2009

Effects of kefirs on glycemic, insulinemic and satiety responses

Kai Ling Kong

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Effects of kefirs on glycemic, insulinemic and satiety responses

by

Kai Ling Kong

A thesis submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Nutritional Sciences

Program of Study Committee:
Suzanne Hendrich, Major Professor
Pamela White
Wendy White

Iowa State University
Ames, Iowa

2009

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DEDICATION

Dedicated to my Lord and Savior, Jesus Christ

Let all that I am praise the Lord;
with my whole heart, I will praise his holy name.

Let all that I am praise the Lord;
may I never forget the good things he does for me.

Psalm 103: 1-2
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**EFFECTS OF KEFIRS ON GLYCEMIC, INSULINEMIC AND SATIETY RESPONSES**

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**GENERAL CONCLUSIONS**

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ACKNOWLEDGMENTS

First and foremost, I would like to thank my major professor, Dr. Suzanne Hendrich, for her enthusiasm, intellectual support, generosity and encouragement during my years in her laboratory at Iowa State University. I thank her for giving me many opportunities to be involved in different projects that have facilitated my growth as a scientist. I thank her for always challenge me and help me to develop creative ideas.

I wish to thank my committee members, Dr. Pamela White and Dr. Wendy White, for giving me comments and suggestions of my project. I thank them for their efforts and time in reviewing my thesis. I also wish to thank Jeanne Stewart who is an Associate Scientist at the Nutritional and Wellness Research Center, Iowa State Research Park. I thank her for her help, discussion, advice and expertise with laboratory instruments, techniques and skills. I thank her for her patience and kindness.

I acknowledge the support and love from my family back in Malaysia, especially my parents, during my study. This thesis would not have been possible without their encouragement. I would like to express my sincere gratitude to Sarah Roberts and her family. I thank her help with developing my writing skills, and help editing of this thesis. I also thank her for her patience, constant encouragement and faithful prayer.

Last but not least, I am grateful to my friends and family members of Walnut Creek Community Church. I thank them for their faithful prayer and spiritual encouragement. It is because of these people that I can truly see God’s plan for my life and how much He loves me.
We hypothesized that three types of kefir (Lifeway® Low Fat Strawberry Kefir, ProBugs Kefir, orange flavor, and Lifeway® Low Fat Plain Kefir) would have low glycemic index (GI), high insulinemic index (II) and high satiety index (SI). Secondarily, we hypothesized that there would be no significant correlations among postprandial satiety, glucose and insulin responses. Lastly, we hypothesized that kefir, like other dairy products, would have dissociation of GI and II. To test our hypotheses, this study was divided into three phases. In Phase I, a portion of Lifeway® Low Fat Strawberry Kefir (S group) and a portion of ProBugs Kefir, orange flavor (O group) containing 50 g of available carbohydrates were tested. In Phase II, a portion of Lifeway® Low Fat Plain Kefir (P group) containing 25 g of available carbohydrates were tested. In Phase III, 240-kcals portions of all three types of kefirs were tested. In all phases a single meal, randomized crossover design was performed in which the test meals were fed to 10 healthy, male and female adults. The total glucose AUC of S group (p< 0.0023), O group (p< 0.0002) and P group (p< 0.0002) were significantly lower compared with their respective glucose controls. A slight, but not significant inverse relationship between glycemic and satiety responses was observed with kefir beverages (r = -0.87; P = 0.13). Using a variance of component analysis, it was found that in the future, a significant relationship between the correlated effects of the treatments on GI and SI can be further tested by increasing the number of subjects to 12. Like other dairy products, kefir showed a dissociation of GI and II. Kefir can potentially be a useful food choice for patients with diabetes who are required to control their blood glucose levels.
GENERAL INTRODUCTION

Introduction

According to the World Health Organization (WHO), by 2015 an estimated 2.3 billion adults will be overweight [Body Mass Index (BMI) of $\geq 25$ kg/m$^2$], and more than 700 million will be obese (BMI of $\geq 30$ kg/m$^2$) (2008a). Obesity greatly affects the overall quality of life. It is the major contributor for chronic diseases such as: type 2 diabetes, cardiovascular disease, hypertension, strokes and some types of cancer (WHO/FAO, 1998; Wild et al., 2004; 2008a). When the per capita nutrient consumption in the United States, between 1909 and 1997 was compared with the prevalence of type 2 diabetes, Gross and colleagues observed a strong correlation between the consumption of refined carbohydrates and the prevalence of type 2 diabetes (Gross et al., 2004). Therefore, carbohydrates, in terms of both quantity and of quality, are receiving significant attention in current laboratory and clinical studies.

Glycemic index (GI) was first introduced by Jenkins and colleagues in 1981 to assess and classify different carbohydrate-rich foods according to their effects on postprandial glycemia (Jenkins et al., 1981). The original purpose of the GI was to provide additional information to help patients with diabetes to better control their blood glucose levels. Low-GI foods cause a smaller insulin response and a slower release of glucose into the bloodstream compared with high-GI foods. Later studies have shown that high-GI diets are independently associated with an increased risk of developing obesity, type 2 diabetes, cardiovascular disease, insulin resistance, and cancer (Livesey et al., 2008). As a result, a great deal of attention has been focused on the health benefits of consuming low-GI diets.
Generally speaking, dairy products have low GI values. Based on the 2002 International Table of Glycemic Index and Glycemic Load Values, four types of dairy products were tested for GI: ice cream, GI = 61 (regular, mean of five studies); milk, GI = 27 (full-fat, mean of five studies); milk, GI = 32 (skim, one study); fermented milk, GI = 11 (3% fat, mean of two studies) and yogurt, GI = 14-38 (from lower value for non caloric sweetener to higher value for caloric sweetener, nonfat to low fat, range of 14 studies) (Foster-Powell et al., 2002). Our study is interested in kefir, the type of milk product that is commonly used in most Eastern Europe countries. Until the present time, no study has measured the GI of kefir. Today, kefir is becoming increasingly popular. Some researchers believe that the various health-promoting properties of kefir outweigh those of yogurt (Lopitz-Otsoa et al., 2006). With the increase of diabetes worldwide, it is worth examining if kefir can bring positive effects in helping to combat this pandemic disease.

Most of the foods tested for GI values have not been measured for their concurrent postprandial insulinemic responses. According to Del Prato et al. (1994), chronic, physiologic hyperinsulinemia can lead to the development of insulin resistance. Besides that, hyperinsulinemia is one of the risk factors in the development of many diseases, such as obesity, diabetes, cancer and dyslipidemia ((DeFronzo et al., 1991; Brouns et al., 2005). While the measurement of postprandial blood glucose responses is important, the measurement of postprandial insulinemic responses is equally important. The concept of insulin index (II) of foods generated by 1000-kJ (240-kcals) was developed by Holt et al. (1997) in order to systematically rate the postprandial insulinemic responses of different type of foods. II is calculated in the same fashion as the GI. The II of different type of kefir drinks will be measured in this study.
In general, pure carbohydrates, sugars and starchy foods have a high correlation between glycemic and insulinemic responses (Lee et al., 1998). However, studies have shown that non-starchy foods can produce higher insulin responses than expected from their GI (Gannon et al., 1988; Holt et al., 1997; Ostman et al., 2001). This is because carbohydrates are not the only stimulus for insulin secretion. There are a number of insulinotropic factors that mediate postprandial insulin secretion including fructose, certain amino acids, fatty acids, and gastrointestinal hormones such as gastric inhibitory peptide, glucagon, and cholecystokinin (Nuttall et al., 1991; Morgan, 1992). Most recently, milk products were shown to elicit unexpectedly high insulin AUCs compared with the predicted insulin AUCs from their GI values (Ostman et al., 2001; Liljeberg et al., 2001). For example, in Ostman et al.’s study, they tested one type of regular milk and two types of fermented milk: ropy milk and filmjolk by using white bread as the standard. The GI values for all three milk products were very low, ranging from 12 to 30; however, the II values were very high relative to their GIs (reported to be similar with the reference meal’s value). Kefir is a kind of fermented milk product, which is somewhat similar with ropy milk and filmjolk. Therefore, the present study is interested in examining the relationship of GI and II of kefir and to further confirm the finding of Ostman et al., which is the dissociation of GI and II of dairy products.

Varied postprandial metabolic events elicited by high GI and low GI diets are hypothesized to have potential effects on satiety (Holt et al., 1995). Many studies have been conducted to examine the relationship between glycemic index and satiety. However, the results of the studies are inconsistent. Some found no effect of GI on satiety and food intake, while others found a significant suppression of hunger and appetite after consumption of the
low GI diets (Bornet et al., 2007). In 1995, Holt and colleagues saw the need for developing a system to produce a table that could demonstrate the energy-satiety ratio of a list of common foods; thus, introducing the concept of satiety index (SI) (Holt et al., 1995). Holt et al. believed that energy-equivalent loads of the different nutrients can have different effects of satiety, thermogenesis, carbohydrate storage and fat storage. Even though a number of studies have shown different types of nutrients and foods satisfy hunger to varying extents, we still have a limited understanding of the complex interacting mechanisms of satiation (Holt et al., 1995). One purpose of the present study is to measure the satiety index of kefir drinks. We are interested in knowing the SI score (%) of kefir compared with the list of 38 foods tested by Holt et al. on an isoenergetic basis. Moreover, in a later publication, Holt et al. used the SI scores (%) of 38 foods to determine whether the postprandial increments in subjective satiety, plasma glucose and insulin responses were interrelated (Holt et al., 1996). This is because Holt and colleagues believed that postprandial increments in plasma glucose and/or insulin are likely to be among the physiological mechanisms responsible for the satiating effects of foods. Therefore, our study is also designed to determine the interrelationships among postprandial satiety, glucose and insulin responses.

In summary, the objectives of this study were: 1. Determine the glycemic, insulinemic and satiety indexes of three types of kefir (Lifeway® Low Fat Strawberry Kefir, ProBugs kefir, orange flavor, and Lifeway® Low Fat Plain Kefir); 2. Determine the interrelationship among postprandial satiety, glucose and insulin responses; 3. Examine the relationship of GI and II of kefir to further confirm the dissociation of GI and II of dairy products.
**Thesis Organization**

This thesis contains a general introduction, a literature review focusing mainly on glycemic index (GI), insulimetic index (II) and satiety index (SI). Kefir-yogurt-like fermented milk product was discussed briefly in the literature review. The paper entitled “Effects of kefirs on glycemic, insulimetic and satiety responses” will be submitted to British Journal of Nutrition. A general conclusion is included following the paper.
LITERATURE REVIEW

Obesity and Diabetes in United States

According to the World Health Organization (WHO), by 2015 an estimated 2.3 billion adults will be overweight [Body Mass Index (BMI) of $\geq 25 \text{ kg/m}^2$], and more than 700 million will be obese (BMI of $\geq 30 \text{ kg/m}^2$) (2008a). The high prevalence of being obese and overweight mostly exists in developed countries with the United States as one of the most severe. 65% of adults in the United States are overweight and 30% are obese (Muoio et al., 2006). Obesity greatly affects the overall quality of life. It is the major contributor for some chronic diseases, for example type 2 diabetes, cardiovascular disease, hypertension, stroke and some types of cancer (WHO/FAO, 1998; Wild et al., 2004; 2008a). Among these diseases, type 2 diabetes has the highest correlation with obesity. 90% of the type 2 diabetes cases in western countries are due to overweight or obesity (2008b). According to the Centers for Disease Control and Prevention, there was a 765% increase in type 2 diabetes cases from the year 1935 to 1996 (Gross et al., 2004). WHO projects in the next 10 years there will be a 50% increase in diabetes deaths worldwide (2008a).

Inevitably, genetic predisposition plays a role in causing obesity and type 2 diabetes; however, we can not deny the fact that sedentary lifestyles and the increased availability of energy-dense, micronutrient-poor foods, promote these conditions in most industrial countries (Perusse et al., 2000; Aguilar-Salinas et al., 2005). Among all the macronutrients, dietary fat has been thought to be an important determinant of body fat, and several mechanisms have been proposed (Van Amelsfort, 1989; Astrup et al., 1993, 1994, 1995). As a result, for the prevention and treatment of diabetes, American Diabetes Association (ADA) guidelines emphasize controlling dietary fat in terms of source and amount (2008c). The
World Health Organization also promotes the minimum intake of fats and advocates the shift of saturated fat to unsaturated fat (2008a). However, does this approach (reduce the intake of dietary fat) work in stopping the rapid increase of obesity and type 2 diabetes? Although the percent of energy consumed from fat has decreased from 42 to 34%, the prevalence of overweight and obese has risen tremendously over the last three decades in the United States (Ludwig, 2000). In 2003, Pirozzo reviewed six different long-term studies on low-fat diets in controlling weight gain (Pirozzo et al., 2003). A total of 594 overweight or obese subjects participated in these six trials. The duration of the intervention varied from 3 to 18 months with 6 to 18 months of follow-up. His review shows that low-fat diets could not sustain weight loss in obese or overweight people. Therefore, these findings suggest that factors other than dietary fat cause the rapid increase of obesity rate.

Gross and colleagues showed that more calories are now obtained from carbohydrates to compensate for the low-fat food intake (Gross et al., 2004). Gross and colleagues examined the correlation between the consumption of refined carbohydrates and the prevalence of type 2 diabetes in the United States. In this study, the per capita nutrient consumption in the United States between 1909 and 1997 obtained from the United States Department of Agriculture was compared with the prevalence of type 2 diabetes obtained from the Centers for Disease Control and Prevention. In a multivariate nutrient-density model, the results showed that there is a strong correlation between the consumption of refined carbohydrates and the prevalence of type 2 diabetes in United States. Therefore, carbohydrate in terms of both quantity and quality is receiving significant attention in the current scientific and clinical studies. Some well-established scientists believe it is the
increased intake of carbohydrate that causes the ever-increasing rate of obesity and type 2 diabetes (Ludwig, 2000; Pawlak et al., 2002; Brand-Miller et al., 2002).

Carbohydrate is the most common source of energy. It is the easiest macronutrient to be absorbed by human body compared with protein and fat. The current focus on carbohydrate is how it can affect postprandial blood glucose. One method that has been developed to rank carbohydrate-rich foods based on their physiological effect is glycemic index (GI) or glycemic load (GL).

**Glycemic Index**

**A) The development of glycemic index**

Glycemic index (GI) was first introduced by Jenkins and colleagues in 1981 to assess and classify different carbohydrate-rich foods according to their effect on postprandial glycemia (Jenkins et al., 1981). This concept was developed to better understand the physiological responses of carbohydrate in the diet. However, before this concept was introduced, carbohydrates in foods were defined as available or unavailable for humans based on their chemical structures (Southgate, 1976). Chemical structures of available carbohydrate are for example, those in the disaccharides (maltose, sucrose, and lactose), α-1,4 linkages of amylose, α-1,4 and α-1,6 linkages of amylopectin; whereas chemical structure of unavailable carbohydrate includes β-1,4 linkages of fiber such as, cellulose, hemicelluloses and pectin. In other words, the available carbohydrate foods for humans are those that can be absorbed by the small intestine and the unavailable carbohydrate foods are foods that can not be absorbed by the small intestine. It was believed that all available carbohydrates in all foods were biologically equivalent. Therefore, in 1950, in order to help patients with diabetes manage their diets, the American Dietetic Association, the American
Diabetes Association, and the U.S. Public Health Service developed a food exchange list (Caso, 1950; Laine et al., 1987). In the exchange list, foods that are alike are grouped together. Foods on each list have approximately the same amount of carbohydrate, protein, fat and calories. All the choices on each list are equal; therefore, any food on the list can be exchanged for any other food on the same list. There are three main groups in the list: carbohydrate group; meat and meat substitute group; and fat group.

