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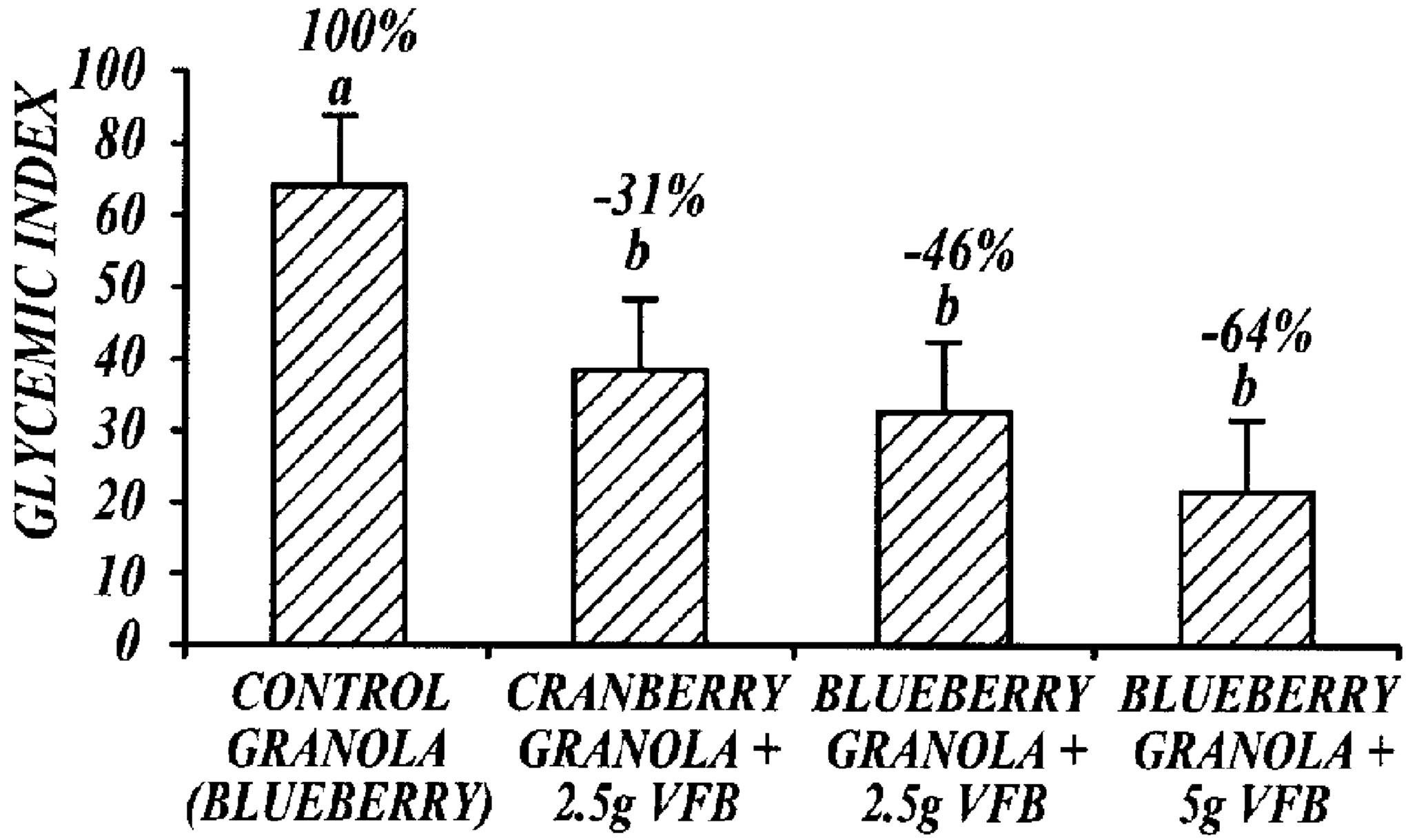
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(54) **Titre : SUPPLEMENT DIETETIQUE ET PROCEDES D'UTILISATION**
(54) **Title: DIETARY SUPPLEMENT AND METHODS OF USE**



(57) **Abrégé/Abstract:**
One aspect of the invention provides dietary fiber compositions comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, and at least one lipid or blend thereof, wherein the lipid or blend thereof comprises at least 20% w/w of the total dietary fiber composition. The invention also provides food products comprising an effective amount of a dietary fiber composition. In other aspects, the invention provides methods for preparing a dietary fiber composition or a food product comprising a dietary fiber composition and methods for promoting satiety, promoting weight loss, lowering blood glucose, or lowering blood cholesterol levels in a mammal.

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ABSTRACT

One aspect of the invention provides dietary fiber compositions comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, and at least one lipid or blend thereof, wherein the lipid or blend thereof comprises at least 20% w/w of the total dietary fiber composition. The invention also provides food products comprising an effective amount of a dietary fiber composition. In other aspects, the invention provides methods for preparing a dietary fiber composition or a food product comprising a dietary fiber composition and methods for promoting satiety, promoting weight loss, lowering blood glucose, or lowering blood cholesterol levels in a mammal.

DIETARY SUPPLEMENT AND METHODS OF USE

FIELD OF THE INVENTION

The invention relates to dietary fiber compositions and their use to suppress appetite, promote weight loss, and to lower blood glucose and cholesterol levels.

BACKGROUND

Obesity and metabolic syndrome, conditions that may lead to the development of Type 2 diabetes, have become more and more common. It has been found that such conditions are due to increasing insulin resistance of the cells. Diabetic conditions are traditionally managed with insulin injections and various pharmaceuticals to regulate blood sugars. However, diet and weight loss play a major role in correcting many metabolic abnormalities associated with diabetes (Yip et al., *Obesity Res. 9*:341S-347S (2001)). Intake of foods with a high glycemic index is known to lead to overeating and obesity (Ludwig et al., *Pediatrics 103*(3):E26 (1999)). Therefore, it is preferable that any agent used in the management of diabetic conditions as well as weight loss be low in glycemic index. It is most preferable if such agents reduce the glycemic index of foods.

A reduction in carbohydrate intake is also required in successful management of diabetic conditions. Diet counseling is helpful, but diabetics experience more food cravings as they experience more frequent states of hypoglycemia (Strachan et al., *Physiol. Behav. 80*(5):675-82 (2004)). Additionally, therapies lowering blood glucose levels in diabetic patients are often associated with the undesirable side effect of body weight gain (Schultes et al., *J. Clin. Endocrinol. Metabol. 88*(3):1133-41 (2003)). It has been reported that diets high in soluble fiber may reduce the risk of diabetes through increased insulin sensitivity (Ylonen et al., *Diabetes Care 26*:1979-85 (2003)). This may result from the possible role of dietary fiber in blood sugar regulation. It has also been reported that high viscosity meals produce a greater sense of fullness compared to low viscosity meals (Marciani et al., *Am. J. Physiol. Gastrointest. Liver Physiol. 280*:G1227-33 (2001)).

Thus, there is a need for dietary fiber compositions that assist in the management of diabetic conditions by lowering blood sugar levels and promoting satiety. The present invention addresses this need and others.

SUMMARY

One aspect of the invention provides dietary fiber compositions. Typically, the dietary fiber compositions comprise effective amounts of glucomannan, xanthan gum, and alginate to produce a desired viscosity. In some embodiments, the dietary fiber composition has a viscosity of at least 2,000 centipoise after 15 minutes under gastric conditions. In some embodiments, the dietary fiber composition has a viscosity of at least 10,000 centipoise after 15 minutes under intestinal conditions. Some embodiments of the dietary fiber composition comprise from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate.

In some embodiments, the invention provides a dietary fiber composition comprising effective amounts of glucomannan, xanthan gum, and alginate to produce an initial viscosity of from about 1 to about 3,000 centipoise and at least a three-fold increase in viscosity within 15 minutes after ingestion in a mammalian subject.

In some embodiments, the invention provides food products comprising an effective amount of a dietary fiber composition comprising glucomannan, xanthan gum, and alginate. Exemplary food products include, but are not limited to, dietary supplements and meal replacements. In some embodiments, the food product comprises from about 2% to about 10% (w/w) of the dietary fiber composition and the dietary fiber composition comprises from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate.

Another aspect of the invention provides a method for preparing a dietary fiber composition. In some embodiments, the methods comprise the step of combining glucomannan, xanthan gum, and alginate to provide a dietary fiber composition comprising effective amounts of glucomannan, xanthan gum, and alginate. In some embodiments, the methods further comprise the step of granulating the dietary fiber composition. The dietary fiber composition prepared according to the methods of the invention may comprise from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In some embodiments, the methods for preparing a dietary fiber composition comprise the step of granulating the composition.

In another aspect, the present invention provides methods of reducing the initial viscosity of a dietary fiber composition comprising glucomannan, comprising the step of granulating the dietary fiber composition.

In another aspect, the invention provides methods of reducing the initial viscosity of a dietary fiber composition comprising glucomannan and xanthan, comprising the step of adding an effective amount of alginate to the composition.

A further aspect of the invention provides methods for promoting satiety, promoting weight loss, lowering blood glucose levels, or lowering blood cholesterol levels in a mammal. In some embodiments, the methods comprise the step of administering to a mammal an amount of a dietary fiber composition effective to promote satiety, to promote weight loss, to lower blood glucose levels, or to lower blood cholesterol levels in the mammal, wherein the dietary fiber composition comprises glucomannan, xanthan gum, and alginate. The dietary fiber composition administered according to these methods may comprise between about 48% and about 70% (w/w) glucomannan, between about 11% and about 13% (w/w) xanthan gum, and between about 9% and about 17% (w/w) alginate.

In another aspect, the invention provides a dietary fiber composition comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, and at least one lipid or blend thereof, wherein the lipid or blend thereof comprises at least 20% w/w of the total dietary fiber composition. In some embodiments, the composition comprises a fiber blend comprising from about 50% to about 80% (w/w) glucomannan, from about 10% to about 20 % (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In some embodiments, the composition comprises a fiber blend comprising from about 60% to about 80% (w/w) glucomannan, from about 10% to about 20 % (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In some embodiments, the composition comprises a fiber blend comprising from about 60% to about 80% (w/w) glucomannan, from about 10% to about 20 % (w/w) xanthan gum, and from about 9% to about 17% (w/w) alginate. In one embodiment, the composition comprises granules in the size range of from about 40 mesh to about 60 mesh.

In another aspect, the invention provides a dietary fiber composition comprising (a) a fiber blend comprising glucomannan, xanthan gum, and alginate; and (b) at least one lipid or blend thereof; wherein the fiber blend and the at least one lipid are each present at

an amount sufficient to allow the dietary fiber composition to exhibit a viscosity in water of from about 1 to about 3,500 centipoise after five minutes and at least a 5-fold increase in viscosity within 15 minutes after exposure to gastric conditions. In some embodiments, the composition comprises a fiber blend comprising from about 50% to about 90% (w/w) glucomannan. In one embodiment, the composition comprises granules in the size range of from about 40 mesh to about 60 mesh.

In another aspect, the present invention provides a food product comprising from 2.5 g to 7.5 g of a composition comprising a fiber blend per 50 g available carbohydrate of the food product, wherein the fiber blend comprises from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In some embodimetns, the composition comprises a fiber blend comprising from about 60% to about 90 % (w/w) glucomannan, from about 5% to about 20% (w/w) xantham gum, and from about 5% to about 30% (w/w) alginate. In some embodiments, the composition comprises a fiber blend comprising from about 50% to about 80 % (w/w) glucomannan, from about 10% to about 20% (w/w) xantham gum, and from about 9% to about 17% (w/w) alginate. In one embodiment, the composition comprises granules in the size range of from about 40 mesh to about 60 mesh.

In yet another aspect, the present invention provides a method for reducing the glycemic index of a food product, the method comprising adding to the food product prior to consumption a composition comprising a dietary fiber blend in an amount effective to reduce the glycemic index of the food product by at least 5 glycemic index units, wherein the fiber blend comprises from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In one embodiment, the composition comprises granules in the size range of from about 40 mesh to about 60 mesh.

In another aspect, the present invention provides a method of reducing the glycemic volatility in a subject in need thereof, comprising administering to the subject in need thereof a composition comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate. In some embodiments, the composition comprises a fiber blend comprising from about 50% to about 80 % (w/w) glucomannan, from about 10% to about 20% (w/w) xantham gum, and from about 9% to about 17%

(w/w) alginate. In one embodiment, the composition comprises granules in the size range of from about 40 mesh to about 60 mesh. In some embodiments, this aspect of the invention includes (a) measuring a subject with a continuous glucose monitoring system for a designated time period to determine the baseline glycemic volatility of the subject; and (b) administering a effective dosage of a fiber blend to the subject, the fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate for a time period effective to reduce the glycemic volatility of the subject as compared to the baseline glycemic volatility measured in step (a).

In another aspect, the invention provides a method of producing a dietary fiber composition comprising: (a) mixing from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate; and (b) adding from about 20% to about 70% of a lipid or blend thereof and mixing to generate the dietary fiber composition. In some embodiments, the method further comprises granulating the mixture of step (a) prior to step (b).

DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 illustrates the effect of different sources of soluble fibers and viscous fiber blend (VFB) on the glycemic response to a 50 g oral glucose load, as described in EXAMPLE 2;

FIGURE 2A provides a comparison of subjective appetite ratings before each meal and bedtime snack at week 0 and week 3 in subjects provided with test breakfasts containing VFB cookies, as described in EXAMPLE 2. Data are expressed as Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk;

FIGURE 2B provides a comparison of subjective appetite ratings before each meal and bedtime snack at week 0 and week 3 in subjects provided with control breakfasts, as described in EXAMPLE 2. Data are expressed as Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk;

FIGURE 3A graphically illustrates the acute postprandial glucose response in subjects provided with control and test breakfasts as measured at the beginning of the study, as described in EXAMPLE 2;

FIGURE 3B graphically illustrates the acute postprandial glucose response in subjects provided with control and test breakfasts as measured during the third week of the study, as described in EXAMPLE 2;

FIGURE 3C graphically illustrates the postprandial insulin response in subjects provided with control and test breakfasts as measured at the beginning of the study, as described in EXAMPLE 2;

FIGURE 3D graphically illustrates the postprandial insulin response in subjects provided with control and test breakfasts as measured during the third week of the study, as described in EXAMPLE 2;

FIGURE 4 shows the area under the curves for postprandial glucose responses at week 0 and week 3 for control and VFB, as described in EXAMPLE 2. All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk;

FIGURE 5 shows the area under the curves for postprandial insulin responses at week 0 and week 3 for control and VFB, as described in EXAMPLE 2. All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk;

FIGURE 6 graphically illustrates the change in percent body fat in subjects that consumed a test breakfast in comparison to subjects that consumed a control breakfast over a three-week period, as described in EXAMPLE 2;

FIGURE 7 graphically illustrates the viscosity profile of various fiber blends over time in distilled water, as described in EXAMPLE 8;

FIGURE 8 graphically illustrates the viscosity profile of various fiber blends over time under gastric conditions, as described in EXAMPLE 8;

FIGURE 9 graphically illustrates the viscosity profile of various fiber blends over time under intestinal conditions, as described in EXAMPLE 8;

FIGURE 10A graphically illustrates the incremental changes in blood glucose after treatment of a plurality of subjects with solid food (white bread), white bread plus VFB100 or white bread plus VFB300, as described in EXAMPLE 11;

FIGURE 10B graphically illustrates the incremental area under the curve (IAUC) in postprandial blood glucose after treatment of a plurality of subjects with the bread treatments shown in FIGURE 10A, as described in EXAMPLE 11;

FIGURE 11A graphically illustrates the incremental changes in blood glucose after treatment of a plurality of subjects with a glucose drink control, glucose drink plus VFB100, or glucose drink plus VFB300, as described in EXAMPLE 11;

FIGURE 11B graphically illustrates the incremental area under the curve (IAUC) in postprandial blood glucose after treatment of a plurality of subjects with the glucose drink treatments shown in FIGURE 11A, as described in EXAMPLE 11;

FIGURE 12 graphically illustrates the change in glycemic index (GI) after consumption with a glucose drink or white bread containing increasing doses (2.5, 5.0, 7.5 g) of VFB, as described in EXAMPLE 12;

FIGURE 13 graphically illustrates the glycemic index for each test meal with or without 5.0 g of VFB per approximately 50 g available carbohydrates, expressed as the Mean ± SEM. As shown in FIGURE 13, addition of VFB to cornflakes, rice, turkey dinner, or yogurt resulted in a 26%, 45%, 24%, and 9% reduction in meal GI, respectively. The percent reductions observed in the GI for cornflakes and rice meals when adding VFB were statistically significant ($p<0.00001$), as described in EXAMPLE 13;

FIGURE 14 graphically illustrates the glycemic index for each test meal with or without VFB, expressed as the Mean ± SEM. As shown in FIGURE 14, addition of VFB reduced the glycemic index of all the granolas, with statistically significant reductions observed, irrespective of the type of granola used ($p<0.0001$), as described in EXAMPLE 14;

FIGURE 15 shows a representative continuous glucose monitoring system (CGMS) graph measuring normal glycemic volatility in a non-obese, non-diabetic subject over a 24-hour period;

FIGURE 16A shows a CGMS graph for an obese, non-diabetic subject (ID:10) measured over a 24-hour period prior to treatment with VFB (baseline);

FIGURE 16B shows a CGMS graph for the subject (ID:10) shown in FIGURE 16A after 5 weeks of consumption of VFB (10-15g/day);

FIGURE 17A shows a CGMS graph for a non-diabetic subject (ID:90) measured over a 24-hour period prior to treatment with VFB (baseline);

FIGURE 17B shows a CGMS graph for the same subject ID:90 shown in FIGURE 17A after 5 weeks of consumption of VFB (10-15g/day);

FIGURE 18A shows a CGMS graph for a non-diabetic subject (ID:20) measured over a 24-hour period prior to treatment with VFB (baseline);

FIGURE 18B shows a CGMS graph for the same subject ID:20 shown in FIGURE 18A after 5 weeks of consumption of VFB (10-15g/day);

FIGURE 19A shows a CGMS graph over a 24-hour period of an obese non-diabetic subject (ID:1098) prior to treatment with a low glycemic index diet (baseline);

FIGURE 19B shows a CGMS graph over a 24-hour period (from the same obese non-diabetic subject shown in FIGURE 19A), after a six month low glycemic index diet;

FIGURE 19C shows a CGMS graph over a 24-hour period of a non-diabetic subject (ID:1146) prior to treatment with a low glycemic index diet (baseline);

FIGURE 19D shows a CGMS graph over a 24-hour period (from the same obese non-diabetic subject shown in FIGURE 19C), after a six month low glycemic index diet;

FIGURE 20A shows a CGMS graph over a 24-hour period from an obese diabetic subject on insulin (ID:60) prior to treatment with VFB (baseline); and

FIGURE 20B shows a CGMS graph over a 24-hour period from the same diabetic subject as shown in FIGURE 20A after treatment with VFB (10-15g/day) for 4 weeks.

