blood glucose levels is expected to optimise overall glycemic control and thus improve long-term outcomes, including reduction of cardiovascular disease and all-cause mortality.<sup>3-6</sup> Nutrition and diet are considered, both by medical professionals and health care organizations, as important tools in optimising blood glucose levels.<sup>1,2,6-8</sup> Nutrition has a profound effect on changes in blood glucose and the postprandial blood glucose response is strongly influenced by the specific composition of the diet. Knowledge on the postprandial blood glucose response to particular foods might be useful in determining optimal nutrition for hyperglycaemic patients. However, the postprandial glucose response is influenced among others by product related factors and therefore cannot be predicted

based on product composition only.<sup>9,10</sup> Both the quantity, as well as the quality of the carbohydrates appears to influence blood glucose response to a meal.<sup>11</sup> The presence of fibre in the diet has been shown to reduce post-prandial hyperglycemia,<sup>12</sup> and the amount of fat in a meal has also been shown to influence the glycemic response to these meals.<sup>13</sup>

In order to compare the effects of specific foods on blood glucose response, Jenkins *et al.*, introduced the Glycemic Index (GI).<sup>14</sup> The GI can be defined as the area under the glucose response curve after consumption of a food containing 50 grams of carbohydrate (CHO), expressed as percentage of the area under the blood glucose response curve after intake of 50 grams of CHO in a standard food (glucose solution or white bread).<sup>10</sup> The standard procedure is to assess the GI in healthy volunteers. Nevertheless, the concept of GI appears to be a useful tool in improving glycemic control in diabetic patients as demonstrated by several clinical trials.<sup>12,15-18</sup>

From a meta-analysis of randomised controlled trials it was concluded that low-GI foods in place of conventional or high-GI foods have a clinically useful effect on medium-

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term glycemic control (glycated proteins) in patients with diabetes. On average, the glycated proteins (HbA1c and fructosamine) were reduced by 7.4% when a low GI diet was compared with a high GI diet, a similar benefit as offered by pharmacological agents that also target post-prandial hyperglycemia. The concept of GI appears to be a useful tool in improving glycemic control in diabetic patients as demonstrated by several clinical trials.<sup>19,20</sup> The GI is considered as an important tool in the dietary treatment of diabetic patients by major diabetic and health care organizations.

Especially in the elderly population the prevalence of diabetes is high, approximately 5–20%. Elderly diabetic patients admitted to nursing- or elderly homes are often malnourished and their nutritional status seems to decline further during admission. In order to provide optimal nutrition to these patients, special diabetic feeds for nutritional support were developed. Such products often have, in comparison to standard feeds, a lower carbohydrate (CHO)/fat ratio, mostly with further adaptations on macro- and micro-nutrient composition (such as fructose, MUFAs, protein and fibre). These products are designed to induce a delayed and limited rise in post-prandial glucose levels. However, the GI of most of these products has never been assessed. For this reason, the GI of different clinical nutrition products were determined in this study. Additionally, the GI scores of special diabetic formulae were compared with those of standard products, still commonly used in this patient group.

### Materials and methods

The randomised, double blinded, cross over study was conducted at Maastricht University in the Netherlands.

The Medical Ethical Committee of Maastricht University approved the study protocol and informed consent was obtained from all participants before the start of the study. Twelve enteral formulas were tested in 7 to 10 healthy volunteers, drawn from a pool of 14. Prior to inclusion volunteers performed an oral glucose tolerance test (OGTT). Criteria for healthy volunteers were a fasting glucose level below 6.5 mmol/l and for the OGTT a 2h glucose level below 7.8 mmol/l and glucose levels below 11.1 mmol/l at all times.<sup>31</sup> Exclusion criteria were any metabolic or inflammatory diseases, age below 18 years and a body mass index (BMI) above 30 kg/m<sup>2</sup>. The six enteral formulas specifically designed for the dietary treatment of diabetic or hyperglycemic patients, and the six standard enteral formulas are all commercially available. Seven of the formulas are drink feeds and five formulas are used as tube-feeds. The macronutrient composition of the formulas is shown in Table 1. As some of the formulas contain a relatively low amount of CHO, portions of 25 grams of CHO were chosen for all tests. This procedure had been approved in previous studies.<sup>9,10,14</sup>