Later, in the 1970s, multiple research studies showed that not all the available carbohydrates in foods gave the same physiological responses. In a series of studies, Crapo and colleagues tested postprandial blood glucose and insulin responses to different types of simple and complex carbohydrates. Their results showed that postprandial blood glucose and insulin responses were not the same for a standard weight of carbohydrate in different carbohydrate-containing foods (Crapo et al. 1976, 1977, 1980, 1981). For example in one study, 50 g carbohydrate in dextrose, rice, potato, corn and bread were tested in 16 normal healthy subjects in a randomized crossover study design. The results showed that dextrose and potato elicited similar and greater plasma glucose and insulin responses compared with rice, corn and bread. Besides that, Jenkins and colleagues believed that the food exchange list used by many patients with diabetes may not reflect the physiological effect of foods. Therefore, in 1981, they developed a standard procedure to measure the glycemic response of different foods by comparing a reference meal with a glucose solution (see Methodology of GI below). They published the first glycemic index list of 62 commonly eaten foods (Jenkins et al., 1981). They used this GI food list to supplement information in food tables. They believed their finding could help patients with diabetes to better control their postprandial blood glucose.
Table 1: Glycemic index of selected foods (adapted from Jenkins et al., 1981)

<table>
<thead>
<tr>
<th>Food</th>
<th>GI Glucose =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bread (white)</td>
<td>69</td>
</tr>
<tr>
<td>Rice (white)</td>
<td>72</td>
</tr>
<tr>
<td>Spaghetti (white)</td>
<td>50</td>
</tr>
<tr>
<td>Sweetcorn</td>
<td>59</td>
</tr>
<tr>
<td>All-Bran</td>
<td>51</td>
</tr>
<tr>
<td>Cornflakes</td>
<td>80</td>
</tr>
<tr>
<td>Carrots</td>
<td>92</td>
</tr>
<tr>
<td>Potato (instant)</td>
<td>80</td>
</tr>
<tr>
<td>Beans (kidney)</td>
<td>29</td>
</tr>
<tr>
<td>Lentils</td>
<td>29</td>
</tr>
<tr>
<td>Banana</td>
<td>62</td>
</tr>
<tr>
<td>Raisins</td>
<td>64</td>
</tr>
<tr>
<td>Ice cream</td>
<td>36</td>
</tr>
<tr>
<td>Milk (whole)</td>
<td>34</td>
</tr>
</tbody>
</table>

B) Methodology of GI

Glycemic index is defined as the incremental area under the blood glucose response curve (IAUC) after the consumption of 50 g available carbohydrates in a meal divided by the incremental area under the curve of 50 g available carbohydrates in a reference meal, which is a glucose solution which is sometimes replaced by 50 g glucose equivalent of white bread (Wolever, 1991).

\[
\text{GI} = \frac{\text{Incremental blood glucose area of test food}}{\text{Incremental blood glucose area of reference food}} \times 100
\]
In order to obtain the greatest precision in GI values, the variation among subjects is recommended to be minimized. Usually, only healthy subjects are recruited for GI test. It is believed that the subjects’ physiological condition, for example insulin sensitivity and glucose tolerance status, could influence the glycemic response to food (Brouns, 2005). Therefore, individuals with type 1 or 2 diabetes, or individuals who are glucose intolerant are excluded. No tobacco use is another exclusion criterion. This is because tobacco may cause acute insulin resistance (Attvall et al., 1993; Frati et al., 1996).

The day before the GI test, subjects are advised to refrain from vigorous physical activity. According to Mikines et al. (1988), vigorous exercise prior to the test can improve insulin sensitivity by increasing muscle glucose uptake. In their study, seven healthy untrained young men were recruited to go through four sequential euglycemic hyperinsulinemic clamps after rest (R), immediately after exercise (E) and 48 h after 60 min of 150 W ergometer exercise (ER). The data demonstrated that the insulin-mediated glucose uptake was higher on E and ER days compared with R days. The GI test is recommended to be done in the morning (at breakfast time) after 10-14 hours of fasting. According to Brouns (2005), this fasted condition is the most stable condition of the subjects because meal influences (breakfast meal) can be avoided in the test. In Wolever & Bolognesi’s study, there was a significant difference in the glycemic response to cereals when tested in the morning and at lunchtime (Wolever & Bolognesi, 1996).

On the day of the meal tolerance test, a portion of food containing 50 g of available carbohydrate (total carbohydrate minus dietary fiber) is recommended to be given to the subjects. However, some foods have a low to moderate amount of carbohydrate per serving. Therefore to avoid an unrealistically large serving of low carbohydrate density food, 25 g of
available carbohydrate portion is allowed with a corresponding 25 g of reference meal (Brouns, 2005). One example of food with very low carbohydrate is carrot (5.1 g of available carbohydrate per 72 g) (Pennington, 1998). In order to get 50 g of carbohydrate, approximately 706 g of carrots would be required to be ingested by the subjects. Therefore it is a very unrealistic portion size, which the subjects would not be able to finish in a short amount of time (15 minute time limit). In this case 25 g of carbohydrate load is permitted to apply for GI test of carrots, but at the same time, the reference meal has to be reduced to 25 g of carbohydrate. Data have shown a range of 25 to 50 g of available carbohydrate is suitable for GI testing. Available carbohydrate of less than 25 g might be considered for foods that have very low available carbohydrate content, but it is not recommended. This is because so far not many GI studies were conducted with less than 25 g of available carbohydrate; therefore the results are difficult to compare (Brouns, 2005).

To date, more than 90% of the GI tests were done by using glucose or white bread as the reference meal (Foster-Powell et al., 2002). The original work of Jenkins was using 50-g of glucose solution as the standard reference meal. However, throughout the course of GI development, some researches prefer white bread over glucose drink. The excessive sweetness of the glucose drink can bring nausea to the subjects. In 1982, Thompson et al. showed that the glucose solution has high osmotic effect; hence it may delay gastric emptying (Thompson et al., 1982). Glucose and white bread do not have the same glycemic response (GI glucose = 100; GI white bread = 70). Therefore, in order to convert from glucose to white bread as the reference meal, the GI value has to be multiplied by 1.4 (Food and Agriculture Organization, 1998). GI values using glucose and white bread correlate very
well \((r = 0.98)\) (Wolever et al., 1991). When compare GI food values, it is advised to know
the reference meal used.

When subjects are given the test or reference meal, they are required to finish the
meal within 5-10 min for liquid food and 10-20 min for solid food (Brouns, 2005). Jenkins
et al. demonstrated that prolonging the time of ingestion from a few minutes to several hours
has a huge impact on glycemic responses on both liquid and solid food (Jenkins et al., 1990).
When the rate of ingestion is decreased, the release of hormones such as gastric inhibitory
polypeptide and insulin is reduced. This delay of hormones secretion reduces the rate of
nutrient delivery to the body, in this case glucose. A baseline blood sample is obtained by
capillary finger-stick before the subjects have their meal. After their first sip/bite of the meal,
subjects resume fasting and subsequent capillary finger-stick blood samples are obtained at
15, 30, 45, 60, 90 and 120 min for normal, healthy subjects and 15, 30, 45, 60, 90, 120, 150,
180 min for patients with diabetes (Brouns, 2005).

The method of blood sampling in GI test plays a crucial role in measuring the
postprandial glycemic response. Arterial blood is the most ideal source of blood sample.
However, it is risky and invasive to obtain arterial blood and as a result, capillary blood is
used in most of the GI studies. Venous sampling was used in some of the GI studies, but
venous and capillary blood show significant differences in postprandial glycemic response.
This is because the tissues consume glucose; therefore the glucose concentration in
peripheral vein is lower than that in artery (Brouns, 2005). Also, it has been confirmed that
venous glucose measurement provides more variation than did the capillary blood. In an
interlaboratory study, GI values of four centrally provided foods (instant potato, rice,
spaghetti and barley) and locally obtained white bread were tested in 8-12 individuals in
each of seven centers using the method recommended by FAO/WHO. The results showed that the standard deviation (s.d.) of center mean GI values was significantly reduced from 10.6 (range 6.8-12.8) to 9.0 (range 4.8-12.6) when venous blood data was excluded (Wolever et al. 2003).

In terms of the area under the curve (AUC) calculation, there are several methods. The methods which are mostly used (Brouns, 2005) include:

1) Total AUC;
2) Incremental area until first return to baseline
3) The area over the baseline under the curve, ignoring area beneath the baseline;
4) Incremental area using the lowest blood glucose as the baseline;
5) The net incremental AUC (apply trapezoid rule for all increments positive and negative)

However, the method recommended by the Food and Agriculture Organization (1998) is the incremental AUC (method 4) (Brouns, 2005). This method does not take into account the area under the fasting concentration, which is zero time point. This is the most widely used method by most of the researchers including the founder of GI concept, Jenkins. When interpreting the results of different GI studies, it is necessary to determine the method used by the authors. This is because GI results do not agree with each other among some of the methods (Brouns, 2005).

When calculating GI, individual IAUC of reference food was advised to be used instead of the average IAUC reference food of a group. This is because overall glycemic response in the blood circulation is the sum of net entry of exogenous glucose from the portal vein and endogenous glucose from hepatic output, and net removal of glucose by tissues
(Englyst et al., 2005). Due to biological variation in hepatic glucose output and tissue glucose uptake among individuals, postprandial glycemic responses can be very different from one subject to another.

C) Glycemic Load

The GI value predicts the blood glucose response after the consumption of a typical 50 g available carbohydrate of a food, but it does not tell us the serving size of this amount of carbohydrate. On the other words, GI values provide a measure of carbohydrate quality of food but not the quantity (Foster-Powell et al., 2002). Therefore, in 1997, the concept of glycemic load (GL) was introduced (Salmeron et al., 1997a; Salmeron et al., 1997b). GL is used to quantify the overall glycemic effect of a serving of food.

\[
GL = \frac{\text{the amount of available carbohydrate contained in a specified serving size of the food}}{100}
\]

High GI food does not always have a high GL value. Let’s take a carrot as an example. Carrot has a high GI value (GI=131). However a 3 oz serving of carrot is small (GL=11.8). This is because carrot is not a high carbohydrate food. There is only 9 g of carbohydrate in 3 oz carrot. As a result, patients with diabetes should not solely refer to GI values of food to make their food choices. In the revised international table of glycemic index, the GL of food per serving is listed (Foster-Powell et al., 2002).
Table 2: Glycemic Load of selected foods (adapted from Foster-Powell et al., 2002)

<table>
<thead>
<tr>
<th>Food</th>
<th>GI Glucose = 100</th>
<th>Available CHO (g/serving)</th>
<th>GL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croissant</td>
<td>67</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Cranberry juice drink</td>
<td>56</td>
<td>29</td>
<td>16</td>
</tr>
<tr>
<td>Gatorade</td>
<td>78</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Baguette (white, plain)</td>
<td>95</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>All-Bran</td>
<td>51</td>
<td>23</td>
<td>9</td>
</tr>
<tr>
<td>Special K</td>
<td>69</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Rice (white)</td>
<td>69</td>
<td>43</td>
<td>30</td>
</tr>
<tr>
<td>Milk (skim)</td>
<td>32</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Apple</td>
<td>40</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Beans, dried</td>
<td>36</td>
<td>30</td>
<td>11</td>
</tr>
</tbody>
</table>

D) Implications of GI on health

The rate of glucose being released into the bloodstream and the duration of the rise in postprandial blood glucose levels is known to cause many hormonal and metabolic changes that could affect health and disease parameters (Brouns et al., 2005). A recent systematic review and meta-analysis by Livesey and colleagues (2008) showed reduced risk markers related to persons who are overweight, obese, diabetic or at risk of coronary heart disease when low GI/GL diets were used in the intervention. This meta-analysis was done by collecting data from 45 controlled dietary intervention trials on GI reported in the literature before January 2005. There were 972 subjects per treatment arm of all ages (study group mean ages 10 to 63 y) with both males (511) and females (461). Several observational studies, clinical trials, meta-analyses and mechanistic studies in animal models also showed that diets with high GI/GL are independently associated with increased risks of developing obesity, type 2 diabetes, and cardiovascular disease. The following thesis will discuss some of these studies and how the use of low GI/GL diets has brought improvement to those diseases.
a) **Weight management and obesity**

Tremendous emphasis has given to the reduction of dietary fat intake when it comes to the prevention and management of overweight and obesity. However, low-fat diets may help with short-term weight loss, but not with long-term effectiveness. This is shown by the Women’s Health Trial Feasibility Study done by Sheppard and colleagues (Sheppard et al., 1991). 303 women who were ≤ 150% of their ideal weight were enrolled in this study and assigned to either the low-fat diet group (fat intake = 22% of energy) or control group (fat intake = 39% of energy). The results demonstrated that women in the low-fat diet group lost 3.2 kg of body weight by six months, but by 24 months some of this was regained and they had lost only 1.9 kg. Consequently, the weight difference between the treatment group and control group after one year was 1.8 kg, which was not significantly different. The reason why low-fat diets are not sustainable are because overweight and obese individuals after losing weight may experience increased hunger (Doucet et al., 2000), decreased resting energy expenditure (Astrup et al., 1999) and decreased fat oxidation (Filozof, 2000). As fat intake is decreased, there is a parallel increase in dietary high GI carbohydrate intake. The GI/GL of the average diet in the United States has been increasing during the past century, especially during the past 20 years based on an ecologic correlation study done by Gross and colleagues when they examined the per capita nutrient consumption in the United States between 1909 and 1997 (Gross et al., 2004). An observational study by Ma et al. revealed that BMI is positively associated with the dietary GI of 572 healthy adults in central Massachusetts. In this study, the average body mass index was 27.4 kg/m² (standard deviation 5.5) and the mean daily dietary glycemic index was 81.7 (standard deviation, 5.5)
(Ma et al., 2005). Many research studies are looking into the relationship of glycemic index with weight management.

Brand-Miller, a researcher who is an advocate of low GI diets, hypothesized that high-GI foods stimulate carbohydrate oxidation and suppress fat oxidation in the postprandial period. This alteration of fuel partitioning hence causes body fat gain (Brand-Miller et al., 2002). Her hypothesis was supported by randomized, controlled, multicenter intervention studies comparing the effects of conventional and low-GI diets on weight control. Ludwig (2002) delineated the mechanism behind Brand-Miller’s hypothesis by evaluating animal studies, human intervention studies and epidemiological studies that examine the relevance of glycemic index for pathophysiological mechanisms affecting body-weight regulation, diabetes, and cardiovascular disease. When a high GI meal is consumed, the glucose released from the meal is rapidly absorbed by the body. A sudden increase of glucose into the bloodstream causes hyperglycemia, which then stimulates insulin release from pancreatic beta cells and inhibits glucagon release from alpha cells. When the ratio of insulin-to-glucagon is high, according to Ludwig, it can alter the normal anabolic responses to food consumption. He believes this condition provokes glycogenesis and lipogenesis, and it suppresses gluconeogenesis and lipolysis. A recent study by Clapp and Lope supported Ludwig’s rationale (Clapp et al., 2007). In this study, after twenty days of low GI diets compared with high GI diets consumption, seven healthy adult women’s caloric requirements were 11% higher, fat oxidation at fasted rest was 27% higher and glucose as well as insulin levels were approximately 40% lower. Ludwig’s own study also showed the circulating levels of fatty acids were lower after consuming high-GI test meals compared with low and medium-GI meals when tested on 12 obese (mean weight 106.6±22.3 kg and height
1.68±0.09 m) teenage boys on three separate occasions using a crossover study protocol (Ludwig et al., 1999). Long-term studies, using animals as models, also demonstrated high-GI diets increased the expression of lipogenic enzymes (fatty-acid synthase) (Kabir et al., 1998) thus increasing lipogenesis.