DETAILED DESCRIPTION

In one aspect, the invention provides dietary fiber compositions comprising glucomannan, xanthan gum, and alginate. As used herein, "glucomannan" refers to a water-soluble dietary fiber with β-(1,4)-linked-D-mannose and β-(1,4)-linked-D-glucose residues in approximately 3:1 ratio and various α-linked galactose end groups. It is most commonly isolated from konjac root (*Amorphophallus konjac*) but can also be isolated from other plant sources. Commercially available glucomannan typically includes up to about 10% (w/w) water. "Xanthan gum" refers to a heteropolysaccharide containing glucose, mannose, potassium or sodium glucuronate, acetate, and pyruvate. Commercially available xanthan gum typically includes up to about 13% (w/w) water. "Alginate" refers to a mixed polymer of mannuronic and guluronic acid. Commercially available sodium alginate typically contains up to about 15% (w/w) water.

The dietary fiber compositions of the invention comprise effective amounts of glucomannan, xanthan gum, and alginate. As used herein, an "effective amount" refers to an amount that produces the desired viscosity. Effective amounts of glucomannan, xanthan gum, and alginate are proportionate amounts of each of these components that produce the desired viscosity when combined. Effective amounts of the dietary fiber

composition are amounts of the composition that produce the desired viscosity when ingested. The proportions of glucomannan, xanthan gum, and alginate in the dietary compositions are generally selected to produce a fiber blend that has an initial viscosity that is palatable, but that increases in viscosity substantially over a 15- to 60-minute time period and that maintains or increases in viscosity under gastric or intestinal conditions. As used herein, the term "initial viscosity that is palatable" refers to a range of viscosity from about 1 centipoise to about 3,000 centipoise. Liquids with a viscosity of greater than about 3,000 centipoise are difficult to ingest and are therefore considered to be non-palatable. As used herein, "initial viscosity" refers to the viscosity of the dietary composition in a 100-fold (w/w) excess of water at a temperature between about 4°C to about 25°C, for example, between about 16°C and about 25°C, or equivalent conditions. "Viscosity under gastric conditions" refers to the viscosity of the dietary composition in a 70-fold (w/w) excess of gastric fluid at a temperature between about 16°C and about 25°C, or equivalent conditions. "Gastric fluid" refers to a solution having a pH of about 1.2 that is made by dissolving 2.0 g of NaCl and 3.2 g of pepsin in 7.0 mL of HCl and sufficient water to make 100 mL (see United States Pharmacopoeia). Gastric conditions may be simulated by adding 10 drops of phosphoric acid to 200 g of distilled water. "Viscosity under intestinal conditions" refers to the viscosity of the dietary composition in a 70-fold (w/w) excess of simulated intestinal fluid at a temperature between about 16°C and about 25°C or equivalent conditions. "Simulated intestinal fluid" refers to a solution having a pH between about 7.5 and about 8.0 that is made as follows: 6.8 g of monobasic potassium phosphate is dissolved in 250 mL of water and mixed; 190 mL of 0.2 N NaOH and 400 mL of water are added. This is followed by adding 10.0 g of pancreatin, mixing, adjusting the solution with 0.2 N NaOH to a pH of 7.5 ± 0.1, and diluting with water to 1,000 mL (see United States Pharmacopoeia).

In some embodiments, the dietary fiber composition has an initial viscosity of between about 1 centipoise (cps) and about 3,000 cps (such as from about 200 cps to about 1,000 cps or from about 400 cps to about 1,000 cps). In some embodiments, the dietary fiber composition has a viscosity under gastric conditions of between about 600 cps and about 5000 cps (such as from about 1,000 cps to about 5,000 cps or from about 1,000 cps to about 3,000 cps) after about 30 minutes. In some embodiments, the dietary fiber composition has a viscosity under intestinal conditions of between about 1,500 cps and about 8,000 cps (such as from about 2,000 cps to about 6,000 cps or from

about 2,500 cps to about 6,000 cps) after about 30 minutes. In some embodiments, the dietary fiber composition comprises effective amounts of glucomannan, xanthan gum, and alginate to produce an initial viscosity of from about 1 to about 3,000 cps and a least a three-fold increase in viscosity within 15 minutes after ingestion by a mammalian subject, as described in EXAMPLE 1.

The proportions of glucomannan, xanthan gum, and alginate in the dietary fiber compositions may be from about 48% to about 90% of glucomannan (such as from about 60% to about 80%, or from about 60% to about 90%, or from about 65% to about 75%, or from about 50% to about 80%, or from about 50% to about 70%, or about 70%), from about 5% to about 20% of xanthan gum (such as from about 10% to about 20% or from about 11% to about 13%, or from about 13% to about 17%, or about 13%, or about 17%), and from about 5% to about 30% of alginate (such as from about 10% to about 20% or from about 13% to about 17%, or about 13%, or about 17%). In some embodiments, proportions of glucomannan, xanthan gum, and alginate in the dietary compositions are about 70% glucomannan, from about 13% to about 17% xanthan, and from about 13% to about 17% alginate, as described in EXAMPLES 1 and 8.

In some embodiments, the dietary fiber compositions are granulated. As used herein, "granulation" refers to any process of size enlargement in which small particles are gathered together into larger, permanent aggregates. Granulation may be accomplished by agitation in mixing equipment, by compaction, extrusion, or globulation. The dietary fiber compositions may be granulated using various mesh sizes. The term "mesh" refers to the size of the particle as determined by its ability to pass through a screen having holes of defined dimensions. The mesh sizes used herein are Tyler equivalents, as set forth in Table 21-12 of the *Chemical Engineers Handbook* (5th ed., Perry & Chilton, eds.). The larger the granulation (i.e., the smaller the mesh size) of the dietary fiber composition, the longer it takes for a desired viscosity to be attained, as shown in EXAMPLE 1. In some embodiments, the dietary fiber composition is granulated using a combined mesh size by separating granulated materials by their particle size, then recombining the particle-size separated granules to give the desired viscosity profile. For example, a combined mesh size of 30 to 60 is obtained by combining granules of 30 mesh (about 600 microns), granules of about 40 mesh (about 400 microns), and granules of about 60 mesh (250 microns).

The dietary fiber compositions of the invention are prepared in a form suitable for oral use according to any method known in the art for the manufacture of oral compositions. For example, the dietary fiber compositions may be prepared as tablets, troches, lozenges, aqueous or oily suspensions, dispersible/dispensable powders or granules (e.g., powders and granules that may be sprinkled on food), emulsions, hard or soft capsules, syrups, elixirs or enteral formulas, or controlled-release compositions. For oral consumption, the dietary compositions may be added to a food or a beverage. For example, a powdered form of the dietary composition may be mixed with an ingestible liquid to form an aqueous beverage or mixed with cookie batter prior to baking. An exemplary formulation of the dietary fiber composition is as hard gelatin capsules, each capsule comprising about 500 mg of the dietary fiber composition.

The dietary fiber compositions of the invention may further comprise additional components. For example, the dietary fiber compositions may additionally comprise magnesium stearate, rice flour, xylitol, lecithin, medium chain triglycerides, flavors, stevia, and/or syloid silica. An exemplary dietary composition comprises about 48% (w/w) glucomannan, about 11% (w/w) xanthan gum, about 9% (w/w) alginate, about 31% (w/w) rice flour, and about 1% (w/w) magnesium stearate. Exemplary dietary fiber compositions are described in EXAMPLES 1, 4, and 5.

In some embodiments, the dietary fiber compositions may include mulberry extract. Mulberry leaf has been shown to possess therapeutic effects on hypoglycemia (see, e.g., *Clin. Chim. Acta 314*(1-2):47-53). Therefore, the addition of mulberry extract may enhance the effect of the dietary fiber composition in the regulation of blood sugar levels. However, the addition of mulberry extract dilutes the concentration of the dietary fibers in the compositions and reduces the viscosity of the overall composition. Therefore, in some embodiments, the dietary fiber compositions of the invention do not include mulberry extract or contain less than 3.5% of mulberry extract.

The dietary fiber compositions of the invention may be consumed before a meal, during a meal, or after a meal. The dietary fiber compositions of the invention control hunger and induce satiety by providing high viscosity in the gastrointestinal tract. The blend of fibers maintains high viscosities under both the acidic conditions of the stomach and the alkaline conditions in the intestines. The dietary fiber compositions of the invention further assist in the management of diabetic conditions by lowering blood glucose levels.

Another aspect of the invention provides food products comprising an effective amount of a dietary fiber composition comprising glucomannan, xanthan gum, and alginate. The food products of the invention may be dietary supplements or meal replacements. In some embodiments, the food products are provided as shakes or smoothies. Typically, the food products of the invention comprise from about 2% to about 30% (such as from about 2% to about 20%, or from about 5% to about 15%, or from about 2% to about 10%) of a dietary fiber composition comprising glucomannan, xanthan gum, and alginate. Typically, the food products comprise between about 2 grams and about 15 grams of the dietary fiber per serving (such as between about 3 to 8 grams or between about 3 and about 6 grams per serving). In some embodiments, the food products of the invention comprise about 9% (w/w) of a dietary fiber composition comprising glucomannan, xanthan gum, and alginate, as described in EXAMPLES 3 and 7.

The food products of the invention may further contain additional components such as proteins or amino acids, carbohydrates, lipids, vitamins, minerals and cofactors, natural or artificial flavors, dyes or other coloring additives, and preservatives. The term "vitamins" includes, but is not limited to, thiamin, riboflavin, nicotinic acid, panthothenic acid, pyridoxine, biotin, folic acid, vitamin B12, lipoic acid, ascorbic acid, vitamin A, vitamin D, vitamin E, and vitamin K. Also included within the term "vitamins" are cofactors and coenzymes such as coenzymes include thiamine pyrophosphates (TPP), flavin mononucleotide (FMM), flavin adenine dinucleotide (FAD), nicotinamide adenine dinucleotide (NAD), nicotinamide adenine dinucleotide phosphate (NADP) Coenzyme A (CoA) pyridoxal phosphate, biocytin, tetrahydrofolic acid, coenzyme B12, lipoyllysine, 11-cis-retinal, and 1,25-dihydroxycholecalciferol. The term "vitamins" also includes choline, carnitine, and alpha, beta, and gamma carotenes. The term "minerals" refers to inorganic substances, metals, and the like, required in the human diet, including, but not limited to, calcium, iron, zinc, selenium, copper, iodine, magnesium, phosphorus, chromium, manganese, potassium, and the like, and mixtures thereof. The mineral may be in the form of a salt, an oxide, or a chelated salt.

Coloring agents include, but are not limited to, titanium dioxide and dyes suitable for food such as those known as FD&C dyes and natural coloring agents such as grape skin extract, beet red powder, beta-carotene, annatto, carmine, tumeric, chlorophyll, and

paprika. The amount of coloring used may range from about 0.0% to about 3.5% dry weight of the total composition, depending on the saturation of the color.

Flavors incorporated in the composition may be chosen from synthetic flavor oils and flavoring aromatics and/or natural oils, extracts from plants, leaves, flowers, and fruits, and combinations thereof. These may include, but are not limited to, cinnamon oil, oil of wintergreen, peppermint oils, clove oil, bay oil, anise oil, eucalyptus, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, oils of citrus fruits (including, but not limited to, lemon and orange) oil of bitter almonds and cassia oil. Suitable flavors include, but are not limited to, vanilla, chocolate, mocha, coffee, ice cream, citrus (including lemon, orange, grape, lime, and grapefruit), apple, pear, peach, mango, strawberry, raspberry, cherry, plum, pineapple, and apricot. The amount of flavoring may depend on a number of factors, including the organoleptic effect desired. Flavors may be present in an amount ranging from about 0% to about 10.0% dry weight based upon the dry weight of the composition. Exemplary food products of the invention are provided in EXAMPLES 2, 3, and 7.

In some embodiments, the food products of the invention do not include bilberry extract, lutein, and/or taurine. Some embodiments of the invention provide food products containing less than 28 g of whey protein or less than 8.9 g of fructose. Some embodiments of the invention provide food products containing more than 0.9 g of medium chain triglycerides.

In a further aspect, the invention provides methods for preparing a dietary fiber composition and methods of preparing a food product comprising a dietary fiber composition. In some embodiments, the methods of preparing a dietary fiber composition comprise the step of combining effective amounts of glucomannan, xanthan gum, and alginate to produce an initial viscosity of from about 1 to about 3,000 centipoise and at least a three-fold increase in viscosity within 15 minutes after ingestion. In some embodiments, the methods of preparing a dietary fiber composition further comprise the step of granulating the dietary fiber composition.

In some embodiments, the methods of preparing a food product comprising a dietary fiber composition comprise the step of adding an effective amount of a dietary fiber composition comprising glucomannan, xanthan gum, and alginate to a food product. The food products of the invention may be consumed once or several times a day.

In another aspect, the invention provides methods of reducing the initial viscosity of a dietary fiber composition comprising glucomannan. In some embodiments, the method includes the step of granulating the dietary fiber composition comprising glucomannan to produce a composition that has a reduced viscosity. In some embodiments, the dietary fiber further comprises xanthan gum and/or alginate. In some embodiments, the method includes the step of adding an amount of alginate to the composition comprising glucomannan effective to reduce the initial viscosity of the composition, while allowing the composition to increase in viscosity over time, such as after a period of about 120 minutes.

Yet another aspect of the invention provides methods for promoting satiety, promoting weight loss, lowering blood glucose levels, or lowering blood cholesterol levels in a mammal. In some embodiments, the methods comprise administering to a mammal an amount of a dietary fiber composition effective to promote satiety in the mammal, wherein the dietary fiber composition comprises glucomannan, xanthan gum, and alginate. In some embodiments, the methods comprise administering to a mammal an amount of a dietary fiber composition effective to promote weight loss in the mammal, wherein the dietary fiber composition comprises glucomannan, xanthan gum, and alginate. In some embodiments, the methods comprise administering to a mammal an amount of a dietary fiber composition effective to lower blood glucose levels in the mammal, wherein the dietary fiber composition comprises glucomannan, xanthan gum, and alginate. In some embodiments, the methods comprise administering to a mammal an amount of a dietary fiber composition effective to lower blood cholesterol levels in the mammal, wherein the dietary fiber composition comprises glucomannan, xanthan gum, and alginate.

Exemplary dietary fiber compositions for use in the methods of the invention are as described above. The dietary fiber compositions may be administered in any form. For example, they may be administered as capsules or they may be administered in a food product.

Exemplary methods of the invention are described in EXAMPLES 2 and 3. As shown in EXAMPLES 2 and 3, the methods of the invention produce significant increases in insulin sensitivity, reduce body fat, and promote satiety and weight loss.

In another aspect, the present invention provides a dietary fiber composition comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan,

from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, and at least one lipid or blend thereof, wherein the lipid or blend thereof comprises at least 20% w/w of the dietary fiber composition.

As described in EXAMPLES 9 and 10, and TABLES 28-31, the addition of a lipid or blend thereof to the various embodiments of dietary fiber compositions of the invention is effective to delay the viscous effects of the fiber blend in water, which is useful to prevent choking during oral administration in a subject, while allowing for a high viscosity within a short time under gastric conditions (*in vivo* conditions post-consumption).

The fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate is described supra.

As used in accordance with this embodiment of the invention, a lipid is defined as a substance such as a fat, oil or wax that dissolves in alcohol but not in water. As used herein, the terms "fat" and "oil" are used interchangeably and comprise fatty acids.

In some embodiments, the lipid for use in the composition comprises a fat selected from the group consisting of a dairy fat (e.g., milk fat, butter fat), an animal fat (e.g., lard) or a vegetable fat (e.g., coconut oil, cocoa butter, or palm oil).

In some embodiments, the lipid for use in the composition comprises an edible oil or a mixture of oils. Such oils include vegetable oils (e.g., canola oil, soybean oil, palm kernel oil, olive oil, safflower oil, sunflower seed oil, flaxseed (linseed) oil, corn oil, cottonseed oil, peanut oil, walnut oil, almond oil, grape seed oil, evening primrose oil, coconut oil, borage oil and blackcurrant oil); marine oils (e.g., fish oils and fish liver oils), or a mixture thereof.

In some embodiments, the lipid for use in the composition comprises oils containing medium-chain triglycerides, such as coconut oil, palm kernel oil and butter or medium-chain triglycerides in purified form.

In some embodiments, the dietary fiber composition comprises an amount of dietary fiber mixture (VFB) in the range of from about 0.01% to about 80% of the total composition (w/w/) and an amount of lipid in the range of from 20% to about 99.99% (w/w). For example, in certain embodiments the ratio of VFB to lipid comprises, (in a weight to weight ratio) 5:95; 10:90; 20:80; 30:70; 40:60; 50:50; 60:40; 70:30; or 80:20.

In some embodiments, the dietary fiber blend for use in the dietary fiber composition comprises from about 50% to about 80% (w/w) glucomannan, from about 10% to about 20% (w/w) xanthan gum, and from about 10% to about 20% (w/w) alginate.

In some embodiments, the dietary fiber blend for use in the dietary fiber composition comprises from about 60% to about 80% (w/w) glucomannan, from about 10% to about 20% (w/w) xanthan gum, and from about 10% to about 20% (w/w) alginate.

In some embodiments, the dietary fiber blend for use in the dietary fiber composition comprises about 70% (w/w) glucomannan, from about 13% to about 17% (w/w) xanthan gum, and from about 13% to about 17% (w/w) alginate.

In one particular embodiment, the dietary fiber composition comprises a dietary fiber mixture (VFB) comprising 70% glucomannan, 13% xanthan and 17% alginate, and a medium chain triglyceride (MCT) at a ratio of 53:47 (w/w).

In some embodiments, the dietary fiber composition further comprises an outer soft gelatin capsule comprising a combination of gelatin, glycerin, and water, as described in EXAMPLE 9.

The dietary fiber composition comprising a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, and at least one lipid or blend thereof can be manufactured by first producing the fiber blend using methods described herein, followed by the addition of the oil (or mixture thereof), and mixing the fiber blend and oil. An exemplary method of producing a dietary fiber composition is described in EXAMPLE 9.

Various embodiments of the dietary fiber blend, as described herein, may be included in food products, either liquid or solid, resulting in a reduced glycemic index of the food product. As described in EXAMPLES 11 to 14 and FIGURES 12 to 14, the benefits of the dietary fiber composition are realized in various types of foods, including without limitation, drinks mixed with the dietary fiber composition, granola, bread, rice, yogurt, cornflakes, turkey, margarine, milk. As described in EXAMPLE 13, the addition of the dietary fiber blend reduced the glycemic index of all of the test meals tested. For example, the addition of the dietary fiber blend to cornflakes, rice, turkey, or yogurt

resulted in a 26%, 45%, 24%, and 9% reduction in the meal glycemic index, respectively, without reducing the palatability of the various foods tested.