Volunteers reported at the laboratory after an overnight fast of at least 10 hours. After a Venflon was placed in a forearm vein and a baseline blood sample was taken, either a portion of product containing 25 gram of available CHO or 25 gram of glucose dissolved in 200 ml of water (reference food) had to be consumed orally within two minutes. Venous blood samples were collected at 15, 30, 45, 60, 90, 120, 150 and 180 minutes after intake of the product. The first 0.5 ml of every sample was discarded because of dilution with saline, and after each

**Table 1a.** Macronutrient composition of the standard enteral formulas per 100 ml.

	Unit	Fortimel†	Nutridrink Multi Fibre†	Biosorb† Drink	Nutrison Standard†	Nutri-drink†	Nutrison Multi Fibre†
Energy	Kcal	100	150	100	100	150	100
Protein	g (En%)	10 (40)	6.0 (16)	4.0 (16)	4.0 (16)	6.0 (16)	4.0 (16)
CHO	g (En%)	10.3 (19)	18.4 (49)	12.3 (49)	12.3 (49)	18.4 (49)	12.3 (49)
Fructose	g	0	0	0	0	0	0
Fat	g (En%)	2.1 (41)	5.8 (35)	3.9 (35)	3.9 (35)	5.8 (35)	3.9 (35)
MUFA	g	1.2	3.5	2.3	2.3	3.5	2.3
Fibre	g	0	2.3	0	0	0	1.5

MUFA: Monounsaturated fatty acids.. †Nutricia N.V., The Netherlands..

**Table 1b.** Macronutrient composition of the diabetes-specific enteral formulas per 100 ml.

	Unit	Diason†	Diasip†	Glucerna‡	Glucerna SR‡	Novasource Diabet§	Diben¶
Energy	Kcal	100	100	100	89	92	90
Protein	g (En%)	4.3 (17)	4.0 (16)	4.2 (16.7)	4.7 (21)	3.4 (15)	4.0 (18)
CHO	g (En%)	11.3 (45)	8.8 (35)	9.6 (34.3)	11.1 (45)	12.5 (54)	8.3 (37)
Fructose	g	2.3	1.9	1.9		3.2	1.6
Fat	g (En%)	4.2 (36)	5.4 (49)	5.4 (49)	3.4 (34)	3.2 (31)	4.5 (45)
MUFA	g	2.8	3.6	3.8	???	1	3.2
Fibre	g	1.5	2.5	1.4	1.18	1.5	2

MUFA: Monounsaturated fatty acids. †Nutricia N.V., The Netherlands; ‡Abbott Laboratories Inc., USA; §Novartis Consumer Health SA, Switzerland; ¶Fresenius Kabi AG, Germany.

sample the catheter was flushed with physiological saline. Glucose concentration was measured in whole blood using a glucose analyser (EML-105, Radiometer, Copenhagen, Denmark). The positive incremental area under the curve (AUC) was calculated according to the trapezoidal rule.<sup>29</sup> For each volunteer the AUC of the test product was expressed as a percentage of the AUC of the reference feed tested in the same volunteer. This results in a value representing the GI for each product. The mean GI for each test product was calculated and a one-factor analysis of variance (ANOVA) was performed to test for differences in GI between the products. In order to determine differences between the products a least significant difference (LSD) post-hoc test was performed. Differences between products were regarded significant when the LSD test showed significant differences (i.e.  $P < 0.05$ ) between the GI's.