Based on the glucostatic theory of food intake regulation introduced by Meyer, low blood glucose is one of the metabolic signals for hunger (Mayer, 1953). However, later studies showed it is the transient declines in blood glucose rather than the absolute blood glucose concentration that gives a signal to glucostatic receptors in the central nervous system that fuel is low and the body needs to be replenished (Louis-Sylvestre et al., 1980; Smith et al., 1993; Campfield et al., 1990). A study done by Melanson et al. showed that the more rapid the decline in blood glucose following a meal-induced peak, the higher the hunger ratings (Melanson et al., 1999). Therefore insulin-induced hypoglycemia caused by high-GI food consumption can encourage over-eating and hence promote weight gain as the body homeostatic system attempts to restore energy. Stephan and colleagues’ research showed that postprandial hypoglycemia is very pronounced in obese subjects (Stephan et al., 1972). An opposite phenomenon is observed with low GI-foods. Many short-term studies have shown low-GI foods minimize postprandial insulin secretion, promote satiety and therefore lower subsequent voluntary food intake (Ludwig, 2000; Roberts, 2000; Pawlak et al., 2002; Brand-Miller et al., 2007). A review article written by Roberts concluded that there is an average of 29% more energy intake after consumption of high-GI meals than low-GI meals (Roberts, 2000). For example, 12 obese (mean weight = 106.6±22.3 kg and height = 1.68±0.09 m) teenage boys were given instant oatmeal (high-GI food) and steel-cut oats (low-GI food) with identical energy and macronutrient content at breakfast and lunch.
Throughout the afternoon, ad libitum food intake was monitored. Energy intake was 53% higher for the high-GI group compared with the low-GI one (Ludwig et al., 1999).

**b) Diabetes**

The original purpose of GI was to supplement the existing carbohydrate exchange list used by people with diabetes in meal planning, so that the patients could have an appropriate intake of glucose according to their physiological requirement (Jenkins DJ et al., 1981). However, Gilbertson’s group suggested that low-GI dietary approach could provide a better quality of life for patients with type 1 diabetes compared with carbohydrate exchange dietary approach (Gilbertson et al., 2001). In this study, 104 children with type 1 diabetes were recruited and HbA1c levels, incidence of hypo- and hyperglycemia, insulin dose, dietary intake, and measures of quality of life by a quality-of-life questionnaire completed independently by the parent and child were collected. The results of this study also showed that the flexible low-GI dietary regimen could improve HbA1c (glycosylated hemoglobin) levels without increasing the risk of hypoglycemia. Numerous epidemiological studies suggest that low GI/GL diets may play a role in the prevention and treatment of type 1 (Buyken et al., 2001) and type 2 diabetes (Salmeron et al., 1997a; Salmeron et al., 1997b). Low GI diets can help by improving the glycemic control (Brand-Miller et al., 2003b) and reducing demand on the pancreatic beta cell in the post-prandial period (Pawlak et al., 2002). This is proven by several intervention studies. In Jenkins and colleagues’ study, six healthy male subjects underwent 2-weeks of metabolically controlled high-GI diets and 2-weeks of low-GI diets in random order (Jenkins et al., 1987). During the 2-week low GI diets, subjects showed significant reductions in serum fructosamine (a marker of glucose concentration) and urinary C-peptide (a marker of insulin secretion). These markers showed that low-GI diets
elicited lower concentrations of glucose and insulin. A randomized crossover study by Jarvi
and colleagues showed that patients with type 2 diabetes who consumed low-GI diet had a
30% lower plasma glucose and insulin compared with a high-GI diet (Jarvi et al., 1999).
Giacco and colleague’s study demonstrated that 63 subjects with type 1 diabetes, aged 28 +/-
9 years, and BMI of 24 +/- 0.6 kg/m² who consume low-GI diet for 24 weeks had a decrease
mean of daily blood glucose concentrations and number of hypoglycemic events (Giacco et
al., 2000). In addition, low GI diets can help with increased insulin sensitivity (Pawlak et al.,
2002; Brand-Miller et al., 2008; Livesey et al., 2008). A randomized crossover, high versus
low-GI study done by Clapp and Lopez showed that various indices of insulin sensitivity
were more than 20% higher in the group of consuming low-GI diets when tested on seven
healthy nonpregnant women (Clapp et al., 2007). More recently, Ma et al. conducted a
randomized clinical trial comparing low-GI versus ADA dietary education among 40
individuals (BMI= 35.8 kg/m²) with poorly controlled type 2 diabetes (Ma et al., 2008). This
study consisted of eight educational sessions focusing on a low-GI or and ADA diet. After 12
months of intervention, patients in low-GI diet group had a reduction in the use of diabetic
medication but achieved equal control of HbA1c and blood lipids with the ADA diet group.

c) Cardiovascular disease (CVD)

High level of postprandial blood glucose after the consumption of high-GI diet may
affect risk for cardiovascular disease. For example, a study done in the Hoorn population
(3553 men and women aged 50-75 years in a small town in the Netherlands) showed that
there was a significant relationship between the eight-year risk cardiovascular death and two-
hour post-load blood glucose concentrations in subjects with normal fasting glucose
concentration after adjustment for known risk factors (DeVegt et al., 1999). During 20 years
of follow-up, 1994 new cases of cardiovascular disease were documented among 82,802 women in the Nurses’ Health Study by using food-frequency questionnaires as the assessment of diet and glycemic load (Halton et al., 2006). Among all these cases, a higher glycemic load, but not protein or fat intake, was strongly associated with an increased risk of cardiovascular disease (relative risk of 1.9 comparing highest and lowest quintiles of GI) after multivariate adjustment. Hyperinsulinemia, which is caused by hyperglycemia with the presence of insulin resistance, is associated with dyslipidemia (high very low-density lipoprotein [VLDL] cholesterol, high triglycerides, and low high-density lipoprotein [HDL]). This is because numerous studies have shown a high-GI diet is negatively associated with HDL-cholesterol and positively associated with triglyceride levels. For example, by using the Third National Health and Nutrition Examination Survey, Ford and Liu revealed that Americans who consumed high-GI/GL diets had a lower HDL-cholesterol level (Ford et al., 2001). A systematic review conducted by Clarke et al. showed that when saturated fat was replaced by carbohydrates (with no change in caloric intake), subjects had a significant decrease in HDL-cholesterol and an increase in triglyceride concentration (Clarke et al., 1997). In contrast, low-GI diets have beneficial effect on lipid metabolism (Jenkins et al., 2002; Clapp et al., 2007). For instance, a clinical trial conducted by Ebbeling and colleagues showed that obese young adults (n=23) who consumed low-GI diets for 12 months had a significant decline in plasma triglyceride (Ebbeling et al., 2005). Also, reanalysis of dietary, anthropometric, and biochemical data from the 1986/87 Survey of British Adults (n=2200) showed that low GI diets promote the synthesis of HDL-cholesterol in human body (Frost et al., 1999). This result is echoed by Liu and colleagues’ study which assessed dietary glycemic load in relation with plasma HDL-cholesterol in 185 healthy postmenopausal
women by using food frequency questionnaires (Liu et al., 2001). Lastly, some researchers believe that low-GI diets may outweigh the conventional low fat diet recommended by the American Heart Association in prevention and treatment of CVD (Ford et al., 2001).

E) Low and high GI/GL foods

High GI foods are rapidly digested and absorbed, whereas low GI foods are digested and absorbed slowly. High GI foods produce a higher rise in postprandial blood glucose levels and a greater overall blood glucose response during the first two hours after consumption compared with low GI foods (Foster-Powell et al., 2002). If a food has a GI number higher than 70, it is classified as a high GI food; if a food has a GI number lower than 55, it is classified as a low GI food. Medium GI foods have GIs in the range of 55-70 (Brand-Miller et al., 1998). Generally, low GI foods consist of non-starchy vegetables, fruits, dairy products, lentils and sugars such as fructose and lactose. Medium GI foods include unprocessed grains and mixed dishes. High GI foods are refined grains, potatoes, rice and some types of bread (Franz, 2006). In 2002, Foster-Powell and colleagues brought together all the relevant data published between 1981 and 2001 to compose a reliable international table of glycemic index and glycemic load values. This table contains approximately 1300 separate entries, representing more than 750 different types of food (see Table 2) (Foster-Powell et al., 2002).

a) GI of dairy products and the introduction of kefir

As mentioned above, dairy products have low GI values. Under the category of dairy products of the International Table of Glycemic Index and Glycemic Load Values:2002, four types of dairy products were tested for GI, they are ice cream, milk, fermented milk, and yogurt (Foster-Powell et al., 2002). The GI values (using glucose as the standard) are as
follow: ice cream, GI = 61 (regular, mean of five studies); milk, GI = 27 (full-fat, mean of five studies); milk, GI = 32 (skim, one study); fermented milk, GI = 11 (3% fat, mean of two studies) and yogurt, GI = 14-38 (from lower value for non caloric sweetener to higher value for caloric sweetener, nonfat to low fat, range of 14 studies). Our study is interested in the type of milk products which are commonly used in most Eastern Europe countries, kefir. Up to the present time, no study has measured the GI of kefir. Today, kefir is becoming increasingly popular. Some researchers believe that the various health-promoting properties of kefir outweigh the benefits of yogurt. With the drastic incline of obesity and diabetes world-wide, it is worth to examine if kefir can bring positive effects in helping to combat this pandemic disease.

Like yogurt, kefir is fermented milk, with a uniform creamy consistency and a slightly sour taste. It is originated in the Caucasus Mountains of Russia centuries ago. In the past, kefir has been prepared by using cows, goats, and sheep milk. Lately the dairy industries have been producing kefir from soy milk. The difference of kefir from the other traditional fermented milks (yogurt) is that it is made only from kefir grains (Lopitz-Otsoa et al., 2006). Being considered a source of family wealth among the tribes of Caucasus, kefir grains were passed from generation to generation in the ancient time. However; today, all over the world, traditional kefir can be made by culturing milk with kefir grains (Roberts and Yarunin, 2000). Kefir grains are a small cluster of microorganisms that resemble miniature cauliflower blossoms. They are a soft, white biological mass, consisting of protein, lipids, and a soluble polysaccharide matrix named kefiran that held the mass together (Lopitz-Otsoa et al., 2006). Compared with yogurt, kefir has a larger and more diverse range of microorganisms in its starter culture, which is composed of yeast and bacteria (Marquina et
The kefir beverages used in this study are from Lifeway Kefir, Lifeway Foods, Inc., Morton Grove, IL. The drinks contain the following cultures: *Lactobacillus lactis*, *Lactobacillus rhamnosus*, *Streptococcus diacetylactis*, *Leuconostoc cremoris*, *Lactobacillus plantarum*, *Lactobacillus casei*, *Bifidobacterium longum*, *Bifidobacterium breve*, *Saccharomyces florentinus*, and *Lactobacillus acidophilus* (Lifeway Foods, Inc., 2005a). The coexistence of bacteria and yeast in the kefir is proven to be beneficial to health (Lopitz-Otsoa et al., 2006).

**b) Food factors influencing GI of dairy products**

The glycemic response is easy to measure; however, the mechanism of the response is complicated to identify. One of the important facts about GI concept is that it is not a direct measure of carbohydrate absorption from the small intestine. Rather, it expresses the combined effect of all the physical and chemical properties of a food that can influence the rate of carbohydrate absorption in the small intestine (Englyst et al., 2005) for example, type of carbohydrate, fat content, protein content, presence of anti-nutrients, ripeness, processing and cooking methods (Jenkins et al., 1981). One might wonder why the GI values of dairy products are generally low and what are factors that cause the low postprandial glycemic response. In terms of dairy products, the GI value can be influenced by the type of carbohydrate, fat and protein contents. For kefir, fermentation might play a role as well.

**i) Type of carbohydrate**

Glucose, fructose and galactose are the monosaccharides. By using white bread as a standard, Lee and Wolever reported GI value for glucose is 149±16 and GI value for fructose is 16±4 (Lee et al., 1998). Maltose, sucrose and lactose are the three major disaccharides. Maltose consists of two glucose molecules attached by an alpha-1,4 linkage; therefore its GI
value is similar with glucose. Sucrose consists of one glucose molecule and one fructose molecule, which are bound by beta-1,4 linkage. The GI value for sucrose is 87±6 by using white bread as standard (Lee et al., 1998). Lactose is composed of glucose molecule and galactose molecule, which are bound by beta-1,4 linkage. The GI of lactose was reported to be 68±8 when using white bread as a standard (Östman et al., 2001). Lactose is the main sugar of milk.

However, in other dairy products such as ice cream, yogurt and kefir, sweeteners are used in order to give desirable taste or flavor. In the United States, the main sugar sweeteners used are high fructose corn syrup and sucrose (Basciano et al., 2005; Malik et al., 2006; Parks et al., 2008). The substantial increase in the amount of dietary fructose consumption has drawn tremendous attention. Fructose consumption has controversial effects on lipid and glucose metabolism. Numerous studies have examined the effect of oral fructose, either given alone or together with a meal on carbohydrate metabolism. In a randomized crossover study, 11 healthy subjects were given 75 g of glucose with or without 7.5 g of fructose. The glucose AUC was 19% less when glucose was administered with fructose (Moore et al., 2000). In another study, when 54 g of fructose was substituted for a similar amount of starch in a meal in six individuals with type 2 diabetes and six individual without type 2 diabetes, the results showed that fructose has lowering glycemic effect and it can induce less insulin secretion compare to starch (Abraha et al., 1998). Studies have shown sucrose has the same effect as fructose which can help to lower glycemic response. When sucrose was supplemented to a maltodextrin challenge, Zucker fatty fa/ fa rats showed a significant decrease of postprandial glycemic response (Wolf et al., 2002). While fructose is believed to have lowering glycemic response effect, other researchers have investigated the effect of
fructose on lipid metabolism. The most recent dietary sugars on lipid metabolism study received great public attention (Parks et al., 2008). In this study, Parks and colleagues showed that acute consumption of fructose significantly increased de novo lipogenesis compared with glucose consumption when six healthy subjects [aged (mean ± SD) 28 ± 8 y; BMI, 24.3 ± 2.8 kg/m²] were tested. Other studies also showed that fructose and sucrose can cause hypertriacylglycerolemia and hypercholesterolemia in animals and humans (Mayers, 1993; Frayn et al., 1995). Therefore, mono- and disaccharides are not necessarily high in GI value as might be expected due to their high bioavailability. In this case, fructose not only has a low GI value, but it also could lower the glycemic response of other carbohydrate rich food when consumed together.

ii) **Fat and protein**

Fat reduces glycemic response by delaying gastric emptying via the secretion of glucose-dependent-insulin-releasing polypeptide (GIP) and glucagons-like polypeptide-1 (GLP-1) (Owen et al., 2003). In Owen et al.’s study, healthy subjects were recruited to consume 50 g available carbohydrate of white bread along with 0, 5, 10, 20, or 40 g fat of non-hydrogenated-fat margarine. The results showed that there was no significant incremental AUC of blood glucose reduction when white bread was consumed with 5, 10 or 20 g of fat, but a significant reduction in the incremental AUC of blood glucose (30%) was observed when 40 g of fat was taken with the white bread. On the other hand, some studies demonstrated that fat has no effect on glycemic responses in insulin resistance or subjects with diabetes. For example, when Gannon et al. fed seven male subjects who had untreated noninsulin-dependent diabetes mellitus (NIDDM) with 50 g carbohydrate alone or 50 g
carbohydrate with 5, 15, 30, or 50 g fat as a butter, the glucose response was not smaller (Gannon et al., 1993). According to Gannon and colleagues, this can be explained by the inability of fat to stimulate GLP-1 secretion.