In accordance with the foregoing, in another aspect, the present invention provides a food product comprising from 2.5 g to 7.5 g of a dietary fiber blend per 50 g available carbohydrate of the food product, wherein the dietary fiber blend comprises from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate.

The dietary fiber blend may be combined with any type of food product, including solid, liquid, or semi-solid food products. Exemplary solid food products include, but are not limited to grains (e.g., rice, cereal (hot or cold)), granola, oatmeal, baked goods (bread, cookies, muffins, cakes and others), pasta (including noodles made with rice or other grains); meat (e.g., poultry, beef, pork, fish), dairy products (e.g., milk, yogurt, cheese, ice cream, butter, and margarine). Exemplary liquid or semi-liquid food products include, but are not limited to, meal replacement drinks, fruit juices, soups (including dry soup mixes), dietary supplements, and smoothies.

The dietary fiber blend may be added to the food product prior to consumption using any suitable method. For example, the dietary fiber blend may be baked into the food product, may be mixed with the food product, or sprinkled onto the food product.

In another aspect, the present invention provides a method of reducing the glycemic volatility in a subject in need thereof, comprising administering to the subject in need thereof a fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate.

The Glycemic Volatility refers to the collective of increased frequency of blood sugar excursions, the rapid nature of the rise and fall of blood sugar and the amount of time spent above an ideal blood sugar level as increased glycemic volatility (in comparison to normal subjects with low glycemic volatility), as measured over time in a subject. The Gycemic Volatility can be measured using a commercially available continuous glucose monitoring system, such as CGMS MiniMed, Medtronic, Inc.

Blood glucose levels in normal human subjects (non-obese, non-diabetic) are between 70 mmol/L to 120 mmol/L, with a low glycemic volatility (only very modest fluctuations from the average over a 24-hour period) as shown in FIGURE 15. In

contrast, as demonstrated in EXAMPLE 16, overweight subjects (based on a BMI from 25-30), and obese subjects (based on a BMI over 30) exhibit increased glycemic volatility (in comparison to normal subjects). As shown in FIGURES 16A, 17A, and 18A, the baseline glycemic volatility of three different obese subjects has peak blood glucose levels exceeding 120 mmol/L. As described in EXAMPLE 16 and illustrated in FIGURES 16B, 17B and 18B, the present inventors have discovered that treatment of obese subjects having increased glycemic volatility with a dietary fiber blend (VFB) comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate, is effective to reduce the obese subject's glycemic volatility as compared to the pre-treatment baseline glycemic volatility. For example, as shown in FIGURE 16B, FIGURE 17B and FIGURE 18B, after treatment with 5g to 15g of VFB per day over at least a 4-week period (such as at least 5 weeks or at least 6 weeks), the glycemic volatility was reduced with peak glucose levels reduced to below 120 mmol/L. The VFB was surprisingly effective and found to be superior than a low glycemic index diet, as further described in EXAMPLE 16.

The glycemic volatility (GV) can be described by the following equations:

$$Gv_1 = \sum_{1\ to\ i} \left| \frac{B_i - B_{i-1}}{t_i - t_{i-1}} \right| \qquad \text{(Eq. 1)}$$

$$Gv_2 = \sum_{1\ to\ i} \frac{(B_i - BL) - |B_i - BL| + |B_i - BU| + (B_i - BU)}{2t} \qquad \text{(Eq. 2)}$$

Where

B_i is the blood glucose level measured at any given point by the CGMS

t_i is the time at which Bi is measured

t is the total time during which blood glucose level is measured by the CGMS

BL is the lowest normal blood glucose level in normal subjects, which, in most cases, is 70 mmol/L

BU is the highest normal blood glucose level in normal subjects, which, in most cases, is 120 mmol/L

The Gv_1 equation shown above (Eq. 1) describes the slope of a CGMS graph and provides a measure of speed and frequency of the fluctuations of blood glucose in a subject over a given time period. An increased Gv_1 value is indicative of increased glycemic volatility in the subject. In some embodiments of the method, the Gv_1 can be calculated for one or more normal individuals (non-diabetic and normal weight) to obtain a Gv_1 reference value and the Gv_1 reference value can be compared to the Gv_1 value from a test subject, wherein a Gv_1 value from the test subject that is increased as compared to the reference Gv_1 value from the reference value is indicative of increased glycemic volatility in the test subject.

The Gv_2 equation shown above (Eq. 2) is a measure of the magnitude of blood glucose fluctuations outside the normal range (e.g., above 120 mmol/L and below 70 mmol/L) in a CGMS graph over a given time period. An increased Gv_2 value is indicative of increased glycemic volatility. In some embodiments of the method, the Gv_2 can be calculated for one or more normal individuals (non-diabetic and normal weight) to obtain a Gv_2 reference value and the Gv_2 reference value can be compared to the Gv_2 value from a test subject, wherein a Gv_2 value from the test subject that is increased as compared to the reference Gv_2 value is indicative of increased glycemic volatility in the test subject.

In some embodiments, this aspect of the invention includes (a) measuring a subject with a continuous glucose monitoring system for a designated time period to determine the baseline glycolic volatility of the subject; and (b) administering a effective dosage of a fiber blend to the subject, the fiber blend comprising from about 48% to about 90% (w/w) glucomannan, from about 5% to about 20% (w/w) xanthan gum, and from about 5% to about 30% (w/w) alginate for a time period effective to reduce the glycolic volatility of the subject as compared to the baseline glycolic volatility measured in step (a). The baseline glycolic volatility measurements may be determined using the continuous glucose monitoring system, using the GO equations (Eq. 1 and/or Eq. 2) as described above.

The continuous glucose monitoring system may be used for a designated time period sufficient to determine the glycolic volatility, such as, for example, at least

12 hours, at least 15 hours, at least 24 hours, or longer. The glycolic volatility of the subject after treatment with the fiber blend may also be determined using the continuous glucose monitoring system, using the GO equations (Eq. 1 and/or Eq. 2) as described above.

In some embodiments, the dosage of the fiber blend is from at least from 5.0 g to 15.0 g VFB per day or greater, such as from 10.0 to 15.0 g VFB per day (e.g., 5.0 g/day, 6.0 g/day, 7.0 g/day, 8.0 g/day, 9.0 g/day, 10.0 g/day, 11.0 g/day,12.0 g/day, 13.0 g/day, 14.0 g/day or 15.0 g/day). The fiber blend may be administered as a powder stirred into a liquid, in a capsule, or sprinkled, baked or mixed into a food product, as described herein.

In accordance with the methods of this aspect of the invention, the dosage of VFB is typically administered for at least 4 weeks, such as at least 5 weeks, at least 6 weeks or longer.

In some embodiments, the dietary fiber blend comprises from about 50% to about 80% (w/w) glucomannan, from about 10% to about 20% (w/w) xanthan gum, and from about 10% to about 20% (w/w) alginate.

In some embodiments, the dietary fiber blend comprises from about 60% to about 80% (w/w) glucomannan, from about 10% to about 20% (w/w) xanthan gum, and from about 10% to about 20% (w/w) alginate.

In some embodiments, the dietary fiber blend comprises about 70% (w/w) glucomannan, from about 13% to about 17% (w/w) xanthan gum, and from about 13% to about 17% (w/w) alginate.

In some embodiments, the dietary fiber blend further comprises at least one lipid or blend thereof, wherein the lipid or blend thereof comprises at least 20% w/w of the total dietary fiber composition.

In one particular embodiment, the dietary fiber blend comprises 70% glucomannan, 13% xanthan and 17% alginate, and a medium chain triglyceride (MET) at a ratio of 53:47 (w/w).

As used herein, the term "subject in need thereof" refers to any mammalian subject with increased glycolic volatility as compared to a normal (non-diabetic, non-obese and non-overweight) subject of the same species, including for example, overweight non-diabetic subjects (based on a BMI from 25-30), obese non-diabetic subjects (based on a BMI over 30), and type II diabetic subjects.

In some embodiments, the method of this aspect of the invention may be used to treat a non-diabetic obese subject having a baseline glycolic volatility with peak glucose levels exceeding 120 mol/L and wherein treatment with the fiber blend reduces the glycolic volatility to a peak glucose level below 120 mol/L, as described in EXAMPLE 16 and shown in FIGURES 16A-18B.

In some embodiments, the method of this aspect of the invention may be used to treat a diabetic obese subject having a baseline glycolic volatility with peak glucose levels exceeding 220 mol/L and wherein treatment with the fiber blend reduces the glycolic volatility to a peak glucose level below 220 mol/L, as described in EXAMPLE 16 and shown in FIGURE 20A and FIGURE 20B.

The following examples merely illustrate the best mode now contemplated for practicing the invention, but should not be construed to limit the invention

EXAMPLE 1

This example describes the selection of fibers in an exemplary dietary fiber composition, referred to as a viscous fiber blend (VFB), which provides desirable viscosity profiles under gastric and intestinal conditions.

In formulating VFB, the main objective was to produce a fiber blend that would increase in viscosity substantially over a 30-to 60-minute time period. To enhance palatability, it is desirable for the initial viscosity of the fiber blend to be thinner and for the maximum thickness of the fiber blend to occur in the stomach and intestines of the subject. Therefore, in selecting fibers, the blend also had to maintain or, more desirably, increase in viscosity under both gastric (acidic) and intestinal conditions. The high viscosity at this point in the digestive system would contribute to a feeling of fullness and also help with blood sugar regulation by modulating carbohydrate absorption.

TABLE 1 shows the viscosity of different fibers tested separately: galactomannan (greater than 80% pure from fenugreek, made by Faunlike), glucomannan (greater than 80% pure from Konjac root), guar gum (commercially sourced galactomannan extract of *Cyanosis tetragonoloba*), xanthan gum (commercially sourced extracellular heteropolysaccharide from *Xanthomonas* bacteria), alginate (commercially sourced medium viscosity sodium alginate from *Ascophyllum nodosum*, and commercial fiber (consisting of 69% glucomannan, 17% xanthan, 9% carrageenan, and 8% guar, supplied

by Dr. Vuksan, and described in U.S. Patent Application Publication No. 2005/0020535). Two grams of each fiber composition were blended with 200 g of water. Viscosity measurements (in centipoise) were recorded at several time intervals.

TABLE 1. Viscosity Results of Fibers Analyzed Separately

	Viscosity (centipoise) at Different Time Points(minutes)										
	5	**10**	**15**	**20**	**25**	**30**	**45**	**60**	**75**	**90**	**120**
Galactomannan (FenuLife)	0	0	50	50	100	200	300	400	450	550	600
Xanthan	1400	1250	1200	1300	1250	1150	1150	1100	1100	1100	1000
Guar Gum	2950	-	3600	3750	3800	3800	3850	3850	4000	3950	3950
Glucomannan	4900	-	33,000	35750	38000	38750	40500	43000	42500	43250	44000
Commercial Fiber	550	800	1000	1100	1150	-	1350	1550	1550	1750	1900
Alginate	0	0	0	0	0	0	0	0	0	0	0

Alginate and galactomannan were the least viscous. Xanthan and guar gum reached their maximum thickness almost immediately. Glucomannan displayed a substantial increase in viscosity over time. However, it seemed excessively thick for our purposes, so we analyzed how glucomannan reacted in combination with other less viscous fibers. Viscosity results for combined fiber blends are shown in TABLE 2.

TABLE 2. Viscosity Results of Fibers Analyzed in Combination

	Viscosity (centipoise) at Different Time Points(minutes)										
	5	**10**	**15**	**20**	**25**	**30**	**45**	**60**	**75**	**90**	**120**
Glucomannan / Alginate (50:50)	200	400	700	1100	1500	2000	3050	3800	4200	4700	5400
Glucomannan / Xanthan (50:50)	1150	1300	1100	1150	1150	1050	1050	1100	1100	1100	1100
Glucomannan / Galactomannan (50:50)	1050	-	2100	3900	4600	4750	5400	5600	5800	5850	5950
Guar Gum / Alginate (50:50)	450	700	950	1100	1250	1350	1550	1700	1750	1820	1900
Glucomannan / Alginate (75:25)	900	2200	3900	-	4700	5450	9500	14500	15600	15800	16300

Alginate, xanthan and galactomannan had a strong, thinning effect in combination with glucomannan. Xanthan's property of immediately reaching maximum viscosity carried over when combined with glucomannan. The drawback with this blend is that the initial viscosity was too thick and it did not continue to thicken over time. The alginate

and glucomannan blend preserved the characteristic of glucomannan in that it continued to thicken over time. However, the initial viscosity was a bit too watery and it thickened too rapidly. The guar gum and alginate blend did not produce adequate viscosity.

From these results, it was determined that glucomannan was a desirable ingredient for the fiber blend due to its high viscosity property. It also had a very smooth texture that enhanced palatability. Alginate helped moderate the strong thickening characteristic of glucomannan and it also achieved a more palatable viscosity during the initial stages of ingestion. Xanthan, too, was selected as part of the blend since it was the only fiber that seemed to curb and thin out glucomannan near the end of the viscosity test (30-60 minutes). Guar gum and galactomannan did not exhibit any new properties that would contribute to the quality of VFB; therefore, they were not selected as part of the fiber blend.

The final composition of VFB created was from 48%-90% glucomannan, from 5%-20% xanthan gum, and from 5%-30% alginate. When glucomannan, xanthan, and alginate are combined at these ratios to produce VFB, this composition exhibits unexpectedly high viscosity values after 120 minutes when blended with water, as shown in FIGURE 7 and described in EXAMPLE 8. The VFB also produces unexpectedly high viscosity values after 10 minutes when blended with gastric juice, as shown in FIGURE 8 and described in EXAMPLE 8.

At a lower glucomannan ratio, the product would not reach desired thickness. At a higher xanthan ratio, the product also did not reach the desired thickness. At a lower xanthan ratio, the fiber blend thickened too quickly. Alginate also had an important role in enhancing palatability by decreasing viscosity during the initial stages of the product.

In a preferred embodiment, VFB compositions were produced that contained 60%-80% glucomannan, 10%-20% xanthan gum, and 10%-20% alginate that had the desirable characteristics mentioned above. For example, a VFB composition was produced that contained 70% glucomannan, 13% xanthan gum, and 17% alginate with desirable characteristics as described herein. Another VFB composition was produced that contained 70% glucomannan, 17% xanthan gum, and 13% alginate with similar desirable properties.

The viscosity profile of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) in comparison to a competing commercial fiber is presented in TABLE 3.

TABLE 3. Viscosity Profile of VFB vs. Commercial Fiber Blend

	Viscosity (centipoise) at Different Time Points(minutes)									
	5	**10**	**15**	**20**	**25**	**30**	**45**	**60**	**75**	**90**
VFB	600	900	1,000	1100	1250	1300	1500	1650	1750	1850
Commercial Fiber	550	800	1,000	1100	1150		1350	1550	1550	1750

The viscosity profile of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) in comparison to a competing commercial fiber in a smoothie is presented in TABLE 4. Five grams of fiber were added to a smoothie mix (see EXAMPLE 6 for composition of exemplary smoothie) and 350 g of distilled water was then added.

TABLE 4. Viscosity Profile of VFB vs. Commercial Fiber Blend in Smoothie

	Viscosity (centipoise) at Different Time Points (minutes)								
	5	**10**	**15**	**20**	**25**	**30**	**45**	**60**	**90**
VFB	2575	3525	4100	4450	4815	5300	6000	6700	7350
Commercial Fiber	865	1050	1140	1290	1375	1400	1690	1725	2050

One of the differences between VFB and the commercial fiber is how they react under simulated digestive conditions. As shown in TABLES 5 and 6, VFB has the ability to increase in thickness under gastric conditions. TABLE 5 compares the viscosity profiles of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) and the commercial fiber when 2 g of fiber are added to 200 g of distilled water with 10 drops of phosphoric acid.

TABLE 5. Viscosity Comparison of VFB and Commercial Fiber Under Gastric Conditions

	Viscosity (centipoise) at Different Time Points (minutes)						
	5	**10**	**15**	**20**	**25**	**30**	**45**
VFB	1000	2800	4100	5100	6150	6500	7150
Commercial Fiber	400	800		2400	3500	4450	6750

TABLE 6 compares the viscosity profiles of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) and the commercial fiber in a smoothie product under gastric conditions. Five grams of commercial fiber or 4 g of VFB were added to a

smoothie mix (see EXAMPLE 6 for composition of exemplary smoothie) and 350 g of gastric fluid was then added.

TABLE 6. Viscosity Comparison of VFB and Commercial Fiber in Smoothie Under Gastric Conditions

	Viscosity (centipoise) at Different Time Points (minutes)							
	5	**10**	**15**	**20**	**25**	**30**	**45**	**60**
VFB	1500	1850	2150	2450	2550	2600	2950	3600
Commercial Fiber	1550	1900	1950	2200	2300	2350	2700	3325

TABLE 7 compares the viscosity profile of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) compared with the commercial fiber under intestinal conditions. Two grams of fiber were added to 200 g of intestinal fluid. Intestinal fluid was made by dissolving 6.8 g of monobasic potassium phosphate in 250 mL of water, mixing, and adding 190 mL of 0.2 N NaOH and 400 mL of water. Ten grams of pancreatin was added, followed by mixing and adjusting the pH with 0.2 N NaOH to a pH of 7.5 ± 0.1. The solution was diluted with water to 1,000 mL (United States Pharmacopoeia).

TABLE 7. Viscosity Profile Comparison of VFB and Commercial Fiber Under Intestinal Conditions

	Viscosity (centipoise) at Different Time Points (minutes)								
	3	**5**	**10**	**15**	**20**	**25**	**30**	**45**	**60**
VFB	2600	6600	15000	3,5000	39250	41000	66500	69500	72000
Commercial Fiber	1150	1350	1700	2250	2600	3000	3000	5850	7900

TABLE 8 compares the viscosity profile of VFB (70% glucomannan, 13% xanthan gum, and 17% alginate) compared with the commercial fiber under intestinal conditions. Five grams of commercial fiber or 4 g of VFB were added to a smoothie mix (see EXAMPLE 6 for composition of exemplary smoothie) and 350 g of intestinal fluid was then added.

TABLE 8. Viscosity Profile Comparison of VFB and Commercial Fiber in Smoothie Under Intestinal Conditions

	Viscosity (centipoise) at Different Time Points (minutes)								
	3	**5**	**10**	**15**	**20**	**25**	**30**	**45**	**60**
VFB	1250	2200	4200	5250		6800	9000	15700	16600
Commercial Fiber	1150	1300	1450	1750	1900	2100	2250	2350	3350

These test results show that under simulated gastric and intestinal conditions, the VFB fiber blend thickened more than the commercial fiber blend, indicating that VFB has a higher viscosity than the commercial fibers in the stomach and may continue to thicken under intestinal conditions.