### Results

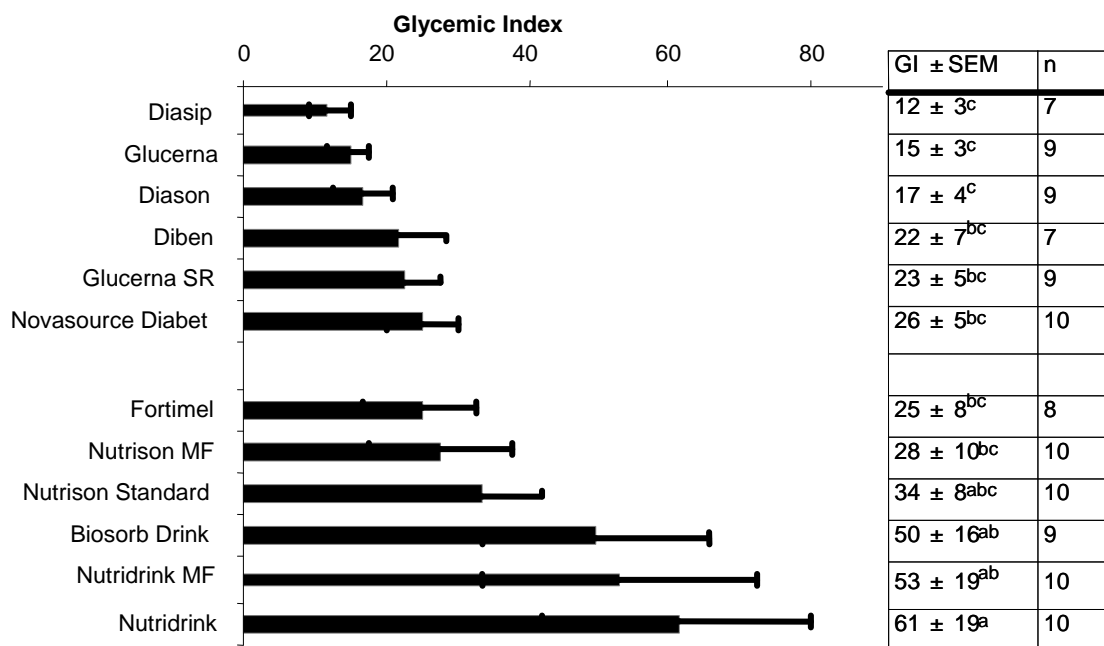
In total 8 male and 6 female volunteers participated in the study. Average age ( $\pm$  standard deviation (SD)) was  $22.6 \pm 2.1$  years, with a range from 20 to 26 and the average BMI ( $\pm$  SD) was  $21.7 \pm 2.0$  (range of 19 to 26). The GI's of the different enteral formulas are shown in Figure 1. The average GI of the diabetes-specific formulas was  $19.4 \pm 1.8$  (mean  $\pm$  standard error of mean (SEM), range 12 to 26). The diabetes-specific formulas showed a significant lower GI ( $P = 0.004$ , Mann Whitney U test) when compared to the GI of the standard formulas ( $42.1 \pm 5.9$ , range 25 to 61).

Analysis of variance (ANOVA) showed that there were significant differences in GI scores between the formulas ( $P = 0.032$ ). In order to find which formulas differed significantly from each other, a LSD multiple-comparison analysis was performed.

The three diabetes-specific formulas Diasip<sup>®</sup>, Glucerna<sup>®</sup> and Diason<sup>®</sup> had significantly lower GI scores than the three standard formulas Nutridrink<sup>®</sup>, Nutridrink Multi Fibre<sup>®</sup> and Biosorb Drink<sup>®</sup>. However, the other three diabetes-specific formulas Diben<sup>®</sup>, Glucerna SR<sup>®</sup> and Novasource Diabet<sup>®</sup> had only significantly lower GI scores when compared with the standard feed Nutridrink<sup>®</sup>. They had no significantly lower GI scores compared to the other standard formulas. Significant results from the LSD test are indicated in Figure 1.