It is believed that protein reduces glycemic response by the amino-acid mediated effects on insulin secretion (Moghaddam et al., 2006). Nuttall et al. conducted a study to determine the effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load (Nuttall et al., 1984). Nine male, subjects with untreated diabetes were recruited. They were given either 50 g of glucose, 50 g of protein or a combination 50 g of glucose with 50 g protein over three consecutive days in a random order. The results showed that protein given with glucose would reduce the plasma glucose rise and increase insulin secretion in some patients with type II diabetes. A more recent study conducted by Moghaddam et al. (2006) agrees with the results of Nuttall et al.. Moghaddam et al. also showed that protein reduced postprandial glycemic responses to a greater extent in subjects (n=20) with higher waist circumference (r = -0.56, P = 0.011) and higher dietary fiber intake (r = -0.60, P = 0.005). They concluded that the effect of protein on glycemic response is highly correlated with subjects’ characteristics.

iii) Fermentation

The production of organic acids during the fermentation process or added organic acid to meals can significantly lower postprandial glucose and insulin responses (Liljeberg & BJORCK, 1998). For example, when 20 g white vinegar was added to a starchy meal (n=10 subjects) (Liljeberg & BJORCK, 1998) or 1 g of vinegar was dressed with lettuce (n=5 subjects) (Brighenti et al., 1991), it lowered the glucose responses in those healthy subjects by more than 30%. Liljeberg and colleagues also demonstrated that consumption of bread
products containing lactic acid, either generated during fermentation or added, decreased postprandial glycemic and insulinemic responses when tested on 11 healthy, normal BMI and aged 26-28 years individuals (Liljeberg et al., 1995; Liljeberg et al., 1996). In terms of regular versus fermented milk products, there is controversial evidence to support the glucose lowering effect of lactic acid. Sanggaard et al. conducted a study to compare whole milk and fermented whole milk, which had the same fat and lactose content (Sanggaard et al., 2004). In this study, they did not observe a lower plasma concentration of glucose and insulin after the fermented milk, but they were able to show that fermented milk certainly had a slower gastric emptying rate than regular milk when tested in eight healthy mean with mean age 23.9 (s.d. 2.7) years and mean BMI 22.8 (s.d. 1.2) kg/m². Another fermented milk study was done by Ostman in Sweden (Ostman et al., 2001). By using regular milk and two commercial Scandinavian fermented milk products (yogurt): ropy milk and filmjolk, Ostman et al. did not observe significantly lower GI values in 10 healthy, normal weight (BMI= 23.4±2.1 kg/m²) subjects for the fermented milk products (GI=15) compare to the regular milk (GI=30). According to Ostman et al., the fermented milk products indeed had a lower GI values; however because regular milk products already have relatively low GI value, the decrease of GI value on filmjolk and ropy milk is not significant. To date, there are two mechanisms proposed to explain this metabolic effect, which fermentation process or added organic acids to meals can significantly lower postprandial glucose and insulin responses. As mentioned in some of the studies above, researchers believed that organic acids delay the rate of gastric emptying therefore flatten the postprandial blood glucose and insulin rise (Hunt and Knox, 1972; Liljeberg et al., 1996).
Insulinemic Index

A) The development of insulinemic index

The GI concept is well established. In order to control the plasma glucose levels in patients with diabetes, postprandial plasma glucose responses have been the focus of many studies. A carbohydrate exchange list is the main tool used by patients with diabetes for controlling their blood glucose levels. Recently, a table of GI values was also introduced as a supplementary tool to those patients. However, most of the foods tested for GI values have not been measured for their concurrent postprandial insulinemic responses. This is because insulin secretion is assumed to be proportional to postprandial blood glucose responses (Brouns et al., 2005). Numerous research studies have shown that a carbohydrate is not the only stimulus for insulin secretion. A number of insulinotropic factors that mediate postprandial insulin secretion include fructose, certain amino acids, fatty acids, and gastrointestinal hormones such as gastric inhibitory peptide, glucagon, and cholecystokinin (Nuttall et al., 1991; Morgan, 1992). Due to these insulinotropic factors, some foods might cause postprandial hyperinsulinemia. Research has shown hyperinsulinemia is one of the risk factors for the development of many diseases, such as obesity, arteriosclerosis, diabetes, cancer and dyslipidemia (DeFronzo et al., 1991; Brouns et al., 2005). According to Del Prato et al., chronic, physiologic hyperinsulinaemia, whether created by exogenous insulin infusion or by stimulation of endogenous insulin secretion, can lead to the development of insulin resistance (Del Prato et al., 1994). Insulin resistance is a key factor that causes metabolic syndrome. As a result, a critic of GI, Hollenbeck, proposed that any estimate of metabolic response should include measurements of both plasma glucose and insulin (Hollenbeck et al., 1986). While the measurement of postprandial blood glucose responses is important for
patients with diabetes in controlling their blood level, the measurement of postprandial insulinemic responses is equally important (Holt et al., 1997).

Insulinemic index (II) is calculated in the same fashion as the GI. The formula for II is as follow.

$$II = \frac{\text{Incremental blood insulin area of test food}}{\text{Incremental blood insulin area of reference food}} \times 100$$

The methodology of II is consistent with the measurement of GI. However, instead of using 50 g of available carbohydrate as the portion of the foods, there are some studies conducted by Holt et al. that used 1000 kJ (240 kcal) portion size (Holt et al., 1996; Holt et al., 1997). This is because 1000 kJ is a more realistic meal in terms of what people habitually eat.

**B) Discrepancy between GI and II of milk**

In general, pure carbohydrate, sugars and starchy foods have a high correlation between glycemic and insulinemic responses (Lee et al., 1998). Combine data from other studies, Björck et al. examined 43 starchy foods and concluded that the postprandial insulin level is higher after the consumption of high-GI, starchy foods than low-GI, starchy foods (Björck et al., 2000). On the other hand, studies have shown that non-starchy foods can produce higher insulin responses than expected from their GI (Östman et al., 2001; Holt et al., 1997).
The GI of milk is in the low range; however, when milk was tested for its postprandial insulin responses, it gives high AUC. Therefore, milk is one of the non-starchy foods which have an inconsistency of GI and II (Ostman et al., 2001; Liljeberg et al., 2001). In Ostman et al.’s single study, they tested one type of regular milk and two types of fermented milk: ropy milk and filmjolk by using white bread as the standard. The GI values for all three milk products were very low, ranging from 12 to 30 which are in accordance with the literature data; however the II values were very high relative to their GIs (reported to be similar with the reference meal’s value). In this study, they also tested the GI and II for lactose solution. The results showed that GI of lactose correlated very well with its II value, suggesting that some milk components can stimulate insulin secretion, but not lactose content. Prior to the study of Ostman et al., inconsistency between GI and II of milk products have been noted in Gannon and colleagues’ study when 50 g carbohydrate of skim milk were given to seven subjects with type 2 diabetes age 64±3 years and with BMI of 32.2±1.7 kg/m² (Gannon et al., 1986). However, this discrepancy has not been acknowledged until the study of Ostman et al. in year 2001. When this intriguing result was observed, Lijeberg and Bjorck decided to conduct a study to confirm the findings of Ostman et al. by supplementing milk to a high-GI white bread and a low-GI spaghetti meal to 10 healthy volunteers, seven men and three women, aged 22-30 years, with normal BMI (Liljeberg and Bjorck, 2001). The insulinotrophic effect of milk in this study is consistent with Ostman et al. which demonstrated that both bread and spaghetti had higher insulin responses when milk was given compared with water. The insulinotrophic effect of milk products has not been understood. There are many potential unexplored mechanisms for the discrepancy of GI and
II. However, two non-carbohydrate components, protein and fat in the milk are believed the most potent insulin secretagogues.

a) Factors causing discrepancy

i) Insulinogenic effect of protein

Different food proteins differ in their effect on glucose metabolism in humans (Holt et al., 1997; Nuttall et al., 1991; Floyd et al., 1966). In term of milk products, according to Nilsson et al., it is the whey fraction of the milk protein which possesses most of the insulinotropic properties in milk products. This is because about 80% of milk proteins are casein and 20% are whey. Casein clots easily to form gel like structure under low pH condition, but not whey. Therefore, when milk gets into the stomach (low pH environment), the only soluble component of milk is whey protein (Nilsson et al., 2004). Whey is then rapidly digested and absorbed to release amino acids into the circulation (Boirie et al., 1997). Studies have shown that certain amino acids are potent insulin secretagogue especially the branched-chain amino acids (leucine, isoleucine and valine) (Schmid et al., 1989). Nilsson and colleagues conducted an experiment mainly to compare an amino acids drink mixture which contains all five amino acids: leucine, isoleucine, valine, lysine, and threonine with whey protein drink (Nilsson et al., 2007). In this study, 12 healthy subjects (aged 20-30; BMI 19.5-25.7 kg/m²) were given drinks consisting of pure glucose or glucose supplemented with free amino acids or whey proteins. Their results showed that the glycemic and insulinemic responses of the amino acid drink mixture mimicked those seen after whey ingestion. All in all, one can say that the whey fraction of milk products which consists of leucine, isoleucine, valine, lysine and threonine are potent stimulators of insulin secretion.
Another possible pathway to explain the insulinotropic effect of milk products proposed by Nilsson and colleagues is via the activation of the incretion system. After a meal digestion, glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) are released. These hormones are important to stimulate the secretion of insulin (Drucker, 2007). Some studies showed that only fat and carbohydrates are the stimulants of GLP-1 and GIP, but less with proteins (Elliott et al., 1993; Hermann et al., 1995; Cataland et al., 1974; Pederson et al., 1975), while other studies have indicated that amino acids do stimulate GLP-1 and GIP release in response to a meal in both healthy subjects and subjects with type 2 diabetes (Simpson et al., 1985; Fieseler et al., 1995; Carr et al., 2008). In Nilsson and colleagues’ study, when whey meal was served to 12 healthy subjects, the AUCs for plasma GIP concentration is significantly higher than the 25 g carbohydrate of white-wheat-bread as reference meal (Nilsson et al., 2004). As a result, this higher GIP response after whey meal may be one of the factors that stimulate insulin secretion.

ii) Insulinogenic effect of fat

Another non-carbohydrate component in milk that is believed to have insulinotropic property is the fat content (Ostman et al., 2001). It is known that fat ingestion can stimulate the secretion of GLP-1 and GIP (Herrmann et al., 1995; Deacon et al., 2005). Collier and O’Dea conducted a study to examine the effect of coingestion of fat on the glucose, insulin, and GIP responses to carbohydrate and protein (Collier and O’Deal, 1983). When eight lean, weight-stable subjects were fed 50 g of carbohydrates (potato) with 50 g of fat (butter), the postprandial glycemic response was reduced but the postprandial insulin response remained as high as the reference meal (50 g of carbohydrate). The results also showed that the addition of fat to carbohydrate meal gave rise to a significant higher plasma
GIP response. As a result, the authors concluded that fat can stimulate the secretion of insulin via the incretin hormone, GIP. Recently, Carr and colleagues conducted a research study that revealed a new perspective towards incretin and islet hormonal responses to fat ingestion in healthy men (Carr et al., 2008). In this study, after fat ingestion, insulin increased immediately and with a peak at 30 to 60 minute time point; however, the circulating incretin levels only began to rise after 30-60 minutes. Therefore, Carr and colleagues proposed that besides activating insulin secretion through a direct action on beta cells, incretins might also stimulate insulin secretion through a neural effect via vagal efferent fibres innervating the pancreas when fat was ingested. Based on the finding of Collier and O’Dea, Hoyt and colleagues decided to investigate if a fat component is the reason causing the dissociation of GI and II in milk products (Hoyt et al., 2005). In this study, they fed nine healthy subjects with both skim milk and whole milk at two separate occasions. However, the results showed that no significant differences existed between GI and II for skim and whole milks. The GI and II for whole milk is 41 and 148 respectively, whereas the GI and II for skim milk is 37 and 140 respectively. Therefore, their results again confirmed with the previous studies that milk is a potent insulin secretagogue, but they ruled out the possible insulinotropic effect of fat content in milk.

b) Milk products and health concern

Hyperinsulinaemia could lead to the development of many other diseases, and milk products have an insulinotropic effect after ingestion. Therefore, should we be drinking milk or consuming dairy products? Since the researchers have not been able to elucidate the mechanism that causes the insulinotropic effect of milk products, should caution be taken
when dietary recommendation of dairy consumption is given to healthy individual or patients with diabetes?

Thus far, there is lack of consensus regarding the effects of milk consumption on the risk of diabetes, obesity, insulin resistance or metabolic syndrome (Pfeuffer and Schrezenmeir, 2006). Few studies have demonstrated an association between higher dairy consumption and lower risk of some metabolic diseases. For example, after 12 years of observation, the 41,254 male participants with no history of diabetes, cardiovascular disease and cancer, at baseline in the Health Professionals Follow-up Study, showed an inverse relationship of dairy intake with risk of type 2 diabetes. In other words, after adjusting for potential confounders, each serving-per-day increase in total dairy intake was associated with a 9% lower risk for type 2 diabetes (multivariate relative risk, 0.91; 95% CI, 0.85-0.97) (Choi et al., 2005). Coronary Artery Risk Development in Young Adults (CARDIA) demonstrated that the 10-year incidence of insulin resistance syndrome was lower by more than two thirds among overweight individuals in the highest category of dairy consumption (≥5/d) compared with those in the lowest category (<1.5/d). Besides insulin resistance, dairy consumption was inversely associated with all other components of the metabolic syndrome as well (Pereira et al., 2002). When the observational study was conducted in the low-income-country Argentina, the same results were shown. In this study, 365 school children age 10±2.3 years from two poor suburbs of Buenos Aires were recruited to determine the association between milk consumption, lifestyle, components of the metabolic syndrome, and insulin resistance. Multiple regression analysis was performed. When insulin resistance was used as the dependent variable, the results showed that there was a significant and positive association between insulin resistance and triglyceridemia (β = 0.007) as well as insulin resistance and
waist circumference ($\beta = 0.024$); however, there was a negative association between insulin resistance and milk consumption ($\beta = -0.135$). As a result, they concluded that increased milk consumption was associated with greater insulin sensitivity, hence decreased risk of type 2 diabetes (Hirchler et al., 2008).