In order to create a product that is more appealing to the consumer, granulated VFB was used to further delay viscosity during the initial stages of ingestion. Granulation is achieved through addition of 30-60% (w/w) water to the VFB blend and then drying off the added water. This process is typically performed through mechanical granulators, fluid-bed granulator/dryers, mechanical agglomerators, or simple mixing followed by oven or vacuum drying.

Non-granulated VFB is quite fine and tends to clump when added with water. It absorbs moisture so quickly that the water actually encapsulates the powder. However, granulated VFB avoids this problem as the larger granules remain separated from each other when wet. Slowly the slurry thickens as the VFB granules gradually dissolve into water.

Determining the proper mesh size of VFB is important in the granulation process. Thirty mesh particles are about 600 microns in diameter, 40 mesh particles are about 400 microns in diameter, 50 mesh particles are about 300 microns in diameter, 60 mesh particles are about 250 microns in diameter, and 80 mesh particles are about 180 microns in diameter. Although it slows viscosity increase, the granulated VFB product still increases to the desirable thickness responsible for generating that full feeling and also regulating blood sugar levels by slowing down absorption of carbohydrates in the intestines. The larger the granulation (i.e., the smaller the mesh size), the more the increase in viscosity is delayed, as shown in TABLE 9.

TABLE 9. Viscosity Comparison of VFB Granulated Using Different Mesh Sizes

	Viscosity (centipoise) at Different Time Points (minutes)

	5	10	15	20	30	60	120
Granulated VFB mesh size 30 (stirred)	0	35	100	195	425	3760	45240
Granulated VFB mesh size 40 (stirred)	55	220	490	2095	6545	28780	>90000
Granulated VFB mesh size 60 (stirred)	590	4295	12090	28755	53035	82630	>90000
Non-granulated VFB (blended)	612.5	1126	2356	3367.5	7880	19400	48860
Non-granulated VFB (stirred)	190	620	5073	7150	15380	56990	>90000
Granulated VFB combined mesh size 30–60	95	315	1115	4330	11215	48800	>90000

A combination of 30-to 60-mesh size granulated VFB product consisting of a 1:1:1 combination of 30-, 40-, and 60-mesh size granules is desirable. A larger proportion of the smaller mesh will delay the increase in viscosity even more.

EXAMPLE 2

This example describes that consumption of an exemplary dietary fiber composition (VFB) of the invention results in improvements in insulin sensitivity and reductions in body fat.

A 5%-10% loss in body fat can decrease the risk factors associated with the metabolic syndrome (Krauss et al., *Circulation* I(18):2284-99 (2000)). Common weight loss strategies such as pharmacological treatments, hypocaloric diets, and fad diets do not target appetite, are difficult and costly to maintain, do not address many of the metabolic abnormalities associated with obesity and Type 2 diabetes, and result in weight regain and reestablishment of comorbidities once they are discontinued.

Prospective studies demonstrate that high dietary fiber is strongly and inversely related to body weight, satiety, and energy intake (Stevens et al., *Am. J. Clin.. Nutr. 46*(5):812-7 (1987); Blundell & Burley, *Int. J. Obes. 11*(Suppl. 1):9-25 (1987); Howarth et al., *Nutr. Rev. 59*(5):129-39 (2001)). Evidence also suggests that high soluble fiber intake is associated with improvements in insulin sensitivity and glycemia (Salmeron et al., *Diabetes Care 20*(4):545-50 (1997); Salmeron et al., *JAMA 277*(6):462-77 (1997); Jenkins et al., *Lancet 2*(7999):1251 (1967); Doi et al., *Lancet 1*(8123):987-8 (1979); Shima et al., *Nutr. Rep. Int. 26*:297-302 (1982)). Consumption of purified, highly viscous fibers (Brand et al., *Diabetes Care 14*(2):95-101 (1991); Wolever et al., *Diabet. Med. 9*(5):451-8 (1992)) such as guar gum (Jenkins et al.,

Lancet 2(8042):779-80 (1977); Aro et al., *Diabetologia 21*(1):29-33 (1981)) and glucomannan (Vuksan et al., *Diabetes Care 23*(1):9-14 (2000)) has resulted in improved insulin sensitivity in subjects with insulin resistance, Type 2 diabetes, and the metabolic syndrome (Chiasson et al., *Diabetes Care 19*(11):1190-3 (1996); Frost et al. *Metabolism 47*(10):1245-51 (1998)).

It is thought that viscous fiber slows digestion and absorption and affects acute and long-term glycemic control and, thus, leads to appetite control (Meyer, *Ann. NY Acad. Sci. 63*:15-32 (1955); Penicaud et al., *Curr. Opin. Clin. Nutr. Metab. Care 5*(5):539-43 (2002)) and increased insulin sensitivity. Insulin is known to help regulate fat metabolism and also plays a key role in diabetes. Lowering insulin levels also makes people feel less hungry and this could also explain its link to weight loss.

The present study tested the hypothesis that a metabolically controlled low-fat diet that is supplemented with a blend of highly viscous dietary fibers would improve postprandial glycemic control and insulin secretion as a result of a decrease in body weight and percent body fat. According to the hypothesis, the highly viscous dietary fibers provide mechanical effects (for example, by affecting gastric distension, gastric emptying, gastrointestinal transit time, nutrient absorption rate, and nutrient contact with gastro-intestinal tract), as well as metabolic effects (for example, by affecting hormone secretion, glycemic and insulin responses, short-chain fatty acids, and fecal energy excretion).

METHODS

1. SUBJECTS

There were 11 participants in the study. The inclusion criteria are shown in TABLE 10, the baseline profile of the participants is shown in TABLE 11.

TABLE 10. Inclusion Criteria

Risk Factor	**Inclusion Criteria**
Hypertension	Blood Pressure: 135/95 mm Hg = 145
Hyperinsulinemia	Fasting Plasma Insulin: > 53 pmol/L
Impaired Glucose Tolerance	2 Hour Post Challenge (Blood) Glucose: 7.8-11.0 mmol/L
Overweight	Body Mass Index: < 30 kg/m^2
Dyslipidemia	High Density Lipoprotein: Men <0.9 mml/l, women < 1.2 mm/l
	Triglycerides: 2.3-4.5 mmol/l
Other	Absence of coronary heart disease, visceral obesity, not taking medications for hyperglycemia, hyperlipidemia or hypertension, less than 2 alcoholic drinks/day, non-smokers

TABLE 11. Participant Profile

Parameter	**Baseline Profile**
Fasting Plasma Insulin	98 ± 13 pmol/l
2-Hour Postprandial Plasma Insulin	439 ± 68 pmol/l
Serum Cholesterol	5.2-6.7 mmol/l
Exercise	Sedentary
Mean Age	55 ± 4 years (range: 46-61)
Body Mass Index	28 ± 1.5 kg/m^2
Waist to Hip Ratio	Men: 0.98 ± 0.2 (waist: 96 ± 12 cm) Women: 0.91 ± 0.4 (waist: 87 ± 19 cm)

2. DESIGN

Randomized, double-blind, placebo-control, crossover design. During the 6-week run-in period, participants consumed the National Cholesterol Education Program Therapeutic Lifestyle Changes (TLC) diet. The experimental phase of the study consisted of two successive 3-week treatment periods, separated by a 2-week washout period (with the TLC diet). During the first treatment period, subjects were randomly assigned to either a TLC diet with the viscous fiber blend (VFB) or wheat bran (WB) alone control. For the second treatment period, participants were crossed over. At week 0 and week 3, participants came to the clinic and consumed a test or control

breakfast, and postprandial glucose and insulin were assessed along with body weight and % body fat. At the beginning and end of each experimental period, participants were tested for glucose and insulin concentrations at 0, 30, 45, 60, 90, 120, and 180 minutes after a test or control breakfast. Insulin sensitivity was calculated as previously described (Matsuda & DeFronzo, *Diabetes Care 22*:1462-70 (1999)). Body fat was determined by infra-red interactance (Futrex-5000) at week 0 and week 3.

3. TEST BREAKFASTS

In a crossover design, participants with reduced insulin sensitivity and the metabolic syndrome were assigned to consume a metabolically controlled diet enriched with either 0.5 g/100 kcal of highly viscous dietary fiber (VFB, test breakfast) or matched wheat bran control (control breakfast) over two 3-week periods, separated by a 2-week washout period. The control breakfast consisted of 49 g of wheat bran cookies, 52 g of bran flakes, 250 mL of 2% milk, and 8 g of butter. The test breakfast consisted of 58 g VFB cookies (containing approximately 10% VFB fibers, 25% sucrose, with a nutrient profile of about 6% protein, 14% fat, 60% available carbohydrates, 1.5% ash, and 2.8% moisture), 69 g bran flakes, 250 mL 2% milk, and 8 g of butter. The two breakfasts were isocaloric and identical in appearance and taste. The nutrient profile of the two breakfasts differed only in the type of fiber, as shown in TABLE 12.

TABLE 12. Nutrient Profile of Control and Test Breakfast

	Control Breakfast	**Test Breakfast**
Energy	673 Kcal	678 Kcal
Protein	10.3%	11.2%
Total Fat	29.0%	28.6%
Available Carbohydrate	61.1%	59.2%
Total Fiber	12.0 g	11.4g
Soluble Fiber	1.2g	5.4g

RESULTS

1. RHEOLOGY

Table 13 shows the viscosity of five different viscous soluble fiber sources compared to viscous fiber blend (VFB). Measurements of the samples were taken by a

Brookfield viscometer (Middleboro, Massachusetts) on a 1% solution at 24-hours using an "F" spindle at a shear rate of 30 rotations per second. Data are the mean of three or more repetitions (cps = centipoises).

TABLE 13. Viscosity Comparison of Different Soluble Fiber Sources

Soluble Fiber Source	Viscosity (centipoise)
Kappa C.	2000
Phyllium	6000
Xanthan	12000
Guar	17000
Konjac 98%	41000
VFB	112000

2. GLYCEMIC RESPONSE

FIGURE 1 and TABLE 14 show the effects of administering 3 g of various sources of soluble fibers and VFB administered on the glycemic response to a 50 g oral glucose load. The control is a 50 g oral glucose load alone.

TABLE 14. Effects of Different Soluble Fiber Sources on Area Under the Curve Glucose Response

Soluble Fiber Source	Under the Curve Glucose Response (mmol/L)
Control	113
Phyllium	100
Xanthan	81
Konjac 98%	80
VFB	39

3. APPETITE CONTROL:

FIGURES 2A-B and Table 15 show a comparison of subjective appetite ratings before each meal and bedtime snack at week 0 and week 3 in subjects provided with test breakfasts with VFB (FIGURE 2A) and control breakfasts (FIGURE 2B). Data are expressed as Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk.

TABLE 15. Comparison of Appetite Ratings in Subjects Provided With Test Breakfasts and Control Breakfasts

	Appetite Score							
	Before Breakfast		Before Lunch		Before Dinner		Before Snack	
	Week 0	Week 3	Week 0	Week 3	Week 0	Week 3	Week 0	Week 3
VFB Treatment								
MEAN	-2.18	-1.55	-1.64	-1.45	-2.18	-1.36	0.09	0.00
SEM	0.23	0.16	0.20	0.21	0.12	0.20	0.25	0.27
Control								
MEAN	-2.36	-2.09	-1.55	-1.73	-2.09	-2.00	0.36	0.27
SEM	0.20	0.25	0.16	0.19	0.21	0.23	0.24	0.27

4, GLUCOSE

FIGURES 3A-B and TABLE 16 show a comparison of the acute postprandial glucose response in subjects provided with control and test VFB breakfasts. Subjects were given either the control breakfast or the test breakfast everyday for three weeks. Their blood glucose response was measured at the beginning of the study (week 0) and at the end of the study (week 3). All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk.

FIGURE 4 shows the area under the curve (AUC) for postprandial glucose response at week 0 and week 3 for control and VFB. All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk.

TABLE 16. Comparison of Blood Glucose Levels in Subjects Provided With Control and Test Breakfasts

	Blood Glucose (mmol/L)							
	0 min	30 min	60 min	90 min	120 min	150 min	180 min	AUC
Week 0: Control								
MEAN	6.28	10.63	11.66	11.26	10.18	9.09	7.67	663.75
SEM	0.56	0.65	0.61	0.77	0.90	1.01	0.97	45.01
Week 0: VFB Treatment								
MEAN	6.62	10.17	11.30	11.66	10.28	8.50	7.62	594.48
SEM	0.75	0.49	0.32	1.07	1.20	1.27	1.26	39.22
Week 3: Control								
MEAN	6.03	10.06	11.48	11.14	10.08	8.69	7.61	666.39
SEM	0.64	0.83	0.72	0.83	0.87	1.07	1.07	46.13
Week 3: VFB Treatment								

	Blood Glucose (mmol/L)							
	0 min	30 min	60 min	90 min	120 min	150 min	180 min	AUC
MEAN	6.01	8.86	9.91	9.30	8.71	7.51	6.46	451.38
SEM	0.59	0.42	0.56	0.85	0.83	0.86	0.80	28.28

5. INSULIN:

FIGURES 3C-D and TABLE 17 show a comparison of the postprandial insulin response in subjects provided with control and test VFB breakfasts. Subjects were given either the control breakfast or the test breakfast everyday for three weeks. Their blood insulin response was measured at the beginning of the study (week 0) and at the end of the study (week 3). All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk.

FIGURE 5 shows the area under the curve (AUC) for postprandial insulin response at week 0 and week 3 for control and VFB. All data points are Means ± SD. Significant differences at $p<0.05$ are indicated by an asterisk.

TABLE 17. Comparison of Insulin Levels in Subjects Provided With Control and Test Breakfasts

	Blood Insulin (pmol/L)				
	0 min	**45 min**	**90 min**	**180 min**	**AUC**
Week 0: Control					
MEAN	78.58	1436.58	1015.08	567.50	139.68
SEM	5.32	149.03	142.08	61.65	16.05
Week 0: VFB Treatment					
MEAN	80.67	1263.25	820.00	472.92	121.61
SEM	5.91	126.49	110.81	48.37	13.94
Week 3: Control					
MEAN	78.33	1420.42	949.75	515.25	138.81
SEM	7.85	161.39	137.58	58.68	17.60
Week 3: VFB Treatment					
MEAN	70.00	808.75	479.75	256.25	69.46
SEM	6.25	65.72	44.71	46.63	6.85

6. PERCENT BODY FAT

An infrared interactance Futrex-5000® system (Futrex Inc., Gaithersburg, Maryland) was used to assess body composition. FIGURE 6 and TABLE 18 illustrate the change in percent body fat from week 0 to week 3 during the control in which

participants consumed the control breakfast compared to the period in which participants consumed the test breakfast. Data are represented as means. Significant differences at $p<0.05$ are indicated by an asterisk.

Table 18. Change in Percent Body Fat in Subjects Provided Control or Test (VFB) Breakfasts

Breakfast	Change in Percent Body Fat From Week 0 to Week 3	
	MEAN	SEM
Control	-1.4	0.7
VFB treatment	-2.8*	0.4

CONCLUSIONS

Areas under the curves for glycemia (-23.13.5% vs. 0.42.3%, P=0.000022) and insulinemia (-40.54.5% vs. 2.02.9%, p=0.000012) were significantly reduced with VFB, compared to control. These decreases translated into a significant increase in insulin sensitivity after consumption of VFB compared to control (55.99.2% vs. 9.74.5%, P=0.00056). In addition, body fat was reduced by 2.8% from baseline following the 3-week period with VFB, compared to the control group, which experienced 1.4% body fat reduction ($p<0.05$). We concluded that prolonged consumption of VFB reduces body fat in individuals with impaired insulin sensitivity in the metabolic syndrome. A possible explanation includes an improvement in insulin sensitivity.

EXAMPLE 3

This example provides an exemplary embodiment of a meal replacement product comprising a dietary fiber composition of the invention.

An exemplary dietary fiber blend (VFB) was made by combining glucomannan (greater than 80% pure from Konjac root), Xanthan gum (commercially sourced extracellular heteropolysaccharide from Xanthomonas bacteria), and alginate (commercially sourced medium viscosity sodium alginate from Ascophyllum nodosum). The composition of an exemplary dietary fiber blend (VFB) is shown in TABLE 19.

TABLE 19. VFB Fiber Blend Composition

Ingredient	Amount
Glucomannan	3500 mg (70%)
Xanthan Gum	850 mg (17%)

Ingredient	Amount
Alginate	650 mg (13%)
Total	5000 mg

A meal replacement product was formulated with the VFB fiber blend as shown in TABLE 20.

TABLE 20. Meal Replacement Composition

Ingredient	Amount
Whey protein	44%
Fructose	14%
VFB fiber blend	9%
Xylitol	8%
Flavor	8%
Lecithin	7%
Vitamins and Minerals	6%
Medium chain triglycerides	4%

TABLE 21 shows the vitamin and mineral provided per serving of the meal replacement product (RE = retinol equivalent units, NE = niacin equivalent units, mcg = microgram, mg = milligram).

Table 21. Vitamin and Mineral Provided Per Serving

Vitamin A	630	RE
Vitamin D	2.5	Mcg
Vitamin E	4.4118	Mg
Vitamin C	20	Mg
Thiamine	750	Mcg
Riboflavin	800	Mcg
Niacin	12	NE
Vitamin B6	750	Mcg
Vitamin B12	0.75	Mcg
Folacin	120	Mcg
Pantothenic acid	2.5	Mg

Biotin	75	Mcg
Calcium	400.5736	Mg
Phosphorus	250	Mg
Iron	2.77324	Mg
Iodide	40	Mcg
Magnesium	120	Mg
Copper	0.5	Mg
Zinc	6	Mg
Potassium	399.6344	Mg
Sodium	354.3036	Mg
Manganese	1	Mg
Selenium	20	Mcg
Chromium	20	Mcg
Molybdenum	25	Mcg

The flavor of the meal replacement can include, but is not limited to, any of the following: chocolate, strawberry, vanilla, pineapple, mango, peach, orange, mocha, and cherry. This meal replacement is a powder form. Each serving is 57 grams, to be mixed with a glass of water. One serving is taken at breakfast and at lunch in place of a regular meal.

EXAMPLE 4

This example illustrates the effects on volunteers of consuming a meal replacement product comprising the dietary fiber composition (VFB) of the invention.