### Discussion

In this study, the diabetes-specific formulas showed statistically significant lower GI values than standard formulas (19.4 versus 42.1 respectively). Although there is some overlap with the GI of diabetes-specific and standard formulas, certain diabetes-specific formulas had very low GIs. These low GI levels found for the diabetes-specific formulas and higher GI levels found for the standard formulae are in line with previous findings on a very limited number of feeds.<sup>30,31</sup> Diets with a low GI have shown beneficial effects on glycemic control<sup>16-19</sup> and even insulin resistance.<sup>15,32,33</sup> Recently it has been reported that consumption of a low GI diet for a period of only 4-weeks by type 2 diabetic patients showed improvement in glycemic control, fasting plasma glucose, HbA1c, glucose utilization and some lipid profiles, in comparison to a high GI diet.<sup>34</sup> This suggests that a low GI diet might play an important role in the treatment and prevention of diabetes and related disorders. In addition, blood lipid status appears to improve as a result of the use of low GI foods.<sup>18,33</sup> This is of particular interest for diabetic patients as they often have dyslipidemia<sup>1</sup> and an increased risk of coronary heart disease.<sup>6</sup> Major health care and diabetic organizations like the World Health Organization<sup>22</sup>



<sup>c/b/a</sup>: GI scores without a common letter differ significantly ( $P < 0.05$ , LSD multiple comparison test)

**Figure 1.** Glycemic Index of tested enteral formulas (mean  $\pm$  SEM)

the Diabetes and Nutrition Group (DNSG) of the European Association for the study of Diabetes<sup>21</sup> and the Dietitians Associations of Australia<sup>24</sup> consider the GI as an important tool in the dietary treatment of diabetic patients.

The GI of the 12 enteral formulas determined in this study vary widely from GI=12 for a diabetes-specific feed up to GI=61 for a standard supplement. The standard errors of some of the enteral formulas are relatively high (>15 for 3 enteral formulas). Methodological issues like testing the reference food only once, measuring plasma glucose levels in venous blood and not in capillary blood and the use of Glucometers could have been attributed to these large standard errors.<sup>35-37</sup> However, despite these large standard errors, three diabetes-specific formulas Diasip<sup>®</sup>, Glucerna<sup>®</sup> and Diason<sup>®</sup> had significantly lower GI scores than the three standard formulas Nutridrink<sup>®</sup>, Nutridrink Multi Fibre<sup>®</sup> and Biosorb Drink<sup>®</sup>. A comparison between the composition of enteral formulas with a low GI (diabetes-specific formulas) and those with a high GI (standard formulas) shows that, in general, a low GI formula is characterized by a lower carbohydrate content, the presence of fructose and a higher fat content containing more MUFA's. Furthermore, the low GI formulas contain relatively high amounts of fibre while standard enteral formulas, especially sip feeds, often do not contain fibre. The fibre containing standard formulas tested here, Nutridrink Multifibre<sup>®</sup> and Nutrison Multi-fibre<sup>®</sup>, contain only 3.1g fibre per portion given while the amount of fibre for the formula with the lowest GI (Diasip<sup>®</sup>) is much higher (7.1g fibre per portion given). This indicates that the presence of fibre could also influence the GI value. Previously, the choice of carbohydrates (e.g. fructose), and fibres has been shown to influence the postprandial glucose responses positively.<sup>11-13, 38, 39</sup>

Similarly to the effect of low GI diets, also diets with a high MUFA and low CHO content have been shown to improve glycemic control as well as lipoprotein status.<sup>40-42</sup> In 1998, the consensus statement on nutritional support of tube-fed patients with diabetes already acknowledged these results and stated that replacing part of the CHO of a product with MUFAs can be an effective way to reach the objectives for good management of diabetes.<sup>43</sup> A meta-analysis of the data concludes that there is good scientific support for high MUFA diets as an alternative to high CHO diets for medical nutrition therapy in diabetes.<sup>44,45</sup> Recently, Hung and co-workers concluded, based on a review of the available evidence, that diets high in MUFAs and fibre and with a low GI appear to be beneficial regarding insulin resistance, glycemic control and blood lipids.<sup>46</sup>