On the contrary, few other recent studies showed negative effect of dairy consumption with some of the metabolic diseases. For example, 1,124 participants of the Hoorn Study demonstrated that higher dairy consumption did not protect against weight gain and development of metabolic disturbances in a Dutch elderly population (Snijder et al., 2008). In the British Women’s Heart and Health Study, 4024 British women ages 60-79 were randomly recruited from primary care centers. Women who never drank milk had lower homeostasis model assessment insulin resistance (HOMA) scores, triglyceride concentrations and body mass index, and higher high-density lipoprotein (HDL)-cholesterol concentrations, than those who drank milk. Therefore, this study implied individuals who do not drink milk may be protected against insulin resistance and the metabolic syndrome (Lawlor et al., 2005).

By and large, the differences in study population, study design, and methodology can contribute to the conflicting results of the beneficial effect of dairy consumption. Before more conclusive results can be proven regarding the negative effects of dairy consumption on metabolic syndrome and insulin resistance, the public should not be advised to avoid dairy consumption. This is because various components of dairy have been suggested to bring other benefits, for example dairy is a good source of calcium and potassium. These two elements are important for the elderly to prevent the development of osteoporosis and for the children to grow. Dairy proteins and peptides enhance the bioavailability of other minerals and trace elements like magnesium, manganese, zinc, selenium and iron (Vegarud et al.,
2000). Besides that, studies have shown dairy intake may promote a healthy lifestyle and better eating habits. Currently in United States, reduction of milk intake among young children and adolescents is a public health concern (Kvaavik et al., 2005). There are numerous epidemiological studies showed that liquid dairy beverages may replace sweetened soda drinks especially in children and adolescents (Johnson et al., 2000; Nielsen et al., 2001; Kranz et al., 2005).

**Satiety index**

**A) Glucostatic theory and postabsorptive metabolic events of low and high-GI diets**

Satiation is defined as the sensation of fullness that develops during the progress of a meal and contributes to meal termination, whereas satiety is defined as the sensation of fullness between one meal and the next (Roberts, 2000). Satiety may determine the length of the intermeal interval and the amount of food consumed during the next eating episode. There are many factors that influence the onset and termination of eating. They can be categorized as external or internal factors. External environment factors include sensory hedonics, tension reduction, social pressure and boredom. Internal factors include humoral and neural signals from the gastrointestinal system and from adipose tissue (de Graaf et al., 2004). One of the external humoral signals that causes the onset and termination of eating is glucose. In 1953, Jean Mayer first proposed the glucostatic theory for short-term appetite regulation. Based on this theory, a decrease in glucose utilization due to its low concentration indicated the onset of meal initiation, whereas an increase in glucose utilization due to its high concentration indicated the termination of meal intake. However, later research studies discovered it is the transient decline in blood glucose rather than the absolute blood glucose concentration that gives a signal to glucostatic receptors in the central nervous system that
fuel is low and the body needs to be replenished (Louis-Sylvestre et al., 1980; Smith et al., 1993; Campfield et al., 1990; Lavin et al., 1996).

Currently, many researchers promote the use of low GI diets to combat the pandemic health issues, obesity and diabetes. Varied postprandial metabolic events elicited by high GI and low GI diets are hypothesized to have potential effects on satiety. Consumption of high GI meals causes a sharp increase in plasma glucose concentration during the early (first hour) postprandial period. The rapid increase of blood glucose stimulates the release of insulin from the pancreatic-beta cells and suppresses the release of glucagon from the alpha cells. According to glucostatic theory, the rise of glucose concentration after the meal will signal satiety and terminate food intake. However, this rapid increase of blood glucose concentration due to the ingestion of rapidly digestible, high GI carbohydrates will only suppress hunger and appetite in the short-term (≤ 1 h). In Anderson and colleagues’ study (2002), fourteen healthy, nonsmoking men, ages 18-35 years with a body mass index of 20-25 kg/m², were recruited to determine the effect of the four carbohydrate sources on subjective measures of satiety and short-term food intake. The results showed that food intake and subjective appetite were inversely associated with blood glucose response in 60 minutes after consumption of the carbohydrates. Two to four hours after the consumption of high GI meal, hyperinsulinaemia persists and results in a rapid fall of blood glucose concentration. This fall of blood glucose concentration often goes below basal concentration which leads to a hypoglycemic stage. Hypoglycemia is caused by high GI diet that accelerates hunger 2-4 hours and beyond (Bornet et al., 2007). On the other hand, low GI diets produce lower and longer postprandial blood glucose rise especially in the early stage. This would gradually release insulin into the blood stream to help with glucose uptake and
the phenomena of hypoglycemia is prevented. According to Ludwig, slower absorption enables prolonged stimulation of nutrient receptors in the gastrointestinal tract and thus causes a prolonged satiety signal to the brain (Ludwig, 2002). As a result, it is hypothesized that low GI diets can attenuate hunger and therefore lead to less food intake.

**B) Studies examining the relationships between GI and satiety**

Many studies have been conducted to examine the relationship between glycemic index and satiety. However, the results of the studies are inconsistent. Some found no effect of GI on satiety and food intake, while others found a significant suppression of hunger and appetite after consumption of the low GI diets. A recent article written by Bornet et al., reviewed 19 human studies, testing carbohydrate foods or mixed meals on the impact of satiety (Bornet et al., 2007). The following part of the thesis will discuss some of these studies. There are many confounding variables that can influence the glycemic responses on satiety; therefore, in this review article, Bornet et al. carefully eliminated those variables. For example, they selected studies that have the same energy content and same carbohydrate, protein and fat contents of the tested meals. This is because macronutrients possess their own satiating powers. Protein is considered to be more satiating than carbohydrates and carbohydrates are more satiating than fat (Rolls et al., 1988; Stubbs, 1995). Even though fiber could influence satiety, the effect of fiber is not controlled by most of the mixed meals human studies; therefore, Bornet et al. were not able to take fiber into account for selection criteria. In this review article, when subjective method of assessment was used in the studies, Bornet et al. showed that 12 of 18 studies supported an inverse relationship between GI diets and satiety, which means low glycemic index food, produces high satiety. Moreover, when
an objective method of assessment was used (ad libitum food intake) in the studies, four of seven showed similar results.

Arumugam and colleagues studied the effects of variations in postprandial glycemia on subjective satiety in overweight and obese women (Arumugam et al., 2008). Fourteen nonsmoking, overweight and obese women between the ages of 35 and 60 years were recruited to participate in this within-subjects’ designed study. In order to model the postprandial effects of high GI meal and low GI meal, the investigators altered the ingestion rate of a glucose beverage. At one visit, the subjects were required to consume a large glucose drink (60 g glucose) with breakfast to mimic the high GI meals; at the other visit, the subjects were served the same amount of glucose but it was divided into eight equal portions, with one portion consumed with breakfast and the seven other portions consumed at 20-minute intervals after the breakfast to mimic the low GI meals. The results showed that subjects experienced higher fullness with the slower ingestion of glucose beverage (low GI meal) compared with the rapid ingestion of glucose beverage (high GI meal) four hours after the breakfast meals.

Ball et al. investigated the effects of low-GI whole-food meals (LWM), high-GI meal-replacement (HMR) and low-GI meal-replacement (LMR) on metabolic, hormonal and satiety responses in 16 overweight adolescents (Ball et al., 2003). It was a randomized, crossover study with three separate 24-hour admissions visits. The results showed that even though no differences were observed in subjective hunger ratings and voluntary energy intake, meals were requested earlier after HMR treatment compared to the LMR treatment (3.1 versus 3.9 hours, respectively). Therefore, the authors concluded that low-GI diets can prolong satiety, which may lead to reduced caloric intake and long-term weight control.
Due to chemical structure differences, amylose and amylopectin have different effects on postprandial glucose and insulin concentrations. Amylose produces a significantly lower postprandial glycemia and insulinemia response compared with amylopectin. Taking advantage of these differences, van Amelsvoort and Weststrate decided to conduct a study examining the postprandial effects of changing the amylose-to-amylopectin ratio (Am:Ap) in the starch fraction of a meal (van Amelsvoort and Weststrate, 1992). Twenty-two normal weight and healthy male volunteers were recruited to participate in this study. They were required to consume hot mixed lunches in which Am:Ap was either 0:100 or 45:55. The results demonstrated that the low-GI meal (high Am:Ap) elicited higher satiety value compared with the high-GI meal (low Am:Ap).

In terms of long-term intervention, Henry and colleagues conducted a study to examine the effects of low- and high-glycemic index breakfasts on food intake in children 8-11 years old (Henry et al., 2007). It was a randomized cross-over design study where children were assigned to one of two groups. On two non-consecutive days per week, for 10 weeks, each group was given low-GI and high-GI breakfasts. After breakfast, subjects would stay for an ad libitum buffet lunch. The foods eaten during the lunch were recorded. In order to obtain daily energy and macronutrient intakes, the subjects were required to record 3-day food dairies and they were interviewed for 24 hour food recall. The results showed that even thought the mean difference of 75 kJ was not statistically significant (P=0.406), there was a tendency towards a reduced energy intake at lunch following the low-GI breakfast compared with the high-GI breakfast. Besides that, 3-day food dairies showed that there was a tendency toward a reduced energy intake during the low-GI study period compared with high-GI study period.
Barkeling and colleagues studied the effects of carbohydrates in the form of pasta and bread on food intake and satiety (Barkeling et al., 1995). By using similar raw material, carbohydrates in the form of pasta produced a low and stable glucose and insulin response (low-GI meal), while carbohydrates in the form of bread produced a high glucose and insulin response (high-GI meal). Sixteen normal weights, elderly men were recruited in this study. They were served a pasta breakfast and a bread breakfast in a randomized cross over design. Their subjective rating of hunger was measured by using 100 mm Visual Analogue Scales from before breakfast to after lunch. Three hours after their breakfast, they were served an ad libitum lunch meal. Their food intakes during the lunch meal were measured by VIKTOR a universal eating monitor. The results of the study demonstrated that even though two types of breakfast meals produced significant difference of insulin and glucose responses, there was no difference in satiety response. Subjects in low-GI breakfast group consumed as much as subjects in high-GI breakfast group during their lunch meal.

C) The development of satiety index

There are two ways of measuring appetite in humans. First, the degree of hunger can be estimated via subjective ratings. Humans have the ability to rate the strength of their conscious drive and motivation to eat (de Graaf et al., 2004). To date, there are two kinds of subjective ratings used by researchers: seven point rating scales and 100 mm visual analogue scales (VAS). Studies have shown that subjective ratings are reproducible, sensitive to exposures of food components, and predictive of food intake (Holt et al., 1995; Flint et al., 2000; Stubbs et al., 2000). The second way to measure one’s appetite is by the actual amount of food eaten after a preload test meal. Foods eaten ad libitum after the test meals are recorded. However, the amount of food eaten should be observed instead of deriving
information from dietary food records or recalls. This is because the food eaten by subjects obtained from dietary records or recalls is not precise and valid (de Vries et al., 1994).

In 1995, Holt and colleagues saw the need for developing a system to produce a table showing the energy-satiety ratio of a list of common foods; thus, introducing the concept of satiety index (SI) to the nutritional field (Holt et al., 1995). Holt et al. believed that energy-equivalent loads of the different nutrients can have different effects of satiety, thermogenesis, carbohydrate and fat storage. Even though a number of studies have shown that different types of nutrients and foods satisfy hunger to varying extents, we still have a limited understanding of the complex interacting mechanisms of satiation (Holt et al., 1995). In the future an international table of satiety index values of foods might be established by using this concept. SI is calculated in the same fashion as the GI; however instead of using 50 g of available carbohydrate as the portion, it uses isoenergetic portions of foods. Rating scale (see Figure 1) instead of the 100 mm VAS was used by Holt and colleagues. The formula for SI is as follows. The denominator also differs slightly from that used in GI. In SI, the group average AUC for the reference food is used instead of the individual’s AUC. This is because some subjects might experience very little fullness for the reference food and express zero results.
One of the purposes of our study is to measure the satiety index of kefir drinks. As mentioned above, the concept of satiety index was first introduced by Holt and Brand-Miller’s lab in order to produce a table showing the energy-satiety ratio of a list of foods (Holt et al., 1995). Therefore, we are interested in knowing the SI score (%) of kefir compared with the list of 38 foods tested by Holt et al. on an isoenergetic basis. Moreover, in a later publication, Holt et al. used these SI score (%) of 38 foods to determine whether the postprandial increments in subjective satiety, plasma glucose and insulin responses were interrelated (Holt et al., 1996). This is because Holt and colleagues believed that postprandial increments in plasma glucose and/or insulin are likely to be among the physiological mechanisms responsible for the satiating effect of foods. Therefore, our study is also designed to determine the interrelationships among postprandial satiety, glucose and insulin

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\text{SI} = \frac{\text{Area under the 120 min satiety curve to 1000 kJ of the test food}}{\text{Area under the 120 min satiety curve for 1000 kJ of white bread}} \times 100
\]
responses. In Holt et al.’s study, the results showed that there were no significant correlations between the glucose and insulin AUC values and satiety AUC values (both $r = 0.06$).

Similarly, there were no significant correlations between the glycemic and insulin index scores and satiety index scores ($r = 0.11$ and $r = -0.08$).

**Literature cited**


EFFECTS OF KEFIRS ON GLYCEMIC, INSULINEMIC AND SATIETY RESPONSES

A paper to be submitted to British Journal of Nutrition

Kai Ling Kong, Suzanne Hendrich

ABSTRACT

We hypothesized that three types of kefir (Lifeway® Low Fat Strawberry Kefir, ProBugs Kefir, orange flavor, and Lifeway® Low Fat Plain Kefir) would have low glycemic index (GI), high insulinemic index (II) and high satiety index (SI). Secondarily, we hypothesized that there would be no significant correlations among postprandial satiety, glucose and insulin responses. Lastly, we hypothesized that kefir, like other dairy products, would have dissociation of GI and II. To test our hypotheses, this study was divided into three phases. In Phase I, a portion of Lifeway® Low Fat Strawberry Kefir (S group) and a portion of ProBugs Kefir, orange flavor (O group) containing 50 g of available carbohydrates were tested. In Phase II, a portion of Lifeway® Low Fat Plain Kefir (P group) containing 25 g of available carbohydrates were tested. In Phase III, 240-kcals portions of all three types of kefirs were tested. In all phases a single meal, randomized crossover design was performed in which the test meals were fed to 10 healthy, male and female adults. The total glucose AUC of S group (p< 0.0023), O group (p< 0.0002) and P group (p< 0.0002) were significantly lower compared with their respective glucose controls. A slight, but not significant inverse relationship between glycemic and satiety responses was observed with kefir beverages (r = -0.87; P = 0.13). Using a variance of component analysis, it was found that a significant relationship between the correlated effects of the treatments on GI and SI can be further
tested in the future by increasing the number of subjects to 12. Like other dairy products, kefir showed a dissociation of GI and II. Kefir can potentially be a useful food choice for patients with diabetes who are required to control their blood glucose levels.

**Keywords:** kefir, glycemic index, insulinemic index, satiety index

**INTRODUCTION**

According to the World Health Organization (WHO), by 2015 an estimated 2.3 billion adults will be overweight [Body Mass Index (BMI) of $\geq 25 \text{ kg/m}^2$], and more than 700 million will be obese (BMI of $\geq 30 \text{ kg/m}^2$) (2008a). Obesity greatly affects the overall quality of life. It is the major contributor for chronic diseases such as: type 2 diabetes, cardiovascular disease, hypertension, strokes and some types of cancer (WHO/FAO, 1998; Wild et al., 2004; 2008a). When the per capita nutrient consumption in the United States, between 1909 and 1997 was compared with the prevalence of type 2 diabetes, Gross and colleagues observed a strong correlation between the consumption of refined carbohydrates and the prevalence of type 2 diabetes (Gross et al., 2004). Therefore, carbohydrates, in terms of both quantity and of quality, are receiving significant attention in current laboratory and clinical studies.