A middle-aged male volunteer took the meal replacement product described in EXAMPLE 3 twice a day for a nine-month trial. At the start of the trial, the volunteer weighed 247.2 pounds, had a BMI of 36, a waist measurement of 45.25 inches, a hip measurement of 47.25 inches, and a body fat measurement of 27.7%. At the end of the nine-month trial, the volunteer weighed 223.75 pounds, has a waist measurement of 43 inches, a hip measurement of 45.5 inches, and a body fat measurement of 25.7%. The volunteer complained of stomachache, loose stools, and hunger in the evening when he did not take the meal replacement.

A middle-aged female volunteer took the meal replacement product described in EXAMPLE 3 twice a day for a nine-month trial. At the start of the trial, the volunteer

weighed 170 pounds, had a BMI of 30.3, a waist measurement of 36.5 inches, a hip measurement of 43 inches, and a body fat measurement of 46.6%. At the end of the nine-month trial, the volunteer weighed 156 pounds, had a waist measurement of 33.5 inches, and a hip measurement of 41 inches. The volunteer complained of diarrhea during the first two days of the trial and found herself drinking more water due to thirst.

A middle-aged female volunteer took the meal replacement product described in EXAMPLE 3 twice a day for a nine-month trial. At the start of the trial, the volunteer weighed 162.5 pounds, had a BMI of 27.9, a waist measurement of 37 inches, a hip measurement of 43 inches, and a body fat measurement of 41.9%. At the end of the nine-month trial, the volunteer weighed 141 pounds, had a waist measurement of 34 inches, a hip measurement of 41 inches, and a body fat measurement of 35.3%. The volunteer complained of minor headache during the first two weeks of the trial.

A middle-aged female volunteer took the meal replacement product described in EXAMPLE 3 twice a day for a nine-month trial. At the start of the trial, the volunteer weighed 172 pounds, had a BMI of 27.7, a waist measurement of 35.75 inches, a hip measurement of 43 inches, and a body fat measurement of 41.6%. At the end of the nine-month trial, the volunteer weighed 143 pounds, had a waist measurement of 31 inches, and a hip measurement of 38.25 inches. The volunteer found the diet plan reasonable and flexible.

EXAMPLE 5

This example provides an exemplary embodiment of a dietary fiber composition (VFB) of the invention formulated as gelatin capsules.

An exemplary dietary fiber composition was formulated as two-piece, hard-gelatin capsules, with each capsule containing 500 mg of the composition shown in TABLE 22.

Table 22. VFB Capsule Composition

Ingredient	**Amount**
Glucomannan	350 mg (47.62%)
Xanthan Gum	85 mg (11.56%)
Alginate	65 mg (8.84%)
Rice Flour	228 mg (31.02%)
Magnesium Stearate	7 mg (0.95%)

Total	735 mg

EXAMPLE 6

This example provides an exemplary embodiment of a dietary fiber composition of the invention formulated as an appetite control powder.

An exemplary dietary fiber composition was formulated as an appetite control power. Each bottle contains 182 g, which represents 26 servings. The contents per serving of the appetite control powder are shown in TABLE 23.

Table 23. Contents per Serving of SlimStyles Appetite Control Powder

Ingredient	**Amount**
Glucomannan	3.5 mg (50%)
Xanthan Gum	0.65002 mg (9.29%)
Alginate	0.85001 mg (12.14%)
Xylitol	0.72898 mg (10.41%)
Lecithin	0.04998 mg (0.71%)
Medium Chain Triglycerides	0.04998 mg (0.71%)
Natural Orange Juice Flavor	0.72002 mg (10.29%)
Orange Flavor	0.36001 mg (5.14%)
Stevia Powder	0.07497 mg (1.07%)
Syloid Silica	0.01603 mg (0.12%)
Total	7 mg

EXAMPLE 7

This example provides an exemplary embodiment of a dietary fiber composition (VFB) of the invention formulated as a meal replacement smoothie.

An exemplary dietary fiber composition was formulated as a meal replacement smoothie. The contents per serving of the meal replacement smoothie are shown in TABLE 24.

Table 24. Contents per Serving of SlimStyles Meal Replacement Smoothie

Ingredient	**Amount**
Whey protein	24.5 g (42.87%)

Ingredient	Amount
Ca (from Ca citrate)	77 mg (0.67%)
Total Ca	400.5736 mg
Mg (from Mg citrate)	120 mg (1.38%)
Iron (from Fe fumarate)	2.5 mg (0.01%)
Zn (from Zn citrate)	6 mg (0.03%)
Se (rice chelate)	20 mcg (0.01%)
Cr (from Cr chelate)	20 mcg (0.00%)
Cu (from Cu chelate)	0.5 mg (0.01%)
Mo (from Mo citrate)	25 mcg (0.01%)
Mn (from Mn citrate)	1 mg (0.01%)
Potassium citrate	20 mg (0.10%)
I (KI)	40 mcg (0.00%)
P (Calcium phosphate dehydrate)	250 mg (2.63%)
Na (sodium chloride)	55 mg (0.24%)
Beta Carotene	6300 iu (0.04%)
Vitamin D2	100 iu (0.00%)
Vitamin E (acetate)	6 iu (0.01%)
B1 thiamin HCl	0.75 mg (0.00%)
B2 riboflavin	0.8 mg (0.00%)
B3 niacinamide	12 mg (0.02%)
Pantothenic acid (Ca Panto)	2.5 mg (0.01%)
Folic Acid	0.12 mg (0.00%)
B6 pyridoxine HCl	0.75 mg (0.00%)
B12 cyanocobalamin	0.5 mcg (0.00%)
Biotin	75 mcg (0.01%)
Vitamin C	20 mg (0.04%)
Glucomannan	3.5 g (6.12%)
Xanthan Gum	0.65 g (1.14%)
Sodium Alginate	0.85 g (1.5%)
Stevia	150 mg (0.26%)
Fructose	7 g (12.25%)
Xylitol	0.72898 mg (10.41%)
Chocolate Flavor	1.3 g (2.27%)

Ingredient	Amount
Cocoa	1 g (1.75%)
Coffee (Rich blend)	2.3 g (4.02%)
Cream Flavor	1.1 g (1.92%)
Lecithin	4.4 g (7.70%)
Medium Chain Triglycerides	2.4 g (4.20%)
Total	(100%)

EXAMPLE 8

This example describes a comparison of the viscosity profile of an exemplary fiber blend (VFB) to other fiber blends under various conditions.

METHODS

A formulation of viscous fiber blend (VFB) was created which included 70% glucomannan (konjac), 13% xanthan and 17% alginate, as described in EXAMPLE 1. The VFB was compared with a konjac/xanthan (70:30) fiber blend and a konjac/alginate (70:30) fiber blend in distilled water, gastric conditions and intestinal conditions as follows.

Compositions Tested:

(1) VFB: konjac (70%)/ xanthan (13%)/ alginate (17%)

(2) KX: konjac (70%)/xanthan (30%)

(3) KA: Konjac (70%)/alginate (30%)

Viscosity Profile Experiments:

Five grams of test material was mixed with 350 g of fluid (either distilled water, gastric, or intestinal juice). The sample was blended for 30 seconds on low speed 2 on a Proctor/Silex blender. Viscosity readings were taken at 5, 10, 15, 20, 30, 45, 60, and 120 minutes. Gastric and intestinal fluids were prepared according to Universal Sample Preparation (USP) methodology.

RESULTS

TABLE 25 and FIGURE 7 compare the viscosity profile of VFB compared with KX and KA under normal conditions (distilled water). TABLE 26 and FIGURE 8 compare the viscosity profile of VFB compared with KX and KA under gastric conditions. TABLE 27 and FIGURE 9 compare the viscosity profile of VFB compared

with KX and KA under intestinal conditions. As shown in FIGURES 7, 8, and 9, the KA (konjac/alginate 70:30) fiber blend consistently has the lowest viscosity of the three fiber blends tested. Under neutral and gastric conditions the KX (konjac/xanthan 70:30) reaches maximum viscosity quickly (e.g., within about 15-20 minutes). The VFB blend (konjac (70%)/ xanthan (13%)/ alginate (17%)) starts at about the same viscosity as KA under neutral conditions, increases in viscosity over time under both gastric and intestinal conditions and eventually reaches a greater viscosity than KX under neutral and gastric conditions. This combination also produces unexpectedly high viscosity values after 10 minutes when blended with gastric juice. Therefore, the addition of alginate to the KX combination unexpectedly provides a decrease in viscosity of VFB at neutral conditions and results in a greater viscosity than KX alone over time.

TABLE 25. Viscosity Profile Comparison of VFB and Various Fiber Blends in Distilled Water

Fiber Blend	5min	10min	15min	20min	30min	60min	120min	avg temp	pH
KX: konjac/xanthan (70:30)	53380	49080	47870	43950	49810	49251	47440	20.2	6.05
KA: konjac/alginate (70:30)	3960	11470	16730	18420	25940	43530	78850	20.2	6.35
VFB (konjac/xanthan/ alginate (70:13:17))	4230	9230	16700	34970	43170	46010	90000	20.8	6.17

TABLE 26. Viscosity Profile Comparison of VFB and Various Fiber Blends Under Gastric Conditions

Fiber Blend	5min	10min	15min	20min	30min	60min	120min	avg temp	pH
KX: konjac/xanthan (70:30)	35500	48020	70150	75400	78720	83290	87680	20.3	1.46
KA: konjac/alginate (70:30)	3210	11820	17664	18820	23580	29130	43460	20.2	3.85
VFB (konjac/xanthan/ alginate (70:13:17))	44880	90000	116500	123600	135200	139600	249000	20.5	3.69

TABLE 27. Viscosity Profile Comparison of VFB and Various Fiber Blends Under Intestinal Conditions

Fiber Blend	5min	10min	15min	20min	30min	60min	120min	avg temp	pH
KX: konjac/xanthan (70:30)	90000	nd	nd	nd	167500	156800	166200	20.2	7.88
KA: konjac/alginate (70:30)	6990	14470	16350	26030	29110	36600	40900	20.1	7.89
VFB (konjac/xanthan/ alginate (70:13:17))	51490	70180	78640	84100	79480	90000	91900	20.5	7.92

EXAMPLE 9

This example describes the preparation of soft gelatin (softgel) capsule containing Viscous Fiber Blend mixed with medium chain triglycerides.

METHODS

Preparation of a soft gelatin capsule containing Viscous Fiber Blend:

INNER FILLING

A soft gelatin capsule was prepared with an inner filling including Viscous Fiber Blend (konjac/xanthan/alginate (70:13:17)) and an oil (e.g., medium chain triglycerides (MCT) at a ratio of from 0.01:99.99 up to 80:20 (w/w VFB:MCT). An example of a ratio of VFB:MCT of 52.7:47.3 w/w is shown below in TABLE 28. The MCT can be substituted with any of the following oils: soy bean oil, palm kernel oil, fish oil, and canola oil.

TABLE 28: Exemplary Inner Filling Ingredients for Capsules

Capsule weight (inner filling)	VFB (konjac/xanthan/ alginate (70:13:17)	Medium chain triglycerides (MCT)
100mg	52.7 mg	47.3 mg
1500 mg	790 mg	710 mg
2,500 mg	1320 mg	1180 mg

OUTER CAPSULE SHELL

The outer capsule shell includes a mixture of gelatin, glycerin, and water.

An exemplary softgel capsule was produced as follows:

Inner Filling:

790 mg VFB

710 mg MCT

Outer Capsule Shell:

2,130 mg of a mixture consisting of gelatin, glycerin and water was used.

The proportion of outer capsule shell to inner filling may be varied to accommodate various capsule sizes, as shown in TABLE 28.

The softgel capsule containing VFB mixed with medium chain triglycerides is effective to delay the VFB viscous effects in water, while allowing for maximum viscosity of the VFB under gastric conditions, as demonstrated in EXAMPLE 10.

EXAMPLE 10

This example demonstrates that VFB encapsulated in an oil-based softgel capsule is effective to delay its viscous effects in water in order to reduce potential choking hazard, while at the same time quickly reaching maximum viscosity under gastric conditions.

METHODS

The viscosity profile of VFB encapsulated in an oil-based softgel capsule was compared in distilled water and gastric juice.

Soft gelatin capsules containing VFB mixed with oil were prepared as described in EXAMPLE 9. Each capsule contained 790 mg VFB (konjac/xanthan/alginate (70:13:17)). Six capsules (a total of 4.74 g VFB) were dissolved in a total volume of either 331.8 distilled H_20 or gastric juice (prepared according to USP guidelines) for a 5 g VFB:350 g H_20 ratio.

The samples were placed in the liquid medium in a vessel placed in a 25°C water bath. After 15 minutes in liquid, the softened capsules were broken open using a spoon. The mixture was then mixed manually for 5 minutes, then put into a blender and mixed mechanically at 4,000 rpm for 30 seconds, followed by mixing at 8,000 rpm for an additional 30 seconds. Viscosity readings were taken at time intervals over a 3-hour period.

RESULTS:

The viscosity profile of VFB softgel capsules in distilled water is shown below in TABLE 29.

TABLE 29: Viscosity Profile of VFB (Konjac/Xanthan/Alginate (70:13:17)) Plus oil (710 mg MCT) Encapsulated in a Softgel Outer Capsule (2,130 mg of a Mixture Consisting of Gelatin, Glycerin, and water) as Measured in Distilled Water

Time (a) (minutes elapsed after capsules were added to water)	**Time (b) (minutes elapsed after capsules were blended in water)**	**Spindle: R3 viscosity (centipoise)**	**RPM**
25	5	3500	10
48	28	9350	5
63	43	19630	2.5
80	60	39660	1
108	88	48350	1
139	119	60180	1
180	160	63590	1

The viscosity profile of VFB softgel capsules in gastric juice is shown below in TABLE 30.

TABLE 30: Viscosity Profile of VFB (Konjac/Xanthan/Alginate (70:13:17)) Plus Oil (710 Mg Mct) Encapsulated in a Softgel Outer Capsule (2130 Mg of a Mixture Consisting of Gelatin, Glycerin, and Water) as Measured in Gastric Juice

Time (a) (minutes elapsed after capsules were added to gastric juice)	**Time (b) (minutes elapsed after capsules were blended in gastric juice)**	**Spindle: R3 Viscosity (centipoise)**	**RPM**
25	5	> 90000	1

TABLE 31: Comparison of Viscosity of VFB Softgel Capsules in Water and Gastric Juice

Time (b) (minutes elapsed after capsules were blended (minutes)	**Viscosity in Water**	**Viscosity in Gastric Juice**
5	3,500	> 90000
28	9350	
43	19630	
60	39660	
88	48350	
119	60180	
160	65590	

As shown in TABLES 30-31, under gastric conditions, the oil-based VFB delivered in softgel capsules thickened quickly (within 5 minutes) after blending,

reaching a viscosity of greater than 90,000 centipoise. In contrast, as shown in TABLES 29 and 31, the oil-based VFB delivered in softgel capsules thickened slowly in distilled water, resulting in a viscosity level of 3,500 at five minutes after blending and gradually increasing to a maximum of 65,000 centipoise at 160 minutes after blending. As shown in TABLE 29, the VFB delivered in softgel capsules took 60 minutes to reach a viscosity of 19,630cps in distilled water and it did not reach 90,000 cps even after over 3 hours. This result is significantly different from the behavior observed for VFB (non-granulated, without oil-based capsule) when stirred into water, which reached 90,000 cps at 120 minutes, as shown in EXAMPLE 1, TABLE 9 herein. In fact, it is noted that the time delay observed in reaching maximum viscosity for VFB delivered in softgel capsules is even more pronounced than that observed for granulated VFB mesh size 40 and mesh size 60, each of which reached 90,000 cps at 120 minutes (see TABLE 9 herein). These results indicate that the addition of oil to VFB is effective to delay its viscous effects when mixed with water. Therefore, the combination of VFB with oil may be used in order to avoid a potential choking hazard during administration of VFB to an individual, since it has been observed that VFB alone becomes viscous very quickly in water and could form large clumps.

Moreover, in contrast to the delayed viscosity observed in water, the VFB delivered in softgel capsules reached 90,000 cps within 5 minutes after contact with gastric conditions, as shown in TABLES 30 and 31. This high viscosity was maintained over time (data not shown). It was surprising that the combination of VFB with oil could reach 90,000 cps within such a short time under gastric conditions. It is important to note that this viscosity profile for VFB in softgel capsules was very different from that observed with VFB alone under gastric conditions (shown in TABLE 6 herein), which was not observed to reach such high viscosities even after 60 minutes. As shown in TABLE 6, VFB alone only reached 3,600 cps after 60 minutes.

Therefore, the results described in this example that were observed with VFB in softgel capsules, including the delay in viscosity in water, and the rapid high viscosity level reached under gastric conditions, demonstrate that the combination of VFB and oil may be used to produce the desired effect of a feeling of fullness in the stomach and reduce the sensation of hunger in an individual while reducing the risk of choking during ingestion.

While not wishing to be bound by theory, the beneficial results described in this example for the combination of VFB and oil may be due to the coating of oil over the fiber. With regard to the delayed viscosity observed in water, it is likely that the oil coats and separates the particles such that water does not cause the particles to clump together and limit their dispersion. However, under gastric conditions, the acidity and gastric enzymes would likely strip off at least a portion of the oil coating such that VFB fibers could quickly reach maximum viscosity. Moreover, in contrast to dispersion of VFB (without oil coating) in water, which yields some clumping, the combination of VFB with oil avoids the clumping in water, which leads to lower initial overall viscosity in water, and thereby allows for an eventual higher viscosity over time because of the ability of the VFB and oil combination to disperse more evenly to allow more fiber particles to react with water instead of forming clumps.

EXAMPLE 11

This example describes the effect of various particle sizes of granulated viscous fiber blend administered in either solid or liquid meals on the postprandial glycemic response in healthy individuals.

RATIONALE

The objective of this study was to determine the glycemic index of two different granule sizes of the viscous fiber blend (konjac/xanthan/alginate (70:13:17), VFB100 (granulated to a smaller mesh size) and VFB300 (granulated to a larger mesh size) administered in solid form (white bread) or in liquid form (glucodex). The VFB100 contains only particles that are finer than 40 mesh. The VFB300 contains only particles that are finer than 20 mesh. Ungranulated VFB (konjac/xanthan/alginate (70:13:17)) has a mesh size of approximately 200 mesh.

METHODS

In a random cross-over designed study, ten healthy individuals (five men and five women, $x \pm SEM$ age: $21 \pm 2y$) were included in this study. Subjects with any known health conditions, such as diabetes, hypertension, and obesity, were excluded from the study. Each study participant received a total of eight treatments in a randomized, double-blind cross-over design. To examine the effects of VFB100 and VFB300 in different food forms, white bread and glucose drink (glucodex) were prepared as follows. VFB100 and VFB300 were prepared as described in EXAMPLE 1. The five white bread treatments included either baked in VFB100, VFB300, or no VFB included as

standardized controls. The three drink treatments included either mixed in VFB100, VFB300, or no VFB (control). All preparations and baking of the white bread with the various VFB granule sizes were done by one person in order to minimize variability between test samples. Study participants were blinded to the identity of the placebo and VFB treatments by coding and by the indistinguishable nature of the fiber in the bread or drinks. To ensure stability, the VFB100 and VFB300 were both stored in a cool, dry location over the course of the study.