Similar to the effect of diets with low GI or low CHO and high MUFA content, the use of an enteral formula with a relative low CHO and high MUFA content for a period of 12 weeks in diabetic patients has shown to reduce fasting and postprandial plasma glucose, plasma lipids and HbA1c. It also improved clinical outcome parameters, i.e. reduction in fevers, pneumonia, urinary tract infection, and pressure ulcers.<sup>47</sup> A reduction in postprandial plasma glucose has most likely lead to the reduction in infectious complications as hyperglycemia is associated with an increased incidence of infectious com-

plications.<sup>3,48-50</sup> In another study, two of the diabetes-specific enteral formulas that were also tested in this study (Diasip<sup>®</sup> and Diason<sup>®</sup>) were compared with the responses of two standard enteral formulas (Biosorb Drink<sup>®</sup> and Nutrison Standard<sup>®</sup>). Again, the diabetes-specific formulas showed a lower postprandial glucose response in diabetic patients.<sup>51</sup>

Some of the enteral formulas tested in this study have a low CHO and a high fat content. The use of a low CHO, high fat diet for diabetic patients is often discouraged because of the concern that such diets may lead to weight gain.<sup>21</sup> It is important to realize that the enteral formulas that were tested in this study are clinical nutrition products. These clinical nutrition products are used to support hospitalised or otherwise institutionalised patients with an insufficient oral intake who require nutritional support. Such products are used under controlled conditions and are given according to the energy requirements of the patient.

In summary, this study shows that diabetes-specific enteral formulas are being characterized by a lower GI than standard formulas. However, only half of the tested diabetes-specific feeds had a very low GI whereas the remaining ones showed some overlap with the GI of standard formulas. As diets with a low GI have been shown to improve glycemic control, it is to be expected that the use of certain diabetes-specific formulas with a low GI show beneficial effects in the nutritional management of diabetic patients in need of nutritional support and should therefore be the preferred option.

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## Original Article

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## 标准的和糖尿病特定肠道配方餐的血糖指数

最近的一项元分析结果表明,低血糖指数 GI 的食物在临床上对糖尿病患者具有控制血糖水平的作用。尽管糖尿病患者口腔摄食不足,通常使用糖尿病特定肠道配方,但对这些配方的 GI 指数知道的不是很多。因此本项研究目的是为了评价几种专门为糖尿病特定配置的肠道配方餐的 GI 指数,以及与标准配方餐进行了比较。本项研究是一项随机的、双盲的、代表性的研究,其在 14 个健康的自愿者中选出 7~10 个对 12 种配方餐进行试验。经过一昼夜的禁食后,我们随机地在不同时段给这些志愿者以任意顺序吃含有 25g 碳水化合物的配方餐或参考餐(每 200ml 含 25g 的葡萄糖)进食 2 个小时后,取静脉血测定餐后血糖浓度,然后计算配方餐和对照餐的正向递增 AUC 值。所调查的配方餐的 GI 指数等于被测配方餐的 AUC 值除上对照餐的 AUC 值。肠道配方餐的 GI 值十分不同,肠道配方餐的特点是 GI 值(平均值±SEM: 19.4 ± 1.8)显著低于标准的配方餐(42.1 ± 5.9) (P=0.004)。但是肠道配方餐和标准配方餐有一个交迭。三种专门为糖尿病患者配置的配方餐的 GI 值要比三种标准餐的 GI 值明显低。尽管有些糖尿病特定配方餐和标准配方餐的 GI 值交迭,某些糖尿病特定配方餐的 GI 值很低,这些 GI 值低的糖尿病特定配方餐在临床上能更好的控制血糖。因此,低 GI 值的糖尿病特定配方餐是对那些需要营养支持的糖尿病患者营养管理的首选。

**关键词:** 糖尿病、高血糖症、临床营养、血糖指标、营养调理。