Glycemic index (GI) was first introduced by Jenkins and colleagues in 1981 to assess and classify different carbohydrate-rich foods according to their effects on postprandial glycemia (Jenkins et al., 1981). The original purpose of the GI was to provide additional information to help patients with diabetes to better control their blood glucose levels. Low-GI foods cause a smaller insulin response and a slower release of glucose into the bloodstream.
compared with high-GI foods. Later studies have shown that high-GI diets are independently associated with an increased risk of developing obesity, type 2 diabetes, cardiovascular disease, insulin resistance, and cancer (Livesey et al., 2008). As a result, a great deal of attention has been focused on the health benefits of consuming low-GI diets.

Generally speaking, dairy products have low GI values. Based on the 2002 International Table of Glycemic Index and Glycemic Load Values, four types of dairy products were tested for GI: ice cream, GI = 61 (regular, mean of five studies); milk, GI = 27 (full-fat, mean of five studies); milk, GI = 32 (skim, one study); fermented milk, GI = 11 (3% fat, mean of two studies) and yogurt, GI = 14-38 (from lower value for non caloric sweetener to higher value for caloric sweetener, nonfat to low fat, range of 14 studies) (Foster-Powell et al., 2002). Our study is interested in kefir, the type of milk product that is commonly used in most Eastern Europe countries. Until the present time, no study has measured the GI of kefir.

Today, kefir is becoming increasingly popular. Some researchers believe that the various health-promoting properties of kefir outweigh those of yogurt (Lopitz-Otsoa et al., 2006). With the increase of diabetes worldwide, it is worth examining if kefir can bring positive effects in helping to combat this pandemic disease.

Most of the foods tested for GI values have not been measured for their concurrent postprandial insulinemic responses. According to Del Prato et al. (1994), chronic, physiologic hyperinsulinemia can lead to the development of insulin resistance. Besides that, hyperinsulinemia is one of the risk factors in the development of many diseases, such as obesity, diabetes, cancer and dyslipidemia ((DeFronzo et al., 1991; Brouns et al., 2005). While the measurement of postprandial blood glucose responses is important, the measurement of postprandial insulinemic responses is equally important. The concept of
insulin index (II) of foods generated by 1000-kJ (240-kcals) was developed by Holt et al. (1997) in order to systematically rate the postprandial insulinemic responses of different type of foods. II is calculated in the same fashion as the GI. The II of different type of kefir drinks will be measured in this study.

In general, pure carbohydrates, sugars and starchy foods have a high correlation between glycemic and insulinemic responses (Lee et al., 1998). However, studies have shown that non-starchy foods can produce higher insulin responses than expected from their GI (Gannon et al., 1988; Holt et al., 1997; Ostman et al., 2001). This is because carbohydrates are not the only stimulus for insulin secretion. There are a number of insulinotropic factors that mediate postprandial insulin secretion including fructose, certain amino acids, fatty acids, and gastrointestinal hormones such as gastric inhibitory peptide, glucagon, and cholecystokinin (Nuttall et al., 1991; Morgan, 1992). Most recently, milk products were shown to elicit unexpectedly high insulin AUCs compared with the predicted insulin AUCs from their GI values (Ostman et al., 2001; Liljeberg et al., 2001). For example, in Ostman et al.’s study, they tested one type of regular milk and two types of fermented milk: ropy milk and filmjolk by using white bread as the standard. The GI values for all three milk products were very low, ranging from 12 to 30; however, the II values were very high relative to their GIs (reported to be similar with the reference meal’s value). Kefir is a kind of fermented milk product, which is somewhat similar with ropy milk and filmjolk. Therefore, the present study is interested in examining the relationship of GI and II of kefir and to further confirm the finding of Ostman et al., which is the dissociation of GI and II of dairy products.
Varied postprandial metabolic events elicited by high GI and low GI diets are hypothesized to have potential effects on satiety (Holt et al., 1995). Many studies have been conducted to examine the relationship between glycemic index and satiety. However, the results of the studies are inconsistent. Some found no effect of GI on satiety and food intake, while others found a significant suppression of hunger and appetite after consumption of the low GI diets (Bornet et al., 2007). In 1995, Holt and colleagues saw the need for developing a system to produce a table that could demonstrate the energy-satiety ratio of a list of common foods; thus, introducing the concept of satiety index (SI) (Holt et al., 1995). Holt et al. believed that energy-equivalent loads of the different nutrients can have different effects of satiety, thermogenesis, carbohydrate storage and fat storage. Even though a number of studies have shown different types of nutrients and foods satisfy hunger to varying extents, we still have a limited understanding of the complex interacting mechanisms of satiation (Holt et al., 1995). One purpose of the present study is to measure the satiety index of kefir drinks. We are interested in knowing the SI score (%) of kefir compared with the list of 38 foods tested by Holt et al. on an isoenergetic basis. Moreover, in a later publication, Holt et al. used the SI scores (%) of 38 foods to determine whether the postprandial increments in subjective satiety, plasma glucose and insulin responses were interrelated (Holt et al., 1996). This is because Holt and colleagues believed that postprandial increments in plasma glucose and/or insulin are likely to be among the physiological mechanisms responsible for the satiating effects of foods. Therefore, our study is also designed to determine the interrelationships among postprandial satiety, glucose and insulin responses.

The objective of this study was to produce a glycemic, insulinemic and satiety indexes of three type of kefir (Lifeway® Low Fat Strawberry Kefir, ProBugs Kefir, orange
flavor, and Lifeway® Low Fat Plain Kefir). The hypothesis tested was that all of the kefir beverages would have low GI, high II and high SI values. In order to test our hypothesis, the study was divided into three phases. A portion of Lifeway® Low Fat Strawberry Kefir and a portion of ProBugs kefir, orange flavor containing 50 g of available carbohydrates were fed to 10 healthy subjects in Phase I. A portion of Lifeway® Low Fat Plain Kefir containing 25 g of available carbohydrates was fed to 10 healthy subjects in Phase II. A 240-kcal portion of all three types of kefirs were fed to 10 healthy subjects in Phase III. Glucose solution was used as the reference food in Phase I and Phase II, and white bread was used in Phase III. Secondarily, we hypothesized that there were no significant correlations among postprandial satiety, glucose and insulin response. Lastly, we hypothesized that kefir, like other dairy products, would have dissociation of GI and II.

SUBJECTS AND METHODS

Study Design

The study was a randomized crossover study with a minimum of 4-day washout period between each treatment visit. It was divided into three phases.

In phase I, the glycemic index of Lifeway® Low Fat Strawberry Kefir (S group), and Lifeway ProBugs Kefir (orange flavor) (O group) were measured. Subjects were required to consume portions of these two types of kefir containing 50 g of available carbohydrates, and two glucose reference solutions (50 g dextrose in 296 mL volume, Fisherbrand Sun-Dex, Fisher Health Care, Houston, TX) for a total of four treatment visits.

In phase II, the glycemic index of Lifeway® Low Fat Plain Kefir (P group) was measured. Subjects were required to consume portions of Lifeway® Low Fat Plain Kefir
containing 25 g of available carbohydrate, and two glucose reference solutions (25 g dextrose in 148 mL volume, Fisherbrand Sun-Dex, Fisher Health Care, Houston, TX) for a total of three treatment visits. This reduction in carbohydrates from 50 g to 25 g is necessary because the low carbohydrate content of plain kefir would necessitate the feeding of an excessive amount of kefir (>1 L) to achieve 50 g carbohydrate intake. It is a very unrealistic portion size and the subjects would not be able to finish it in a short amount of time (15 minute time limit).

In phase III, insulin and satiety index of the same beverages (Lifeway kefir- low fat plain kefir, low fat strawberry kefir and ProBugs orange flavor kefir) were measured. However, white bread (as opposed to glucose solution) was used as the reference food and the portion sizes of the test and reference foods were standardized by energy content, not carbohydrate content. This is because nutrients other than carbohydrate can stimulate insulin secretion (Holt et al., 1997) and energy content is a key variable that affects satiety (Holt et al., 1995). Subjects were required to consume 240-kcal (1000-kJ) portions of the white bread and each type of kefir.

**Test meals**

Table 1 shows the portion sizes of three type of kefir required to provide 25 g or 50 g available carbohydrates for Phase I and II of the study and their individual nutrient composition. The reference food of these two phases was 25 g (148 mL) or 50 g dextrose (296 mL), Fisherbrand Sun-Dex, Fisher Health Care, Houston, TX respectively. For phase III, subjects were required to consume 240-kcal (1000-kJ) portions of each type of kefir (Lifeway® Low Fat Strawberry Kefir, ProBugs kefir, orange flavor, and Lifeway® Low Fat Plain Kefir). Table 2 shows the portion sizes of the kefir drinks and their individual nutrient
compositions. The reference food of this phase was 240-kcal of Sara Lee® White Bread. In each phase, subjects were given 4 oz (~118 mL) of water to help with ingestion. All of the nutrient composition and the feeding portion sizes are derived from the product labels.

**Subjects**

A study protocol was approved by the Iowa State University Human Subject Protection Committee. Individuals who showed interest were invited to the Iowa State University, Nutrition and Wellness Research Center for screening tests. Those who were recruited to be the subjects of the study were healthy adults, ages 18-45 years, with no history of diabetes, glucose intolerance, gastrointestinal disorders or use of tobacco. Their fasting plasma glucose concentrations were less than 100 mg/dL and their body mass index were less than 30 kg/m². They were also interviewed and completed detailed questionnaires on medical conditions, use of medications or dietary supplements that could affect glucose tolerance.

A total of 30 subjects were recruited for this study. Relevant characteristics of the subjects are listed in Table 3. For the female subjects, none showed positive results for the pregnancy tests. These 30 subjects were divided into three groups for three phases of the study. Phase I comprised of five males and five females with a mean age (± standard error of the mean) of 22 ± 2 years, mean BMI of 22.2 ± 3.4 kg/m² and mean fasting plasma glucose level of 88 ± 6 mg/dL. Phase II comprised of five males and five females with a mean age of 23 ± 3 years, mean BMI of 22.6 ± 3.0 kg/m² and mean fasting plasma glucose level of 91 ± 4 mg/dL. Phase III comprised of five male and five females with a mean age of 25 ± 4 years, mean BMI of 24.2 ± 3.5 kg/m² and mean fasting plasma glucose level of 93 ± 5 mg/dL. Due to an error during blood collection, the insulin and glucose AUC for O group in Phase III of the study was calculated from nine subjects instead of ten subjects.
Feeding protocol

Three days prior to each visit, subjects were asked to consume at least 150 g per day of carbohydrates and record them in a 3-days dietary food record. Subjects were required to fast eight to ten hours overnight before for the meal tolerance test. They also had to refrain from vigorous exercise for 12 hours before the visit (Brouns et al., 2005).

Subjects arrived at the Iowa State University, Nutrition and Wellness Research Center (NWRC) between 0700 and 0730 hour. Upon their arrival, the subjects’ body weight was measured and there was a 30-minute resting period to allow stabilization of blood glucose. During the resting period, the 3-day dietary records were analyzed for carbohydrate intake by using Nutritionist V diet analysis software. After the rest period, a baseline blood sample (approximately 1-2 mL) was obtained by a capillary finger-stick. Then the subject preceded to the dining area for the test meals. The order of the test meals was randomized. Subjects were directed to consume the required portion of either the test or reference meals within 15 minutes. The timing for the meal tolerance test started with the first sip or first bite of their meal. Subjects resumed fasting after consuming the meal and subsequent capillary finger-stick blood samples were obtained at 15, 30, 45, 60, 90, and 120 min. Subjects were allowed to resume their normal diet and physical activity patterns after collection of the last blood sample.

In Phase III, in addition to all the meal tolerance test procedures as described above, subjects in this phase were required to provide self-reported feelings of satiety on an equilateral seven-point rating scale (see Figure 1) before each of the blood sampling time points (Holt et al. 1995). This scale was anchored 1 (extremely hungry) to 7 (extremely full). Subjects did not discuss or compare their hunger ratings with each other.
Analysis of plasma glucose and insulin concentrations

Blood samples were collected at 0, 15, 30, 45, 60, 90, and 120 minute time points. The whole blood samples (approximately 1-2 mL) were collected in 1.5 mL micro-centrifuge tubes. Samples were then centrifuged at 16,000 relative centrifugal force (rcf) x g for 15 minutes at 4 °C to obtain serum. Serum was stored frozen at -80 °C until it was thawed for analysis. Serum glucose concentrations were determined in duplicate using the glucose analyzer (Beckman Coulter Glucose Analyzer 2; Beckman Coulter Inc, Fullerton, CA) for Phase I and II and biochemical analyzer (YSI Model 2700 Select Biochemical Analyzer; Yellow Springs Instrument Co. Inc, Yellow Springs, OH) for Phase III. Insulin concentrations in the serum were determined in duplicate using an enzyme-linked immunoassay (ALPCO Insulin EIA).

Analysis of carbohydrate content of Lifeway® Kefir

1.00 mL of each type of kefir drink was put into 1.5 mL micro-centrifuge tubes. The samples were then centrifuged at the speed of 16,000 rcf x g for 15 minutes at 4 °C. After centrifugation, the supernatant of each sample was transferred into a clean 1.5 mL micro-centrifuge tube for glucose, sucrose and lactose analysis using the biochemical analyzer kits that have been validated by YSI Inc. (Yellow Spring, OH).

Statistical analysis

The AUC was calculated via the trapezoidal rule with fasting levels as the baseline and truncated at zero. Any negative area was ignored (Wolever et al. 1991). The formula for glycemic index (GI), glycemic, insulinemic index (II) and satiety index (SI) scores are as follows:
A glycemic score was used instead of glycemic index score in Phase III because the portion sizes of the meals were standardized by energy content (240-kcal), not carbohydrate content. As shown in Table 2, carbohydrate contents in all three kefir drinks were varied in Phase III.

For the satiety index score, a group average was used instead of the individuals’ AUC for reference food because there was one subject who experienced no satiety from the white bread and therefore gave a zero value to the denominator for the formula.

AUC for glycemic, insulinemic and satiety and all of the three indexes (GI, II and SI) were analyzed by crossover ANOVA. Significance was defined as $P<0.05$. For the response variable in each phase, a carryover effect was first tested after adjusting for gender, sequence, period and treatment effects. If the carryover effect was not significant, the carryover terms were removed from the model before all other effects (gender, sequence, period and treatment) were tested. A Tukey-Kramer adjustment was used for multiple pair wise comparisons among treatments. Equal variance and normality assumption were checked using residual versus predicted values plot, and histogram of residuals respectively for each model.

To find the sample size needed to observe a significant correlation between GI and SI the ratio of the covariance and product of the standard deviations was calculated for different
values of N. The covariance of the population means was estimated by the covariance of the sample means since independent errors were assumed. The variance of GI and SI were estimated using a variance components analysis for the data on GI and SI.

T-tests were also used to test for differences between the actual and predicted GI values of all Lifeway® Kefir beverages.

RESULTS

The models for all phases including carryover terms showed there was no significant carryover effect (P-value > 0.5), so carryover terms were removed from the final model for all phases. There were no significant gender, sequence and period effects when they were tested in all phases.