Each subject was given eight treatments as follows:

50 g of white bread control with no VFB, consumed with 300 ml water (solid food control was repeated 3 times by each subject)

50 g of white bread with 3 grams of VFB100 consumed with 300 ml water

50 g of white bread with 3 grams of VFB300 consumed with 300 ml water

50 g of glucodex (liquid control) consumed with 300 ml water

50 g of Glucodex diluted in 300 ml with 3 grams VFB100

50 g of Glucodex diluted in 300 ml with 3 grams VFB300

Study participants were given eight treatments on eight separated mornings after a 10-to 12-hour overnight fast. The study was done over a two month period. To minimize carry-over effects, there were at least three days of separation between each treatment. Each participant was instructed to maintain the same dietary and exercise pattern the evening before each treatment and to consume at least 150 g of carbohydrates each day for three days before each treatment. To ensure that these instructions were followed, participants completed a questionnaire that detailed pre-session information about their diet and lifestyle patterns for each visit. No adverse effects were reported by any of the study participants.

At the start of each treatment, a blood sample was obtained from each participant using a 250 μL fasting finger prick capillary collected with a Monoejector Lancet Device (Owen Mumford Ltd., Woodstock, Oxon, England). One of the eight treatments was then administered over a period of 5 minutes. An additional finger-prick blood sample was obtained at 15, 30, 45, 60, 90, and 120 minutes after the start of treatment (t=0), for a total of seven collection tubes per participant per treatment.

Blood Glucose Analysis:

All blood samples were collected in tubes containing fluoride oxalate, frozen immediately at -20°C pending analysis, and analyzed within three days of collection. The

glucose concentration was determined by the glucose oxidate method with the use of a YSI 2300 Stat glucose/L-lactate analyzer, model 115 (Yellow springs, Ohio). The interassay CVs of this method for two sample pools were 3.3% (3.99 ± 0.013 mmol/L; n=91) and 1.8% (14.35 ± -/26 mmol/L; n=89).

Statistical Analysis:

The postprandial serum blood glucose curves were plotted as the incremental change in blood glucose over time and the positive incremental area under the curve (AUC) was calculated geometrically for each participant. Blood glucose concentrations were used to control for fasting differences between the treatments. The Number Cruncher Statistical System (NCSS statistical software, Kaysville, Utah) was used for the statistical analysis purposes. The independent and interactive effect of treatment doses and meals on AUC was assessed by repeated measurements of two-way analysis of variance (ANOVA). Repeated measurements of two-way ANOVA assessed the interactive and independent effects of each pairing of each of the two factors; treatment x administration time, treatment x sampling time, and administration time x sampling time. If the interaction term was significant, then further two-way ANOVAs assessed the interactive and independent effect of treatment and administration time on incremental glycemia at each postprandial sampling point (15, 30, 45, 60, 90, 120 minutes) and on the AUCs. Adjustment with Tukey-Kramer test was done for contrasting means among both the treatment doses and the administration times to control for multiple comparisons. Repeated measurements of one-way ANOVA were used to measure the pair-wise differences between treatments in AUC and incremental glycemia at each time point in the test (15, 30, 45, 60, 90, and 120 minutes). The results are expressed as Mean ± SD and $p<0.05$ is considered statistically significant.

RESULTS

Two-way ANOVA showed a significant effect of treatment ($p<0.001$) and time ($p<0.001$) on incremental glycemia with a significant interaction ($p<0.0001$). Because the interaction terms for the two-way ANOVA were significant, the effect of treatments was assessed at each postprandial sampling time point and for the AUCs.

SOLID FOOD (WHITE BREAD)

FIGURE 10A graphically illustrates the incremental changes in blood glucose for each treatment with solid food (white bread), white bread plus VFB100 or white bread plus VFB300. Repeated measurements of two-way analysis of variance (ANOVA)

applied to these data demonstrated a significant effect of time and treatment, as well as a significant interaction ($p=0.0007$). The "*" symbols in FIGURE 10A represent a significant difference ($p<0.05$) in blood glucose levels between treatment and control at a particular time point. As shown in FIGURE 10A, at 30, 45, and 60 minutes, the blood glucose levels in VFB300 were significantly lower than that in the control ($p<0.05$). There was no significant difference between VFB100 and VFB300 and the white bread control (w/o VFB) at 0, 90, and 120 time points. In addition, at 15-, 30-, 45-and 60-minute time points there were no significant differences between VFB100 and VFB300 bread treatments. At the 30-minute time points, both VFB100 and VFB300 bread treatments were significantly lower than the white bread control ($p<0.05$). FIGURE 10B graphically illustrates the incremental area under the curve (IAUC) in postprandial blood glucose in a plurality of subjects after treatment with solid food (white bread), white bread plus VFB100 or white bread plus VFB300. The "*" symbol in FIGURE 10B represents a significant difference ($p<0.05$) in blood glucose levels between treatment and control. As shown in FIGURE 10B, the IAUC in VFB300 treatment is significantly lower when compared to the mean white bread controls ($p<0.05$), but the IAUC in VFB100 treatment and the white bread did not differ significantly. In addition, no significant difference was detected between the VFB100 and VFB300 treatments in bread.

LIQUID (GLUCOSE DRINK)

The incremental changes in blood glucose for each treatment with glucose control drink, glucose drink plus VFB100, or glucose drink plus VFB300 are shown in FIGURE 11A. The "*" symbols in FIGURE 11A represent a significant difference ($p<0.05$) in blood glucose levels between treatment and control at a particular time point. As shown, repeated measures of two-way analysis of variance (ANOVA) found that there was a significant effect of time and treatments, as well as a significant interaction ($p=0.0007$). There was no significant difference observed between VFB100 and VFB300 and the glucose drink (glucodex) control at 0-, 90-, and 120-minutes points. At 30, 45, and 60 minutes, VFB100 was found to significantly lower blood glucose levels as compared to the control ($p<0.05$). At 15-, 45-, and 60-minute time points there was no significant difference observed between VFB100 and VFB300 drink treatments. At 15-and 60-minute time points, both VFB100 and VFB300 drink treatments were observed to significantly lower blood glucose as compared to the control ($p<0.05$). Also,

at the 30-minute time point, the VFB100 drink was significantly lower than the VFB300 drink treatment (p=0.003). At the 45-minute time point, the VFB100 drink was significantly lower than the control (p=0.025); however at this time point there was no significant difference observed between VFB300 and the control.

FIGURE 11B graphically illustrates the IAUC in postprandial blood glucose after treatment with the glucose control drink, glucose drink plus VFB100, or glucose drink plus VFB300. The "*" symbols in FIGURE 11B represent a significant difference ($p<0.05$) in blood glucose levels between treatment and control. As shown in FIGURE 11B, the IAUC in VFB100 treatment and in VFB300 treatment were significantly lower when compared to the control ($p<0.05$), but there was no significant difference observed between the IAUC in VFB100 drink treatment and the VFB300 drink treatment.

SUMMARY AND CONCLUSION:

In bread, both VFB100 and VFB300 were observed to lower plasma blood glucose. When compared to the bread control without VFB, a trend was observed wherein the larger VFB300 granules produced a greater effect on postprandial blood glucose than the finer VFB100 granules. While not wishing to be bound by theory, it is likely that the larger particles (VFB300) are less accessible to water molecules before the baking process of bread, and therefore more particles may be available for binding with water molecules after the consumption of bread, whereas the smaller particles (VFB100) are likely saturated with the binding of water molecules during the baking process and before consumption. Hence, a larger particle size (e.g., 300) of VFB displays a more viscous gelling and performs better than a smaller particle size (e.g., 100) of VFB in trapping glucose in the GI tract when consumed with white bread.

When mixed into drinks, both the VFB100 and VFB300 generated a greater postprandial glycemic response in comparison to the control than that observed in the breads, likely due to the direct absorption of glucose when drinks were consumed as compared to breads. However, the smaller particle size (VFB100) resulted in a greater reduction of blood glucose in drinks as compared to the larger size (VFB300). While not wishing to be bound by theory, it is likely that the faster absorption rate of glucose in drinks contributes to this result, since smaller particles are able to bind to water molecules more easily, which leads to better gel formation. This mechanism is likely different from

that in bread because the VFB in drinks does not undergo any processing and can directly interact with water molecules and trap glucose.

CONCLUSION:

These results indicate that the administration of a smaller particle size of VFB (e.g., VFB100) in the drink form is best for healthy subjects to improve their glycemic response. The administration of a larger particle size of VFB (e.g., VFB300) in the solid food form (e.g., bread) is best for healthy subjects to improve their glycemic response.

EXAMPLE 12

This example describes a dose response study to determine the glycemic index lowering potential of various doses of VFB added to liquid and solid food formulations before consumption.

METHODS:

The glycemic index reducing potential of VFB100 and VFB300 was determined when added to liquid (glucose drinks) and solid (white bread plus margarine) food formulations. Three different doses were administered and the glycemic index was calculated for each dose. Healthy subjects underwent treatments of separate days, with each subject performing up to two tests per week with at least one day between tests. On each test day, subjects arrived to the test site in the morning after a 10-to 14-hour overnight fast. After being weighed and after a fasting sample was obtained by finger prick, the subject then consumed a test meal within 10 minutes and further blood samples were obtained at 15, 30, 45, 60, 90, and 120 minutes after the start of the test meal. Subjects were also given a choice of one to two cups of either water, tea, or coffee, with or without milk. The beverage consumed by each subject remained the same on each test day.

GLUCOSE SERIES

SUBJECTS

The glucose series was tested in ten healthy subjects including five males and five females, age 35.6±13.2 years; body mass index 24.6±2.1 kg/m2, as shown below in TABLE 32.

TABLE 32: Subject Details Glucose Series

ID	Sex	Ethnicity	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m2)
247	F	Caucasian	56	167.0	70.0	25.1
249	M	Caucasian	61	182.0	79.1	23.9
174	M	Caucasian	29	185.2	92.0	26.8

124	F	Caucasian	29	162.5	54.0	20.4
161	F	Caucasian	40	157.0	56.7	23.0
208	M	Caucasian	34	175.0	79.0	25.8
126	F	Caucasian	20	157.4	62.5	25.2
253	M	East Asian	25	167.0	76.4	27.4
313	M	Caucasian	33	175.0	71.5	23.3
311	F	Caucasian	29	158.0	63.6	25.5
		Mean ±SD	**35±10.3**	**168±10.3**	**70.5±11.6**	**24.6±2.1**

Test Meals (Glucose Series)

The test meals in the glucose series consisted of 50 g of glucose mixed with 200ml of water to which the VFB was added using a small hand mixer. In addition to the test foods, each subject in the glucose series was also given a standard glucose control matched for carbohydrate content on three separate occasions.

TABLE 33: Nutrient Content of Glucose Series

Test Meal	Abbrev	Amount (g)	Protein (g)	Fat (g)	Total CHO (g)	Dietary fiber (g)	Available CHO (g)
Glucose	Gluc	50	0	0	50	0	50
Glucose +2.5 g VFB	VFB2.5	52.5	0	0	52.5	2.5	50
Glucose + 5.0 gVFB	VFB5.0	55	0	0	55	5.0	50
Glucose + 7.5 g VFB	VFB7.5	57.5	0	0	57.5	7.5	50

*weight may vary slightly between batches, depending on moisture content, CHO=carbohydrate.

WHITE BREAD SERIES

SUBJECTS

The white bread series was tested in ten healthy subjects including three males and seven females, age 33.5±11.1 years, body mass index 26.3±5.2 kg/m2, as shown below in TABLE 34.

TABLE 34: Subject Details White Bread Series

ID	Sex	Ethnicity	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m2)
141	F	Caucasian	26	144.0	50.0	24.11
12	M	Caucasian	42	174.0	80.0	26.40
308	F	Caucasian	21	158.0	50.0	20.03

303	F	Caucasian	19	167.0	89.8	32.20
316	F	Caucasian	36	163.0	69.7	26.20
290	F	Caucasian	20	159.0	50.8	20.09
207	M	Caucasian	50	168.0	76.1	26.96
199	M	Caucasian	41	179.0	116.0	36.20
210	F	Caucasian	41	153.0	67.3	28.75
93	F	Caucasian	39	162.0	58.0	22.10
		Mean±SD	**33.5±11.1**	**162.7±10.1**	**70.8±21.0**	**26.3±5.2**

TEST MEALS (WHITE BREAD SERIES)

The white bread series consisted of portions of white bread containing 50 g available carbohydrate (defined as total carbohydrate minus dietary fiber). The white bread was baked in a bread maker in loaves containing 250 g available carbohydrate. The ingredients for each loaf (250 ml warm water, 340 g all purpose flour, 7 g sugar, 4 g salt, and 6.5 g dry yeast) were placed into the bread maker according to instructions and the machine turned on. After the loaf had been made, it was allowed to cool for an hour, and then weighed and after discarding the crust ends, the remainder was divided into portion sizes containing 50 g available carbohydrate. These portions were frozen prior to use, and reheated in the microwave prior to consumption.

To avoid loss of VFB and increase palatability, 10 g of Becel margarine was added to the white breads that had VFB sprinkled on it. To control for any effect the margarine may have had on the glucose tolerance, an extra white bread with margarine only was also consumed. All test meals were given in random order. An extra test meal of white bread with margarine was also given in the white bread series to match the margarine given with the VFB.

TABLE 35: Nutrient Content of White Bread Series

Test Meal	**Abbrev**	**Amount (g)**	**Protein (g)**	**Fat (g)**	**Total CHO (g)**	**Dietary fiber (g)**	**Available CHO (g)**
White Bread	WB	104*	7.6	1.6	52.8	2.8	50
White Bread + Margarine	WB+M	114	1.1	9.6	52.8	2.8	50
White Bread + Margarine +VFB2.5 g	VFB2.5	114	1.1	9.6	55.3	5.3	50
White Bread + Margarine +VFB5.0 g	VFB5.0	114	1.1	9.6	57.8	7.8	50

Test Meal	Abbrev	Amount (g)	Protein (g)	Fat (g)	Total CHO (g)	Dietary fiber (g)	Available CHO (g)
White Bread+Margarine +VFB7.5 g	VFB7.5	114	1.1	9.6	60.3	10.3	50

*weight may vary slightly between batches, depending on moisture content, CHO=carbohydrate.

ASSAY METHODS:

Blood glucose was measured after fasting and at 15, 30, 45, 60, 90, and 120 minutes after eating the test meal. Incremental areas under the blood glucose response curves (IAUC) were calculated using the trapezoid rule and ignoring area beneath the baseline. Each subject's IAUC after consumption of each test food was expressed as a percentage of the mean IAUC of the three white bread controls taken by the same subject.

The glycemic index was calculated by expressing each subject's glucose IAUC for the test food as a percentage of the same subject's average response after reference white bread. The mean of the resulting values was the food GI based on the glucose scale (i.e., GI of glucose = 100). The blood glucose concentrations at each time and the IAUC values were subjected to repeated measures analysis of variance (ANOVA) examining for the effect of the test meal.

After demonstration of significant heterogeneity, the significance of the differences between individual means was assessed using Tukey's test to adjust for multiple comparisons. In addition, the significance of the differences between blood glucose concentrations and increments for each test food and white bread were assessed by paired t-test. To estimate the GI-lowering potential of 1 g of VFB, the GI change for each individual dose was averaged and calculated per gram of VFB.

WITHIN-SUBJECT VARIATION:

The incremental areas under the blood glucose response curves (IAUC) after the three tests of white bread control were calculated (data not shown). Although the difference in the IAUC between subjects was highly significant, there was no effect of order using the ANOVA statistical method. The mean within-subject coefficients of variation (CV) for IAUC for the glucose and white bread series were 21.7±4.9%

and 26.5±5.2%, respectively, which is average for normal subjects. Values less than 30% were considered to be satisfactory in the study.

Palatability was rated on a 100 mm visual analogue scale anchored at very "unpalatable" at one end and "very palatable" at the other end. Therefore, a higher number corresponds to a subject's perception of a more palatable product.

RESULTS

BLOOD GLUCOSE RESPONSE FOR GLUCOSE TEST MEAL

The results of the glucose test meal study are summarized below in TABLE 36. The "*" symbol indicates a statistically significant difference between the test condition and glucose control at the indicated time point.

TABLE 36: Summary of Blood Glucose Response for Glucose Test Meal

Test Condition	**0min (mean)**	**15min**	**30min**	**45min**	**60min**	**90min**	**120min**	**AUC**
Glucose Control (50 g)	4.36± 0.13	6.5± 0.22	7.86± 0.49	7.83± 0.64	6.87± 0.64	4.9± 0.45	3.76± 0.30	216.4± 28.4
Glucose +VFB2.5 g	4.44± 0.15	5.72± 0.28*	7.19± 0.45	7.27± 0.68	6.97± 0.71	5.32± 0.45	4.31± 0.38	190.1± 36.4
Glucose + VFB 5.0 g	4.35± 0.15	5.64± 0.26*	6.75± 0.34*	6.87± 0.48*	6.28± 0.57	5.26± 0.42	4.57± 0.26	170.1± 29.6
Glucose + VFB 7.5 g	4.48± 0.15	5.67± 0.33*	6.71± 0.27*	6.66± 0.38*	6.31± 0.44	5.37± 0.29	4.77± 0.26*	156.7± 23.5

As shown above in TABLE 36, Glucose + VFB 2.5 g as compared to glucose control showed a statistically significant decrease in blood glucose level at the 15-minute time point (p=0.0001). Glucose + VFB 5.0 g as compared to glucose control showed a statistically significant decrease in blood glucose levels at 15 minutes (p=0.026), at 30 minutes (p=0.009), at 45 minutes (p=0.023), and at 120 minutes (p=0.014) after test meal consumption. Glucose + VFB 7.5 g as compared to glucose control showed a statistically significant decrease in blood glucose levels at 15 minutes (p=0.016), 30 minutes (p=0.010), 45 minutes (p=0.011), and at 120 minutes (p=0.003).

BLOOD GLUCOSE RESPONSE FOR WHITE BREAD TEST MEAL

The results of the white bread test meal are summarized below in TABLE 37. The "*" symbol indicates a statistically significant difference between the test condition and glucose control at the indicated time point.

TABLE 37: Summary of Blood Glucose Response for White Bread Test Meal

Test Conditions	0min (mean)	15min	30min	45min	60min	90min	120min	AUC
White Bread Control	4.21± 0.07	4.79± 0.12	6.30± 0.16	6.67± 0.14	6.28± 0.22	5.54± 0.16	4.86± 0.13	174.2± 13.5
White Bread + Margarine Control	4.17± 0.08	4.81± 0.13	6.22± 0.17	6.45± 0.22	6.09± 0.35	5.37± 0.26	4.89± 0.20	164.7± 16.9
White Bread + VFB2.5 g	4.40± 0.07	4.66± 0.11	5.73± 0.21*	5.75± 0.27*	5.69± 0.34*	5.54± 0.30	5.18± 0.23	121.1± 21.0
White Bread+VFB5.0 g	4.26± 0.12	4.34± 0.12*	5.28± 0.17*	5.66± 0.23*	5.33± 0.24*	5.13± 0.16	4.83± 0.15	96.6± 20.1
White Bread+VFB7.5 g	4.15± 0.12	4.4± 0.14*	5.25± 0.17*	5.35± 0.16*	5.15± 0.14*	4.71± 0.13*	4.59± 0.12	85.1± 12.3

As shown above in TABLE 37, there was no significant difference observed in blood glucose concentrations after consumption of the white bread alone control as compared to the white bread plus margarine control. However, white bread plus margarine plus VFB 2.5 g as compared to white bread control showed a statistically significant difference at 30 minutes (p=0.008), 45 minutes (p=0.002), and 60 minutes (p=0.018) after consumption of the test meal. White bread plus margarine plus VFB 5.0 g as compared to white bread control showed a statistically significant difference at 15 minutes (p=0.006), 30 minutes (p=0.0001), 45 minutes (p=0.001), 60 minutes (p=0.001), and 90 minutes (p=0.0001). White bread plus margarine plus VFB 7.5 g as compared to white bread control showed a statistically significant difference at 15 minutes (p=0.029), 30 minutes (p=0.0001), 45 minutes (p=0.0001), 60 minutes (p=0.0001), and 90 minutes (p=0.001).

PALATABILITY AND GLYCEMIC INDEX

The palatability scores and GI values for the glucose and bread series were calculated as described above and are shown below in TABLE 38. With regard to palatability, all test meals were well tolerated, however, the palatability scores of the glucose with VFB for all three doses was significantly lower when compared to the control glucose, likely because gelling of the glucose (after addition of VFB) took place before all was consumed.

TABLE 38: Glucose Drink Series: Palatability and Glycemic Index

Test Meal	Abbrev	Palatability (mm)	Glycemic Index
Glucose	Gluc	53.7±6.4[a]	100[a]
Glucose+2.5 g VFB	VFB2.5	35.6±10.4[b]	83.7±9.0[ab]
Glucose+5.0 gVFB	VFB5.0	34.0±9.6[b]	77.7±8.2[ab]
Glucose+7.5 gVFB	VFB7.5	26.2±8.8[b]	71.5±5.9[b]

Values with different letters in the superscript are significantly different ($p<0.001$)

TABLE 39: White Bread Series: Palatability and Glycemic Index

Test Meal	Abbrev	Palatability (mm)	Glycemic Index
White Bread	WB	65.7±7.8	71[a]
White Bread+Margarine	WB+M	72.7±8.2	66.8±3.6[a]
White Bread +Margarine+VFB2.5 g	VFB2.5	75.6±3.2	47.5±5.9[b]
White Bread + Margarine + VFB5.0 g	VFB5.0	73.8±5.7	37.3±5.9[b]
White Bread + Margarine + VFB7.5 g	VFB7.5	64.9±6.3	33.9±3.6[b]

With regard to glycemic index, in the glucose series the GI value of the 7.5 g VFB was significantly lower than the control glucose test meal (see TABLE 38), while in the bread series, all three doses of VFB (2.5, 5.0, 7.5 g) were significantly lower than both the white bread and the white bread and margarine control (see TABLE 39).

The glycemic index reducing potential of VFB was then determined when added to liquid (glucose) and solid (white bread plus margarine) food formulations. The glycemic index was calculated for each dose of VFB (2.5, 5.0, 7.5 g). Incremental areas under the blood glucose response curves (IAUC) were calculated as described above. Each subject's IAUC after consumption of each test food was expressed as a percentage of the mean IAUC of the three white bread controls taken by the same subject. The mean of the resulting values was the food GI based on the glucose scale (i.e., GI of glucose = 100). In addition, the glycemic index lowering potential of each formulation was estimated. The glycemic index and change in glycemic index per gram of VFB (ΔGI/gVFB) are provided below in TABLE 40 for the glucose drink test meals, and are provided below in TABLE 41 for the white bread test meals.

TABLE 40: Average change in Glycemic Index when VFB is added to glucose drink

Test Meal	**GI**	**ΔGI/gVFB**
50 g Glucose Control	100^{a}	
50 g Glucose +2.5 g VFB	$83.7\pm9.0^{a,b}$	-6.5
50 g Glucose + 5.0 g VFB	$77.7\pm8.2^{a,b}$	-4.5
50 g Glucose + 7.5 g VFB	72.5 ± 5.9^{b}	-3.7
	Average change in GI per gram of VFB	**-4.9±0.9**

Numbers with different letters in the superscript are statistically different ($p<0.05$).

Table 41: Average Change in Glycemic Index When VFB is Added to White Bread

Test Meal	**GI**	**ΔGI/gVFB**
White Bread Control	71^{a}	
White Bread + Margarine	66.8 ± 3.6^{a}	
White Bread + Margarine + 2.5 gVFB	47.5 ± 5.9^{b}	-9.4
White Bread + Margarine + 5.0 g VFB	37.3 ± 5.9^{b}	-6.7
White Bread + Margarine + 7.5 g VFB	33.9 ± 3.6^{b}	-5.0
	Average change in GI per gram of VFB	**-7.0±1.3**

Numbers with different letters in the superscript are statistically different ($p<0.05$).

SUMMARY AND CONCLUSIONS

The results in this example demonstrate that the addition of VFB reduced the glycemic index of all of the meals, irrespective of the type of meal it was added to. FIGURE 12 graphically illustrates the change in glycemic index after consumption with a glucose drink or white bread containing increasing doses of VFB. As shown in FIGURE 12, increasing the dose of VFB causes a corresponding decrease in GI values, although the relationship is not linear.

To obtain an estimate of the GI lowering potential of VFB, the mean of the reduction observed per gram of VFB at each dose level was calculated and the results are shown above in TABLE 40 and TABLE 41. As shown in TABLE 40, the glycemic index

lowering potential of VFB when added to a liquid meal (glucose drink) is -4.9 ±0.9 in the glucose series. As shown in TABLE 41, the glycemic index lowering potential of VFB when added to a solid meal (white bread plus margarine) is -7.0±1.3 in the white bread series. As there was no significant change in GI observed with the addition of margarine (see TABLE 37), the GI lowering potential for the white bread series was calculated using the control white bread GI value. Therefore, the addition of VFB to a liquid in the dose range of 2.5-7.5 g will result in a reduction of GI of the food product by approximately five GI units for a liquid food product, and seven GI units when added to a solid food product.

EXAMPLE 13

This example demonstrates that the addition of VFB to various foods is effective to reduce the glycemic index of the food to which it was added.

METHODS

SUBJECTS

Ten healthy subjects (four male and six female), aged 37.3 ±3.6 years with a body mass index of 23.8±1.3 kg/m2 were studied. The individual details are shown below in TABLE 42.

TABLE 42: Subject Details

ID	Sex	Ethnicity	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m2)
93	F	Caucasian	39	163.0	56.9	21.4
190	F	Caucasian	24	167.0	58.0	20.8
201	M	Asian	28	171.0	71.0	24.3
209	M	Asian	41	167.0	66.5	23.8
233	F	Caucasian	47	158.0	53.1	21.3
254	F	Caucasian	46	170.0	77.4	26.8
258	F	Asian	40	153.0	49.5	21.1
281	M	Caucasian	23	186.5	84.7	24.4
312	F	Caucasian	58	178.0	86.3	27.2
318	M	Caucasian	23	186.5	84.7	24.4
		Mean±SD	**37.3±3.6**	**169.8±3.4**	**69.3±4.7**	**23.8±1.3**

TEST MEALS

The following food types were included in this study:

Study 1: Corn flakes, Rice, Roast Turkey, Yogurt, White bread,

Study 2: Granola 1B, 1C, 2B, 3B, Slimfast

All test meals consisted of portions of each food containing 50 g available carbohydrate (defined as total carbohydrate minus dietary fiber). Five grams of VFB300 (granulated (konjac/xanthan/alginate (70:13:17)) was sprinkled onto the portion of cornflakes, rice, roast turkey dinner, or yogurt immediately prior to consumption. The cornflakes were consumed with 125 ml of milk.

To control for any effect the milk may have had on the glucose tolerance, an extra white bread with milk was also consumed. The white bread was baked in a bread maker in loaves containing 250 g available carbohydrate. The ingredients for each loaf (250 ml warm water, 340 g all purpose flour, 7 g sugar, 4 g salt, and 6.5 g dry yeast) were placed into the bread maker according to instructions and the machine turned on. After the loaf had been made, it was allowed to cool for an hour, and then weighed and after discarding the crust ends, the remainder was divided into portion sizes containing 50 g available carbohydrate. These portions were frozen prior to use and reheated in the microwave prior to consumption.

TABLE 43: Nutrient Content of Test Foods

Test Meal	Abbrev	Amount (g)	Protein (g)	Fat (g)	Total CHO (g)	Dietary Fiber (g)	Available CHO (g)
White Bread	WB	104*	7.6	1.6	52.8	2.8	50
White Bread + 125ml 2% milk	WB+M	104+125ml	8.1	4.1	58.8	2.8	56
Cornflakes + 125ml 2% milk	CF	60+125ml	8.3	2.5	56	0	56
Cornflakes + 125ml milk + VFB (5g)	CF+VFB	60+125ml+5g	8.3	2.5	61	5	56
Rice	Rice	62.5	4.2	0	50.0	0	50
Rice + VFB (5g)	Rice + VFB	62.5+5	4.2	0	55	5	50
Turkey Dinner	Rturk	422	21.6	11.3	55.4	5.6	50
Turkey Dinner + VFB (5g)	RT+VFB	422+5	21.6	11.3	60.4	10.3	50
yogurt	yogurt	250	8	4	50	0	50
yogurt+VFB (5g)	Yog+VFB	250+5	8	4	55	5	50

ASSAY METHODS

Each subject underwent treatments on separate days, with each subject performing up to two tests per week with at least one day between tests. On each test day, subjects arrived in the morning after a 10-to 14-hour overnight fast. After being weighed and having a fasting blood sample obtained by finger prick, the subject then consumed a test meal within ten minutes and further blood samples were obtained at 15, 30, 45, 60, 90, and 120 minutes after the start of the test meal. Subjects were given a choice of one to two cups of water, tea, or coffee, with or without milk. The beverage consumed by each subject remained the same on each test day.

Blood samples were collected into 5 ml polypropylene tubes containing a small amount of sodium fluoride/potassium oxalate, mixed by rotating the tube vigorously, and placed into a refrigerator. After the last blood sample, tubes were stored at -20°C prior to analysis of glucose using an automatic analyzer (Model 2300 STAT, Yellow Springs Instruments, Madison, Wisconsin). All blood samples were analyzed within one week of collection. Blood glucose was measured after fasting and at 15, 30, 45, 60, 90, and 120 minutes after eating the test meal. Incremental areas under the plasma glucose curves (IAUC) were calculated using the trapezoid rule and ignoring area beneath the baseline. The glycemic index was calculated by expressing each subject's glucose IAUC for the test food as a percentage of the same subject's average response after the reference white bread. The mean of the resulting values was the food glycemic index (GI) based on the glucose scale (i.e., GI of glucose = 100). The blood glucose concentrations at each time point and the IAUC values were subjected to repeated measures analysis of variance (ANOVA) examining for the effect of the test meal. After demonstration of significant heterogeneity, the significance of the differences between individual means was assessed using Tukey's test to adjust for multiple comparisons. In addition, the significance of the differences between blood glucose concentrations and increments for each test food and white bread were assessed by paired t-test. The percent reduction in GI was calculated for each meal with VFB was also calculated.

Palatability was rated on a 100 mm visual analogue scale anchored at very "unpalatable" at one end and "very palatable" at the other end. The higher the number, the higher the perceived palatability of the test food.

RESULTS

The results of the blood glucose tests for the various test foods are summarized below in TABLE 44. The "*" symbol indicates a statistically significant difference between the test condition and the white bread control at the indicated time point.

TABLE 44: Summary of Blood Glucose Responses for Test Foods

Test Condition	**0min (mean)**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**AUC**
Cornflakes	4.37± 0.13	5.14± 0.19	7.12± 0.30	7.64± 0.52	6.80± 0.55	5.13± 0.23	4.38± 0.27	184.9± 28.5
Cornflakes+ VFB	4.41± 0.13	4.90± 0.25	6.33± 0.41	6.58± 0.40*	6.15± 0.39	5.01± 0.23	4.72± 0.11	132.7± 23.5
Rice	4.41± 0.12	5.43± 0.23	7.23± 0.27	7.08± 0.44	6.38± 0.50	5.71± 0.26	4.63± 0.13	185.6± 31.7
Rice+VFB	4.44± 0.13	4.86± 0.13	5.84± 0.23*	5.75± 0.29*	5.44± 0.31*	5.16± 0.11	4.86± 0.11	98.8± 17.1
Roast Turkey	4.39± 0.08	5.44± 0.21	7.34± 0.35*	6.68± 0.54*	5.64± 0.49*	4.29± 0.08*	4.04± 0.13*	126.8± 22.5
Roast Turkey + VFB	4.43± 0.11	5.29± 0.25	6.51± 0.29	5.98± 0.36*	5.06± 0.26*	4.50± 0.10*	4.41± 0.11	89.1± 12.0
Yogurt	4.43± 0.11	5.60± 0.26	6.92± 0.25	5.90± 0.36*	4.72± 0.26*	3.97± 0.09*	3.85± 0.07	92.4± 11.8
Yogurt + VFB	4.41± 0.14	5.54± 0.31	6.52± 0.34	5.71± 0.42*	4.82± 0.33*	4.20± 0.13*	4.08± 0.14*	84.9± 14.5
White Bread	4.37± 0.12	5.12± 0.32	6.54± 0.40	6.73± 0.40	6.36± 0.37	5.26± 0.25	4.77± 0.12	158.9± 20.7

As shown above in TABLE 44, the blood glucose concentration after consumption of cornflakes was higher than the white bread control, with a statistical difference observed at 45 minutes ($p=0.001$). The blood glucose concentration after consumption with cornflakes plus VFB was reduced as compared to cornflakes alone and was very similar to that observed after consumption with the white bread control.

As shown in TABLE 44, the blood glucose concentration after consumption of rice was very similar to that observed after consumption of the white bread control. However, after consumption of rice plus VFB, the blood glucose concentration was reduced at statistically significant lower levels at 30 minutes ($p=0.049$), 45 minutes ($p=0.005$), and 60 minutes ($p=0.002$) after test meal consumption as compared to the white bread control.

As shown in TABLE 44, the blood glucose concentration after consumption of roast turkey was initially higher than that observed for the white bread control with a significantly higher level observed at 30 minutes (p=0.025) then trended lower, with a statistically significant lower level observed at 60 minutes (p= 0.037), 90 minutes (p=0.001), and 120 minutes (0.011). After consumption of roast turkey with VFB, the initial blood glucose levels were similar to the white bread control, then trended lower than those observed for white bread, with a statistically significant lower level observed at 45 minutes (p=0.006), 60 minutes (p=0.001), and 90 minutes (p=0.012) as compared to the white bread control.

Finally, as further shown in TABLE 44, the blood glucose concentration after consumption of yogurt was initially higher than that observed for the white bread control, then trended lower with a statistically significant lower level observed at 45 minutes (p=0.021), at 60 minutes (p=0.00), and at 90 minutes (p=0.001) as compared to the white bread control. After consumption of yogurt with VFB, the blood glucose concentration was initially the same as the white bread control, then trended lower with a statistically significant lower level observed at 45 minutes (p=0.007), 60 minutes (p=0.00), 90 minutes (p=0.00), and 120 minutes (p=0.00) as compared to the white bread control.

PALATABILITY AND GLYCEMIC INDEX

The palatability scores and glycemic values for the test meals are shown below in TABLE 45.

TABLE 45: Palatability and Glycemic Index

Test Meal	**Abbrev**	**Palatability (mm)**	**Glycemic Index (GI)**	**Glycemic Index Category[1]**
Cornflakes+125ml 2% milk	CF	66.5±4.5	83.4±8.0	High
Cornflakes+125ml 2% milk +VFB	CF+VFB	58.8±5.2	58.0±6.9	Medium
Rice	Rice	42.0±4.4	82.0±7.5	High
Rice+VFB	Rice+VFB	41.4±6.5	44.7±4.4	Low
Roast Turkey	RT	78.1±5.5	55.2±4.7	Low
Roast Turkey + VFB	RT+VFB	75.5±6.4	41.1±3.5	Low
Yogurt	Yog	75.1±8.3	44.2±4.1	Low
Yogurt+VFB	Yog +VFB	77.0±5.5	37.5±2.9	Low
White Bread	WB	71.3±5.0	71.0±0.0	High
White Bread + 125ml	WB+M	67.2±4.6	83.7±9.0	High

2% milk				

[1] The Glycemic Index Category is defined as follows: GI ≤ 55 is categorized as "Low"; 56 < GI < 69 is categorized as "Medium"; GI ≥ 70 is categorized as "High" (See the Canadian Diabetes Association website, www.diabetes.ca/Section About glycemic.asp, accessed July 26, 2007).

As shown above in TABLE 45, the addition of VFB reduced the glycemic index (GI) of all of the test meals irrespective of the type of meal to which it was added. In particular, it is noted that the addition of VFB to cornflakes reduced the GI of the cornflakes from the high GI category to the medium category, and the addition of VFB to rice reduced the GI of the rice from the high GI category to the low GI category.

FIGURE 13 graphically illustrates the glycemic index for each test meal with or without 5.0 g of VFB per approximately 50 g available carbohydrates, expressed as the Mean ± SEM. As shown in FIGURE 13, addition of VFB to cornflakes, rice, turkey dinner or yogurt resulted in a 26%, 45%, 24%, and 9% reduction in meal GI, respectively. The percent reductions observed in the GI for cornflakes and rice meals when adding VFB were statistically significant ($p<0.00001$).

With regard to palatability, all test meals were well tolerated. It is noted that the addition of VFB to the various food types did not significantly reduce the palatability of the particular food product. Therefore, these results demonstrate that the addition of VFB reduced the GI of all of the test meals irrespective of the type of meal to which it was added and did not significantly affect the palatability of the test meals.