Phase I: Glycemic responses of Lifeway® Low Fat Strawberry Kefir, and Lifeway ProBugs Kefir (Orange Flavor)

The serum glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), and Lifeway ProBugs Kefir (orange flavor) (O group) are shown in Figure 2 and Table 4. The total blood glucose AUC of subjects consuming strawberry-flavored kefir (S group, p< 0.0023) and orange-flavored kefir (O group, p< 0.0002) was significantly lower compared with the reference meal (50 g of glucose solution). Total AUC for O group was not significantly different compared with S group. The GI of strawberry-flavored kefir was 60 ± 10, which was significantly lower than the reference meal (GI = 100 ± 0); the GI of orange-flavored kefir was 48 ± 10, which was significantly lower than the reference meal (Table 7).

Phase II: Glycemic response of Lifeway® Low Fat Plain Kefir
The serum glucose response to Lifeway® Low Fat Plain Kefir (P group) is shown in Figure 3 and Table 5. P group showed a significantly lower total glucose AUC compared with the reference meal (glucose solution, \( p < 0.0002 \)). The GI of P group was 36 ± 9, which was significantly lower than the reference meal (GI = 100 ± 0) (Table 7).

**Phase III: Glucose, insulin and satiety responses of Lifeway® Low Fat Strawberry Kefir, Lifeway ProBugs Kefir (Orange Flavor), and Lifeway® Low Fat Plain Kefir**

The insulinemic and satiety index values of Lifeway® Low Fat Strawberry Kefir were 142 ± 48 and 85 ± 19 respectively, Lifeway ProBugs Kefir (orange flavor) were 124 ± 47 and 121 ± 27 respectively and Lifeway® Low Fat Plain Kefir were 112 ± 36 and 122 ± 16 respectively. Glycemic scores, insulinemic index and the satiety index were not significantly different among all the treatments and reference meal (white bread) (Table 6b). In term of the interrelationships among glucose, insulin and satiety responses, there were no significant correlations between the glycemic and satiety index scores (\( r = -0.87; P = 0.13 \)) or insulinemic index and satiety index scores (\( r = -0.44; P = 0.56 \)). However, by performing a variance of components analysis and calculating the covariance between the means of the treatments for GI and SI, the correlation between GI and SI was predicted to be -0.96 if there were 12 subjects in the study, assuming subjects similar to those in the present study. Thus, an N of 12 would be proposed for future work on the satiety index of kefirs.

**Dissociation between glycemic index and insulinemic index of kefir**

Table 7 is a summary of GI and II of three type of kefir from all the phases. As mentioned above, the GI of S, O and P groups were significantly lower than those after the control meals. No differences in GI were found between S group and O group. Even though there were differences of GI between kefir beverages and the control meals, the insulinemic
indexes for all the kefir beverages did not differ significantly from those for the control; indeed they were higher than the reference meal. No differences in insulinemic indexes were found among the beverages. These results showed that the blood insulin responses were not proportional to blood glucose responses after consuming the kefir beverages. With higher insulin released, kefir might have an insulinotropic effect after ingestion.

**Different types of carbohydrates content in Lifeway® Kefir**

The amount of glucose, sucrose and lactose content in Lifeway® Low Fat Strawberry Kefir, Lifeway ProBugs Kefir (orange flavor) and Lifeway® Low Fat Plain Kefir were measured. Table 8 shows the amount of each type of carbohydrate contained in all three beverages. In 546 mL of Lifeway® Low Fat Strawberry Kefir, there were 13.2 g of glucose, 0.3 g of sucrose and 35.9 g of lactose; in 548 mL of Lifeway ProBugs Kefir (orange flavor), there were 3.1 g of glucose, 28.7 g of sucrose and 35.5 g of lactose; in 667 mL of Lifeway® Low Fat Plain Kefir, there were 0.1 g of glucose, 0 g of sucrose and 47.5 g of lactose.

**Actual and predicted glycemic indexes of Lifeway® Kefir**

By using the data from the carbohydrate analysis of Lifeway® Kefir, the predicted glycemic indexes of all three types of kefir were determined using the GI mixed meals calculation method (Wolever et al., 1986). Table 10 shows the actual and predicted GI values. By running a t-test, it was found that there was no significant difference between the actual and predicted GI values for all of the beverages (S group, p-value = 0.4602; O group, p-value = 0.1587; P group, p-value = 0.1335).

**DISCUSSION**

Based on the classification of GI value by Brand-Miller (1998), the results of present study showed that Lifeway® Low Fat Strawberry Kefir is a medium GI food (GI = 60).
Lifeway ProBugs Kefir (orange flavor) (GI = 48) and Lifeway® Low Fat Plain Kefir (GI = 36) are low GI foods. By observing the ingredient information on the food labels, we believe the reason Lifeway® Low Fat Plain Kefir had the lowest GI value was because it did not contain any added sweeteners. On the other hand, both Lifeway® Low Fat Strawberry Kefir and Lifeway ProBugs Kefir (orange flavor) have added cane juice and juice concentrate in order to give desirable taste and flavor. Cane juice (cane sugar) mainly consists of sucrose (glucose α-1,2 fructose), a disaccharide and some glucose. The GI value for sucrose is 68 by using glucose as standard (Lee et al., 1998). The carbohydrate analysis which was done on all three types of Lifeway® beverages confirmed our assumption. The data showed that both strawberry and orange flavored kefir contained glucose and sucrose but not plain kefir. Dairy products generally have a GI value ranging from 11 to 36 (Foster-Powell et al., 2002); however, sweetener can increase the GI value of dairy products which are otherwise a low GI food.

The reason we used 25 g of carbohydrates in Phase II was to provide a realistic portion size of meals to the subjects. Plain kefir is a low carbohydrate content food, therefore it would necessitate the feeding of an excessive amount of kefir (>1 L) to achieve 50 g carbohydrate intake. According to the Glycemic Index Methodology of Brounds, 25 g of carbohydrate load is permitted to apply for GI test, but at the same time, the reference meal must be reduced to 25 g of carbohydrates. In addition, Lee and Wolever’s study showed that the mean glucose AUC increased linearly as the dose of carbohydrates increased. In other words, when the amount of carbohydrate intake is increased, the glucose response AUC will increase in a dose-response fashion (Lee and Wolever, 1998). However, our study did not show this dose-response fashion. When 50 g dextrose in 296 mL volume was fed to the
subjects in phase I, the total AUC of this control is $3272 \pm 229 \text{ mg x min/dL}$; while when 25 g dextrose in 148 mL volume was fed to the subjects in phase II, the total AUC of this control was $2888 \pm 331 \text{ mg x min/dL}$; a difference of only $384 \text{ mg x min/dL}$. The volume of the drink might have an effect on glycemic response since we fed the subjects with different volumes of dextrose in two phases. However, according to the study of Gregersen et al., the volume of test meal had no effect on glycemic response (Gregersen et al., 1990). They showed that an increase of water volume (given as tap water) from 90 to 600 mL did not alter the glycemic or insulinemic responses. One difference between our study and Lee and Wolever’s dose-response study is that we used two completely different groups of subjects in Phase I and Phase II, but they fed the same group of subjects with 25 g and 50 g of glucose in a randomized order. Studies have shown there is a high interindividual variability of glycemic index value. For example, in a Vega-Lopez and colleagues’ study, when white bread was fed to 25 healthy subjects, the glycemic index values ranged from 44 to 132, with a CV of 30% (Vega-Lopez et al., 2007). Besides that, another report showed that the CV of the white bread AUC for subjects with type 2 diabetes was 33%, and for subjects with type 1 diabetes it was 39% (Wolever et. al., 1987). Therefore, we concluded that the reason we did not see the dose-response fashion was due to the high interindividual variability.

Both Lifeway ProBugs Kefir (orange flavor) and Lifeway® Low Fat Plain Kefir were more satiating than the control food; however, this difference was not significant. In terms of the interrelationships among glucose, insulin and satiety responses, statistically, the correlations between the glycemic score and satiety index or insulin index and satiety index were not significant. However Lifeway® Low Fat Strawberry Kefir which had the highest glycemic score had the lowest SI value. Both of the Lifeway ProBugs Kefir (orange flavor)
and Lifeway® Low Fat Plain Kefir had similar glycemic scores and so did their SI values. Many studies have been conducted to examine the relationship between glycemic index and satiety. However, the results of the studies are inconsistent. Some found no effect of GI on satiety and food intake, while others found a significant suppression of hunger and appetite after consumption of the low GI diets. A most recent review article written by Bornet et al., investigated 19 human studies, testing carbohydrate foods or mixed meals’ effects on satiety (Bornet et al., 2007). In this review article, when a subjective method of assessment was used in the studies, Bornet et al. showed that 12 out of 18 of the studies supported an inverse relationship between GI diets and satiety, which means low glycemic index food, produces high satiety. Moreover, when an objective method of assessment was used (ad libitum food intake) in the studies, four out of seven showed the similar results. In the present study, a variance of components analysis showed that a sample size of 12 subjects would give enough power to find a significant relationship between the correlated effects of the treatments on glycemic score and satiety index values.

As mentioned above, the ingredient information on the food labels showed that both strawberry and orange-flavored kefir had added cane juice and juice concentrate, which might contribute to the GI value difference among three types of kefir drinks. For this reason, a carbohydrate analysis was performed to determine the different types of carbohydrate contained in the beverages. The results of this analysis showed that all three types of kefir contained varied amount of glucose, sucrose and lactose. By using the GI mixed meals calculation method introduced by Wolever and Jenkins (1986), we proceeded to predict the GI values of each type of kefir with the data obtained from the carbohydrate analysis. From
the calculation, we were able to show that there was no significant difference between the actual and the predicted GI value of the beverages.

In addition, the results of Phase III in our study showed dissociation between the GI and II of kefir. Even though the GI values for all Lifeway® kefir beverages were significantly lower than the control, their insulinemic responses were not. The insulinemic responses of all three type of kefir were not significantly different from those for the white bread (control). In fact, all of the II values for kefir drinks exceeded the control as shown by Table 7. Therefore, the finding of our study is in agreement with the results of Ostman et al. (2001). In Ostman and colleagues’ study, they tested one type of regular milk and two types of fermented milk: ropy milk and filmjolk by using white bread as the standard. The GI values for all three milk products were very low (GI = 15 to 30); however, the II values were very high relative to their GIs (reported to be similar with the reference meal’s value). In this study, they also tested the GI and II for lactose solution. The results showed that GI of lactose correlated very well with its II value, suggesting that some milk components, but not lactose content can stimulate insulin secretion. Prior to the study of Ostman et al., inconsistency between GI and II of milk products had been noted in Gannon and colleagues’ study when 50 g carbohydrate of skim milk were given to seven subjects with type 2 diabetes, ages 64±3 years, and with BMI of 32.2±1.7 kg/m² (Gannon et al., 1986). Liljeberg and Bjorck’s study also confirmed the findings of Ostman et al. by supplementing milk to a high-GI white bread and a low-GI spaghetti meal to 10 healthy volunteers (Liljeberg and Bjorck, 2001). The results of the study demonstrated that both bread and spaghetti had higher insulin responses when milk was given compared with water. The insulinotrophic effect of milk products has not been understood. There are many potential unexplored mechanisms for the discrepancy of GI and
II of milk. Two non-carbohydrate components, protein and fat in the milk, are to believe to be the cause of this discrepancy. However, later when Hoyt et al. (2005) studied the GI and II for skim milk and whole milk, they ruled out the possible insulinotropic effects of fat content in milk. This is because both skim and whole milk showed discrepancy of GI and II although their fat content was different. Most recently, Nilsson et al. (2004) and Frid et al. (2005)’s studies showed that the insulinotropic effect of milk is most probably related to the whey protein fraction of milk. The mechanism of this effect remains unknown; however, they proposed that whey might contain specific insulinogenic amino acids and bioactive peptides, either naturally present in whey or produced during digestion that can stimulate insulin secretion. Besides that, they also proposed that the incretin hormones, glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) might play an important role because both of these hormones were significantly elevated after the ingestion of whey protein. All in all, further research is needed to elucidate the mechanism of the insulinotropic effect of whey protein in milk.

In summary, our data from healthy male and female subjects demonstrated that Lifeway® Low Fat Strawberry Kefir is a medium GI food (GI = 60), and Lifeway ProBugs Kefir (orange flavor) (GI = 48) as well as Lifeway® Low Fat Plain Kefir (GI = 36) are low GI food. Therefore, potentially Lifeway® kefir could be an ideal food to recommend to patients with diabetes. There is a high interindividual variability in GI testing. This is because we could not show the dose-dependent fashion when 25 and 50 g of dextrose were fed to two different groups of subjects. Moreover, our data showed a slight but not significant inverse relationship between glycemic and satiety responses. This possibility can be further tested by
increasing the number of subjects. Lastly, our data showed that kefir, like other dairy products, showed the dissociation of GI and II.

REFERENCES:


<table>
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<tr>
<th></th>
<th>Phase I</th>
<th>Phase II</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>ProBugs kefir, orange flavor</td>
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<tr>
<td>Portion size (mL)</td>
<td>546</td>
<td>548</td>
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<tr>
<td>Available carbohydrate (g)</td>
<td>50</td>
<td>50</td>
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<tr>
<td>Energy (kcal)</td>
<td>396</td>
<td>481</td>
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<tr>
<td>Protein (g)</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Lifeway® Low Fat Plain Kefir</td>
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</table>
Table 2. The portion sizes and nutrient composition of the test foods for Phase III

<table>
<thead>
<tr>
<th></th>
<th>Lifeway Low Fat Strawberry Kefir</th>
<th>ProBugs kefir, orange flavor</th>
<th>Lifeway Low Fat Plain Kefir</th>
<th>Sara Lee White Bread</th>
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<tbody>
<tr>
<td>Portion size (mL)</td>
<td>331</td>
<td>273</td>
<td>479</td>
<td>-</td>
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<tr>
<td>Energy (kcal)</td>
<td>240</td>
<td>240</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>Available carbohydrate (g)</td>
<td>30</td>
<td>25</td>
<td>18</td>
<td>37</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>19</td>
<td>16</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>3</td>
<td>9</td>
<td>4</td>
<td>4</td>
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</table>
Table 3. Subject characteristics of each phases

<table>
<thead>
<tr>
<th>Phase</th>
<th>Age (y)</th>
<th>Ethnicity</th>
<th>BMI (kg/m²)</th>
<th>Fasting plasma glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (n = 5 M, 5 F)</td>
<td>22 ± 2</td>
<td>2 Asian; 8 Caucasian</td>
<td>22.2 ± 3.4</td>
<td>88 ± 5.6</td>
</tr>
<tr>
<td>II (n = 5 M, 5 F)</td>
<td>23 ± 3</td>
<td>10 Caucasian</td>
<td>22.6 ± 3.0</td>
<td>91 ± 4.0</td>
</tr>
<tr>
<td>III (n = 5 M, 5 F)</td>
<td>27 ± 4</td>
<td>2 Asian; 8 Caucasian</td>
<td>24.2 ± 3.4</td>
<td>93 ± 4.6</td>
</tr>
</tbody>
</table>

¹ values represent means ± SD
Table 4. The area under the 120 min plasma glucose response curves (AUC) (mean ± SEM) for Phase I¹²

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total glucose AUC (mg (0-120 min)/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>1929 ± 305 ⁷</td>
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<tr>
<td>ProBugs kefir, orange flavor</td>
<td>1604 ± 305 ⁷</td>
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<tr>
<td>Reference meal (glucose)</td>
<td>3272 ± 229a</td>
</tr>
</tbody>
</table>

¹ Values represent means ± SEM (n=10);  
² Treatments bearing different letters were significantly different (p<0.05 level of significance) by crossover ANOVA, after Tukey adjustment
Table 5. The area under the 120 min plasma glucose response curves (AUC) (mean ± SEM) for Phase II¹²

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total glucose AUC (mg (0-120 min)/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifeway® Low Fat Plain Kefir</td>
<td>866 ± 245 b</td>
</tr>
<tr>
<td>Reference meal (glucose)</td>
<td>2888 ± 331 a</td>
</tr>
</tbody>
</table>

¹Values represent means ± SEM (n=10);
²Treatments bearing different letters were significantly different (p<0.05 level of significance) by crossover ANOVA, after Tukey adjustment
Table 6a. The area under the 120 min plasma glucose, insulin, and satiety response curves (AUC) (mean ± SEM) for Phase III ¹ ²

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total glucose AUC (mg/dL min)</th>
<th>Total insulin AUC (µIU/mL min)</th>
<th>Total satiety AUC (RS units min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>1530 ± 324&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>1187 ± 270&lt;sup&gt;a&lt;/sup&gt;</td>
<td>107 ± 25&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>ProBugs kefir, orange flavor</td>
<td>1098 ± 324&lt;sup&gt;b&lt;/sup&gt;</td>
<td>769 ± 277&lt;sup&gt;a&lt;/sup&gt;</td>
<td>155 ± 25&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Lifeway® Low Fat Plain Kefir</td>
<td>1116 ± 324&lt;sup&gt;b&lt;/sup&gt;</td>
<td>894 ± 270&lt;sup&gt;a&lt;/sup&gt;</td>
<td>167 ± 25&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Reference meal (white bread)</td>
<td>2286 ± 288&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1243 ± 270&lt;sup&gt;a&lt;/sup&gt;</td>
<td>130 ± 25&lt;sup&gt;a&lt;/sup&gt;</td>
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¹ Values represent means ± SEM (n=10);
² Treatments bearing different letters within the column were significantly different (p<0.05 level of significance) by crossover ANOVA, after Tukey adjustment.
Table 6b. The glycemic scores, insulinemic index and satiety index of Phase III

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Glycemic score (%)</th>
<th>Insulin index (%)</th>
<th>Satiety index (%)</th>
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<tbody>
<tr>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>87 ± 24 a</td>
<td>142 ± 48 a</td>
<td>85 ± 19 a</td>
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<tr>
<td>ProBugs kefir, orange flavor</td>
<td>44 ± 9 a</td>
<td>124 ± 43 a</td>
<td>121 ± 27 a</td>
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<tr>
<td>Lifeway® Low Fat Plain Kefir</td>
<td>41 ± 12 a</td>
<td>112 ± 36 a</td>
<td>122 ± 16 a</td>
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<tr>
<td>Reference meal (white bread)</td>
<td>100 ± 0 a</td>
<td>100 ± 0 a</td>
<td>100 ± 0 a</td>
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</table>

¹ Values represent means ± SEM (n=10); ² Treatments bearing different letters within the column were significantly different (p<0.05 level of significance) by crossover ANOVA, after Tukey adjustment
Table 7. Glycemic and insulinemic indexes of all Phases⁴

<table>
<thead>
<tr>
<th>Treatments</th>
<th>GI</th>
<th>II</th>
<th></th>
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<tr>
<td></td>
<td>Phase I</td>
<td>Phase II</td>
<td>Phase III</td>
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<tr>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>60 ± 10ᵇ</td>
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<td>142 ± 48ᵃ</td>
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<td>124 ± 43ᵃ</td>
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<td>Lifeway® Low Fat Plain Kefir</td>
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<td>36 ± 9ᵇ</td>
<td>112 ± 36ᵃ</td>
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</tr>
<tr>
<td>Reference meal</td>
<td>100 ± 0ᵃ</td>
<td>100 ± 0ᵃ</td>
<td>100 ± 0ᵃ</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Values represent means ± SEM (n=10);
² Treatments bearing different letters were significantly different (p<0.05 level of significance) within the same phase by crossover ANOVA, after Tukey adjustment
³ Phase I and II used glucose solutions as reference, whereas Phase III used white bread
⁴ All the treatments were compared against 100% of the reference food
Table 8. The different types of carbohydrate content in Lifeway® Kefir

<table>
<thead>
<tr>
<th>Types of carbohydrate (g)</th>
<th>Lifeway® Low Fat Strawberry Kefir(^2)</th>
<th>ProBugs kefir, orange flavor(^3)</th>
<th>Lifeway® Low Fat Plain Kefir(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>13.2 ± 0.4</td>
<td>3.1 ± 0.1</td>
<td>0.1 ± 0</td>
</tr>
<tr>
<td>Sucrose</td>
<td>0.3 ± 0.5</td>
<td>28.7 ± 0.6</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Lactose</td>
<td>35.9 ± 0.9</td>
<td>35.5 ± 1.0</td>
<td>47.5 ± 1.4</td>
</tr>
<tr>
<td>Total</td>
<td>49.5</td>
<td>67.3</td>
<td>47.6</td>
</tr>
</tbody>
</table>

\(^1\) Values represent means ± SD (n=3);
\(^2\) Amount of glucose, sucrose and lactose were measured in 546 mL of Lifeway® Low Fat Strawberry Kefir
\(^3\) Amount of glucose, sucrose and lactose were measured in 548 mL of Lifeway ProBugs Kefir (orange flavor)
\(^4\) Amount of glucose, sucrose and lactose were measured in 667 mL of Lifeway® Low Fat Plain Kefir
Table 9. The predicted GI values of three types of Lifeway® Kefir

<table>
<thead>
<tr>
<th>Type of carbohydrate</th>
<th>Lifeway® Low Fat Strawberry Kefir ¹</th>
<th>ProBugs kefir, orange flavor ³</th>
<th>Lifeway® Low Fat Plain Kefir ⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carbohydrate</td>
<td>Carbohydrate</td>
<td>Carbohydrate</td>
</tr>
<tr>
<td></td>
<td>GI² g Proportion of total GI contribution</td>
<td>g Proportion of total GI contribution</td>
<td>g Proportion of total GI contribution</td>
</tr>
<tr>
<td>Glucose</td>
<td>100 13.2 0.267 26.7</td>
<td>3.1 0.046 4.6</td>
<td>0.1 0.002 0.2</td>
</tr>
<tr>
<td>Sucrose</td>
<td>68 0.3 0.006 0.4</td>
<td>28.7 0.426 29</td>
<td>0 0 0</td>
</tr>
<tr>
<td>Lactose</td>
<td>46 35.9 0.727 33.4</td>
<td>35.5 0.527 24.2</td>
<td>47.5 0.998 45.9</td>
</tr>
<tr>
<td>Total</td>
<td>49.4 60.5</td>
<td>67.3 57.8</td>
<td>47.6 46.1</td>
</tr>
</tbody>
</table>

¹ GI values are taken from reference (Foster-Powell et al., 2002)
² Amount of glucose, sucrose and lactose were measured in 546 mL of Lifeway® Low Fat Strawberry Kefir
³ Amount of glucose, sucrose and lactose were measured in 548 mL of Lifeway ProBugs Kefir (orange flavor)
⁴ Amount of glucose, sucrose and lactose were measured in 667 mL of Lifeway® Low Fat Plain Kefir
Table 10. The actual GI values were not significantly different compared with the predicted GI of Lifeway® Kefir

<table>
<thead>
<tr>
<th>Beverages</th>
<th>Actual GI values</th>
<th>Predicted GI values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifeway® Low Fat Strawberry Kefir</td>
<td>60 (^a)</td>
<td>61 (^a)</td>
</tr>
<tr>
<td>ProBugs kefir, orange flavor</td>
<td>48 (^a)</td>
<td>58 (^a)</td>
</tr>
<tr>
<td>Lifeway® Low Fat Plain Kefir</td>
<td>36 (^a)</td>
<td>46 (^a)</td>
</tr>
</tbody>
</table>

\(^1\) T-tests were used to test for differences between actual and predicted GI values

\(^2\) Treatments bearing different letters within the row were significantly different (p<0.05 level of significance)
FIGURES:

Figure 1. The visual analog scale used in satiety index testing.
Figure 2. Blood glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), and control (mg/dL, over 120 minutes).
Figure 3. Blood glucose responses to Lifeway® Low Fat Plain Kefir (P group), and control (mg/dL, over 120 minutes).
Figure 4. Blood insulin responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (µU/mL, over 120 minutes).
Figure 5. Satiety responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (RSU, over 120 minutes).
GENERAL CONCLUSION

Low-GI diets have received a considerable attention due to their positive effects on risk factors for certain chronic diseases. In recent decades, low-GI diets became one of the strategies to combat obesity in this country. Studies have established that dairy products generally have low GI values. Kefir, a type of milk product that is commonly used in most Eastern Europe countries, has low GI value compared with reference meal. However, when sweetener is added to kefir, it can increase the GI value of this dairy product.

Pure carbohydrates, sugars and starchy foods have a high correlation between glycemic and insulinemic responses. However, certain foods can produce higher insulin responses than expected from their GI. Milk is one of the non-starchy foods that shows an insulinotropic effect. In our study, kefir is proved to have the same effect. Whey fraction of milk products which consists of leucine, isoleucine, valine, lysine and threonine, are believed to be the potent stimulators of insulin secretion.

Many studies have been conducted to examine the relationship between glycemic index and satiety; however, the results are inconsistent. Our data showed a slight but not significant inverse relationship between glycemic and satiety responses. We believe that if the number of subjects were increased, it would provide a better power to detect the relationship of glycemic score and satiety index value.

In conclusion, kefir is a medium to low GI food depending on the added sweetener. Therefore, kefir can potentially be a useful food choice for patients with diabetes who are required to control their blood glucose levels.
APPENDIX A. INDIVIDUAL SUBJECT CHARACTERISTICS OF ALL PHASES

Table 11a. Individual subject characteristics of phase I

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Age (y)</th>
<th>Ethnicity</th>
<th>BMI (kg/m²)</th>
<th>Fasting plasma glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>25</td>
<td>Caucasian</td>
<td>25.0</td>
<td>85</td>
</tr>
<tr>
<td>102</td>
<td>20</td>
<td>Caucasian</td>
<td>22.5</td>
<td>99</td>
</tr>
<tr>
<td>103</td>
<td>22</td>
<td>Asian</td>
<td>29.2</td>
<td>86</td>
</tr>
<tr>
<td>104</td>
<td>21</td>
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<tr>
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<td>81</td>
</tr>
<tr>
<td>108</td>
<td>23</td>
<td>Asian</td>
<td>18.9</td>
<td>89</td>
</tr>
<tr>
<td>109</td>
<td>19</td>
<td>Caucasian</td>
<td>19.5</td>
<td>87</td>
</tr>
<tr>
<td>110</td>
<td>22</td>
<td>Caucasian</td>
<td>18.7</td>
<td>81</td>
</tr>
</tbody>
</table>

Table 11b. Individual subject characteristics of phase II

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Age (y)</th>
<th>Ethnicity</th>
<th>BMI (kg/m²)</th>
<th>Fasting plasma glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>201</td>
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</tr>
<tr>
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<td>87</td>
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<td>Caucasian</td>
<td>24.2</td>
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</tr>
<tr>
<td>207</td>
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<tr>
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<td>95</td>
</tr>
<tr>
<td>209</td>
<td>19</td>
<td>Caucasian</td>
<td>22.4</td>
<td>94</td>
</tr>
<tr>
<td>210</td>
<td>28</td>
<td>Caucasian</td>
<td>19.9</td>
<td>89</td>
</tr>
</tbody>
</table>
### Table 11c. Individual subject characteristics of phase III

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Age (y)</th>
<th>Ethnicity</th>
<th>BMI (kg/m²)</th>
<th>Fasting plasma glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>301</td>
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<td>303</td>
<td>25</td>
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<tr>
<td>304</td>
<td>35</td>
<td>Asian</td>
<td>22.3</td>
<td>98</td>
</tr>
<tr>
<td>305</td>
<td>20</td>
<td>Caucasian</td>
<td>29.2</td>
<td>97</td>
</tr>
<tr>
<td>306</td>
<td>25</td>
<td>Caucasian</td>
<td>25.7</td>
<td>89</td>
</tr>
<tr>
<td>307</td>
<td>27</td>
<td>Caucasian</td>
<td>27.0</td>
<td>86</td>
</tr>
<tr>
<td>308</td>
<td>26</td>
<td>Caucasian</td>
<td>28.9</td>
<td>89</td>
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<tr>
<td>309</td>
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<td>Caucasian</td>
<td>22.4</td>
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<tr>
<td>310</td>
<td>20</td>
<td>Caucasian</td>
<td>22.9</td>
<td>97</td>
</tr>
</tbody>
</table>
APPENDIX B. INDIVIDUAL GLUCOSE, INSULIN AND SATIETY AUC GRAPHS OF ALL PHASES

Phase I: Blood glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), and two controls (glucose solutions) (mg/dl, over 120 minutes).

Subject 101

Subject 102
Phase I: Blood glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), and two controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 103

Subject 104

Subject 105
Phase I: Blood glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), and two controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 106

Subject 107

Subject 108
Phase I: Blood glucose responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), and two controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 109

Subject 110
Phase II: Blood glucose responses to Lifeway® Low Fat Plain Kefir (P group), and controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 201

Subject 202

Subject 203
Phase II: Blood glucose responses to Lifeway® Low Fat Plain Kefir (P group), and controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 204

Subject 205

Subject 206
Phase II: Blood glucose responses to Lifeway® Low Fat Plain Kefir (P group), and controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 207

Subject 208

Subject 209
Phase II: Blood glucose responses to Lifeway® Low Fat Plain Kefir (P group), and controls (glucose solutions) (mg/dL, over 120 minutes).

Subject 210
Phase III: Blood insulin responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (µIU/mL, over 120 minutes).

Subject 301

![Graph showing insulin levels for Subject 301](image)

Subject 302

![Graph showing insulin levels for Subject 302](image)

Subject 303

![Graph showing insulin levels for Subject 303](image)
Phase III: Blood insulin responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (µU/mL, over 120 minutes).

Subject 304

Subject 305

Subject 306
Phase III: Blood insulin responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (µIU/mL, over 120 minutes).

Subject 307

Subject 308

Subject 309
Phase III: Blood insulin responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (µIU/mL, over 120 minutes).

Subject 310
Phase III: Satiety responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway Low Fat Plain Kefir (P group), and white bread control (RSU, over 120 minutes).

Subject 301

Subject 302

Subject 303
Phase III: Satiety responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (RSU, over 120 minutes).

Subject 304

Subject 305

Subject 306
Phase III: Satiety responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway Low Fat Plain Kefir (P group), and white bread control (RSU, over 120 minutes).

Subject 307

Subject 308

Subject 309
Phase III: Satiety responses to Lifeway® Low Fat Strawberry Kefir (S group), Lifeway ProBugs Kefir (orange flavor) (O group), Lifeway® Low Fat Plain Kefir (P group), and white bread control (RSU, over 120 minutes).

Subject 310