EXAMPLE 14

This example demonstrates that the addition of VFB to various types of granola is effective to reduce the glycemic index of the granola to which it was added.

METHODS

SUBJECTS

Ten healthy subjects (four male and six female), aged 37.3±3.6 years with a body mass index of 23.8±1.3 kg/m2 were studied. The individual details of the subjects that participated in this study are described in TABLE 42 of EXAMPLE 13.

TEST MEALS

All test meals consisted of portions of each food containing 50 g available carbohydrate (defined as total carbohydrate minus dietary fiber). The white bread control

was generated as described in EXAMPLE 13. VFB may be incorporated into granola by blending selective dry and liquid granola ingredients with VFB (konjac/xanthan/alginate (70:13:17)) and then processing the overall mixture through baking or other drying methods. The following test granola meals were prepared by baking the VFB into the granola:

Granola 1C = Cranberry Granola with 2.5 g VFB per 60 g serving (50 g available CHO)

Granola 1B = Blueberry Granola with 2.5 g VFB per 60 g serving (50 g available CHO)

Granola 2B = Blueberry Granola with 5.0 g VFB per 60 g serving (50 g available CHO)

Granola 3B = Blueberry Granola control (no VFB) 60 g serving (50 g available CHO)

TABLE 46: Nutrient Content of Test Foods

Test Meal	Abbrev	Amount (g)	Protein (g)	Fat (g)	Total CHO (g)	Dietary Fiber (g)	Available CHO (g)
Blueberry Granola (control)	Gran3B	92	9.3	14.6	62.3	12.3	50
Cranberry Granola + 2.5 g VFB	Gran1C	93	10.3	14.7	61.9	11.8	50
Blueberry Granola + 2.5 g VFB	Gran1B	92	10.0	14.3	61.4	11.4	50
Blueberry Granola + 5g VFB	Gran2B	98	10.4	15.2	65.8	15.8	50
Slimfast	Slimfast	470ml					50
White Bread	WB	104*	7.6	1.6	52.8	2.8	50

ASSAY METHODS

Each subject underwent treatments on separate days, with each subject performing up to two tests per week with at least one day between tests. On each test day, subjects arrived in the morning after a 10-to 14-hour overnight fast. After being weighed and having a fasting blood sample obtained by finger prick, the subject then consumed a test meal within ten minutes and further blood samples were obtained at 15, 30, 45, 60, 90,

and 120 minutes after the start of the test meal. Subjects were given a choice of one to two cups of water, tea, or coffee, with or without milk. The beverage consumed by each subject remained the same on each test day.

Blood glucose was measured after fasting and at 15, 30, 45, 60, 90, and 120 minutes after eating the test meal using the methods described in EXAMPLE 13. Palatability was measured using the methods described in EXAMPLE 13.

RESULTS

The results of the blood glucose tests for the various granola test meals and controls are summarized below in TABLE 47. The "*" symbol indicates a statistically significant difference between the test condition and the white bread control at the indicated time point.

TABLE 47: Summary of Blood Glucose Responses for Test Foods

Test Conditions	**0min (mean)**	**15min**	**30min**	**45min**	**60min**	**90min**	**120min**	**AUC**
Gran1B	4.49± 0.14	4.96± 0.24	6.16± 0.29	5.61± 0.25*	4.86± 0.27*	4.77± 0.15	4.68± 0.09	73.1± 16.2
Gran1C	4.38± 0.13	4.79± 0.21	5.85± 0.33*	5.81± 0.33*	5.36± 0.30*	4.69± 0.17*	4.51± 0.14	86.6± 15.3
Gran2B	4.49± 0.14	4.82± 0.15	5.47± 0.20*	5.26± 0.21*	4.86± 0.22*	4.68± 0.17*	4.56± 0.11	50.3± 10.1
Gran3B	4.44± 0.12	5.36± 0.22	6.93± 0.33*	6.76± 0.53	6.40± 0.51	4.88± 0.27	4.28± 0.13	147.7± 25.7
Slimfast	4.45± 0.12	5.40± 0.21	6.09± 0.34	5.11± 0.27	4.41± 0.24	4.22± 0.16	4.12± 0.15	59.8± 8.8
WB	4.37± 0.12	5.12± 0.32	6.54± 0.40	6.73± 0.40	6.36± 0.37	5.26± 0.25	4.77± 0.12	158.9± 20.7

As shown above in TABLE 47, the blood glucose concentration after consumption of granola 3B (control) was similar to the glucose concentration after consumption of white bread, with a statistically significant decrease observed at 30 minutes ($p=0.034$) after test meal consumption. The blood glucose concentration after consumption of granola 1B (with 2.5 g VFB) was significantly lower than that observed for the white bread control, with a statistically significant difference observed at 45 minutes ($p=0.001$) and 60 minutes ($p=0.0001$) after test meal consumption. The blood glucose concentration after consumption of granola 2B (with 5.0 g VFB) was further reduced as compared to the white bread control, with a statistically significant reduction

observed at 30 minutes (p=0.002), 45 minutes (p=0.0001), 60 minutes (p=0.0001), and 90 minutes (p=0.036) after test meal consumption. The blood glucose concentration after consumption of granola 1C (with 2.5 g VFB) was also significantly lower than that observed for the white bread control, with a statistically significant reduction observed at 30 minutes (p=0.034), 45 minutes (0.001), 60 minutes (0.001), and 90 minutes (0.022) after test meal consumption.

PALATABILITY AND GLYCEMIC INDEX

The palatability and glycemic index was analyzed as described above in EXAMPLE 13. The results are shown below in TABLE 48. With regard to palatability, all test meals were well tolerated; however the palatability score of the blueberry granola with 5 g VFB (Gran2B) was significantly lower when compared to the white bread control.

TABLE 48: Palatability and glycemic Index

Test Meal	Abbrev	Palatability	Glycemic Index	GI Category1
White Bread	WB	71.3±5.0	71.0±0.0	High
Blueberry Granola (control)	Gran3B	52.7±8.7	63.8±6.3	Medium
Blueberry Granola + 2.5 g VFB	Gran1B	45.2±8.1	32.6±4.8	Low
Cranberry Granola + 2.5 g VFB	Gran1C	45.2±8.9	38.4±4.0	Low
Blueberry Granola + 5g VFB	Gran2B	40.8±8.6	21.6±3.0	Low
Slimfast	Slimfast	43.0±8.6	30.4±5.4	Low

With regard to the Glycemic Index, all of the granolas containing VFB were significantly lower that the white bread control or the granola control. FIGURE 14 graphically illustrates the glycemic index for each test meal with or without VFB, expressed as the Mean ± SEM. As shown in FIGURE 14, addition of VFB reduced the glycemic index of all the granolas, with statistically significant reductions observed irrespective of the type of granola used ($p<0.0001$). As compared to the control granola (blueberry), the cranberry granola (2.5 g VFB), blueberry granola (2.5 g VFB) and blueberry granola (5.0 g VFB) reduced the GI by 31%, 45%, and 64%, respectively.

This study demonstrates that VFB can be incorporated into granola and other foods as an effective and palatable method to moderate the spike in blood glucose levels after ingesting foods with medium or high glycemic indices. Not only did the addition of VFB reduce the GI in a dose-dependent fashion, it also lowered the glycemic index

category of the granola from medium to low. The addition of VFB to other medium or high glycemic index category foods can be expected to have similar effects.

EXAMPLE 15

This Example describes a 14-week study with overweight and obese human subjects demonstrating that Viscous Fiber Blend (VFB) is effective to reduce weight, lower cholesterol levels, and decrease fasting glucose when administered daily.

Rationale:

The purpose of this observational retrospective clinical analysis was to examine the efficacy of VFB micro-granules (VFB100) (granulated konjac/xanthan/alginate (70:13:17)) on weight loss, body mass index, waist circumference, waist-hip ratio, plus laboratory measurements including total and LDL cholesterol, triglycerides, fasting insulin, fasting glucose and 2 hour glucose tolerance test for 14 weeks in overweight and obese adults.

Subjects:

A total of 29 sedentary adults (23 women; 6 men in generally good health), aged 20 to 65 years with a body mass index (BMI) range of approximately 23 kg/m^2 to 36 kg/m^2 were invited to participate through a series of advertisements placed in local newspapers. Subjects gave their written consent for participation in the program and were required to attend group lectures on general health, diet, and exercise, every two weeks given by one of the study directors for a maximum of 14 weeks.

Methods:

Screening and evaluation of the subjects were performed by a medical doctor or naturopathic physician for height (inches), weight (pounds), and waist-hip measurements on a bi-weekly basis. Percent body fat was determined using bioelectrical impedance testing at baseline and every two weeks thereafter. A computerized analysis (RJR Systems) was further employed on all subjects in order to determine BMI and percent body fat. While all subjects enrolled in the program were initially evaluated for HDL, LDL, total cholesterol, triglycerides, fasting glucose, fasting insulin, 2 hour fasting insulin, and 75 gram glucose tolerance test at baseline, only those with aberrant risk factors were re-tested using the latter laboratory parameters at week 14. During this time frame, volunteers were required to take up to 10 grams of VFB micro-granules (VFB100) with 12 to 16 oz of water in divided doses throughout the day.

Significance was determined using the paired T-test analysis with assistance from the Short Term Consulting Service, Department of Statistics, University of British Columbia.

Results:

Weight Loss and Other Parameters: During the 14 weeks of VFB use, there were significant reductions in group weight (-12.78 ± 7.84 pounds), waist measurements (-4.75 ± 2.19 inches), % body fat (-2.43 ± 2.39 %), and BMI (-2.26 ± 1.24 kg/m^2). Similarly and in concert with these latter outcomes, both sexes individually demonstrated significant reductions in the tested weight loss variables as noted in the following tables:

TABLE 49: Group 1: Men and Women Combined

Test	*Sample size*	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*%Change*
*Weight	29	198.38"	± 31.82	185.6	± 30.52	-12.78	± 7.84	-6.44
*Waist	29	40.78""	± 5.03	36.03	± 5.10	-4.75	± 2.19	-11.65
*Hip	29	45.79""	± 3.02	42.06	± 2.93	-3.73	± 1.62	-8.14
*%fat	29	40.30	± 8.28	37.87	± 8.88	-2.43	± 2.39	-6.02

*p < 0.05 from week 0

" weight is in pounds

"" waist and hip is in inches

TABLE 50: Group 1: Men (n=6)

Test	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*% Change*
*Weight	246.50	± 20.10	228.20	± 28.78	-18.32	± 6.15	-7.43
*Waist	47.69	± 3.80	41.98	± 4.05	-5.71	± 1.81	-12.00
*Hip	47.47	± 3.00	43.45	± 2.91	-4.02	± 1.43	-8.00
*%Fat	26.58	± 3.01	24.62	± 2.97	-1.97	± 1.15	-7.00

* p < 0.05 from week 0

TABLE 51: Group 2: Women (n=23)

Test	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*% Change*
*Weight	185.83	± 17.31	174.49	± 19.33	-11.34	± 7.69	-6.00
*Waist	38.97	± 3.54	34.47	± 4.16	-4.50	± 2.25	-12.00
*Hip	45.35	± 2.65	41.70	± 2.89	-3.65	± 1.69	-8.00
*%Fat	43.88	± 4.52	41.33	± 6.15	-2.55	± 2.63	-6.00

* $p < 0.05$ from week 0

TABLE 52: BMI for all the Groups Combined

Gender	*Sample size*	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*% Change*
*Male	6	35.03"	± 4.09	32.47	± 3.78	-2.56	± 1.22	-7.31
*Female	23	33.45"	± 7.57	31.27	± 8.17	-2.18	± 1.26	-6.52
*All	29	33.78"	± 6.96	31.52	± 7.43	-2.26	± 1.24	-6.70

* $p < 0.05$ from week 0

" BMI in kg/m^2

Lipid levels:

Compared to baseline values, those subjects employing VFB micro-granules for the 14-week study period had a significant reduction of 19.26% (n = 17; $p < 0.05$) and 25.51% (n= 16; $p < 0.05$) in total and LDL cholesterol values respectively. Although there was a trend towards a reduction in triglyceride and an increase in HDL cholesterol values, the resulting changes were not statistically significant.

Fasting Insulin and Glucose:

As a group and by the end of the study period, those participants employing VFB experienced a 6.96% reduction in fasting glucose (n=20; $p < 0.05$), a 12.05% decline in 2 hour glucose tolerance (n=21; $p < 0.05$), and 27.26% (n=17; $p < 0.05$) reduction in fasting insulin levels compared to baseline (see graph 2). Although there was a trend towards a reduction in 2 hour fasting insulin levels, the results were not statistically significant.

TABLE 53 is a summary of the overall laboratory data obtained during the 14-week trial with VFB micro-granules:

TABLE 53: Laboratory Data Analysis Group Results:

Test	*Sample size*	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*% Change*
*Total cholesterol (mmol/L)	17	5.69	±1.07	4.60	±0.82	-1.09	±0.63	-19.26
Triglycer-ides (mmol/L)	17	1.92	±0.98	1.52	±0.56	-0.40	±0.89	-20.97
HDL	17	1.48	±0.53	1.53	±0.77	0.05	±0.67	3.33

Test	*Sample size*	*Week 0 mean*	*SD*	*Week 14 mean*	*SD*	*Change*	*SD*	*% Change*
(mmol/L)								
*LDL (mmol/L)	16	3.40	±0.96	2.53	±0.64	-0.87	±0.56	-25.51
*Fasting glucose (mmol/L)	20	5.75	±0.78	5.34	±0.49	-0.40	±0.65	-6.96
*2 hr Glucose (mmol/L)	21	6.09	±2.10	5.35	±1.81	-0.73	±1.43	-12.05
*Insulin Fasting (pmol/L)	17	89.41	±44.84	65.04	±33.21	-24.37	± 36.29	-27.26
2 hr Insulin (pmol/L)	17	433.53	± 270.32	355.76	±332.44	-77.76	± 196.51	-17.94

** $p < 0.05$ from baseline*

Analysis of efficacy using self-reporting scales:

In a self-reporting scale completed by the participants at the end of the study, 97.7% of the VFB users noted that they had a positive response to the product both in curbing food cravings and hunger.

Side effects of the test preparation:

VFB was generally well tolerated by the participants with gastrointestinal (GI) symptoms comprising the majority of all the reported complaints. Symptoms such as gas, bloating, bowel cramping, constipation, and diarrhea were noted by the volunteers. Sixty-eight percent noted that their GI symptoms resolved within approximately 3 weeks of beginning VFB. A full 32% of the participants found that they had mild GI side effects throughout the study but that these were not sufficient in severity for them to discontinue use.

Discussion:

The results of this retrospective analysis clearly demonstrate that the use of VFB micro-granules (VFB100) along with general changes in diet and physical activity, over a 14-week time period, is of benefit in modifying the metabolic and cardiovascular risk factors in those who are overweight and/or obese. Overall, there was a significant reduction in group weight (-12.78 ± 7.84 pounds), waist measurements (-4.75 ± 2.19 inches) and percent body fat (-2.43% ± 2.39%). Moreover, these latter changes were

paralleled by a significant decrease in fasting LDL (-25.51%), fasting glucose (-6.96%), and fasting insulin (-27.26%) levels over a relatively short time span of 14 weeks. This wide range of clinical benefits provided by VFB micro-granules is reflective of its unique physiological advantages in improving metabolic control.

Consuming 5 to 10 grams of foods rich in viscous soluble fiber has been reported to decrease serum LDL cholesterol and subsequent CVD events by 10% to 15% (Shamliyan, et al., *J. Fam. Pract.* 55:761-9 (2006)). Based on the results obtained from this study, VFB has been shown to be more effective in reducing LDL cholesterol by 25.1%. In comparison, research has shown that those who employ a "portfolio" of cholesterol-lowering foodstuffs for a minimum of 3 months have a stable reduction in LDL cholesterol by approximately 14% ($p < 0.001$) (Jenkins, et al., *Am. J. Clin. Nutr. 83*:582-91 (2006)).

Moreover, the reduction in LDL cholesterol values seen in the current investigation is noteworthy as the percent decrease obtained with VFB falls within the range of effectiveness (20% to 55%) reported for statin-type medication (Ritishauser, *Swiss Med. Wkly 136*:41-9 (2006)).

The results of this study demonstrate that VFB is effective in promoting short-term weight loss over a 14-week time period. The results obtained (-12.78 pounds; 5.81 kg) are similar to those who have taken the anti-obesity medication orlistat. In a controlled study, overweight (BMI > 25 kg/m^2) Type 2 diabetic patients who employed the drug orlistat at a dose of 120 mg tid over a 12-week time period lost 2.5 kg compared to 0.4 kg in the placebo group ($p < 0.05$) (Kuo, et al., *Int. J. Clin. Pract. 60*(8):906-10 (2006)). Extended use (12 months) of prescription weight loss medications including sibutramine and orlistat has resulted in a mean weight loss of 4.5 kg and 2.9 kg, respectively, compared to a placebo (Dixon, *Australian Fam. Phys. 35*:576-79 (2006)).

It is interesting to note that in the current 14-week investigation, men lost more weight on average (-18.32 ± 6.15 pounds) than the women (-11.34 ± 7.69 pounds). This change could be ascribed to the basic sex differences seen in resting energy expenditure. A study by Dr. Robert Ferraro and his associates has shown that the sedentary 24-hour energy expenditure is approximately 5% to 10% lower in women compared to men after statistical adjustments for age, activity, and body composition (Ferraro, et al., *J. Clin. Invest. 90*:780-784 (1992)).

In this study, through the use of a portable indirect calorimeter (MedGem device by HealtheTech), it was determined that women had a lower average resting/basal metabolic rate (1841.18 kilocalories) score compared to men (2346.67 calories) at the outset of the study.

This study also demonstrated that in tandem with the reduction in weight, BMI scores were also lowered in significant fashion by 2.26 ± 1.24% from baseline ($p < 0.05$) in subjects that consumed VFB. BMI is a commonly employed measure to assess the degree of overweight/obesity and its overall impact on health risk (usda.gov/cnpp/Insights/Insight16b.pdf). For example, both genders with a BMI of greater than or equal to 30 have a higher mortality risk than those who are classified as being overweight (BMI from 25 kg/m^2 to 29.9 kg/m^2) (Villareal, et al. *Am. J. Clin. Nutr.* *82*:923-34 (2005)).

In addition to modifying weight and cholesterol levels, the results of this study show that VFB significantly decreased fasting glucose, 2-hour glucose and fasting insulin levels, demonstrating that VFB is of great value in improving glycemic control. In particular, the results of the current study show that overall fasting insulin levels decreased from 89.41 ± 44.84 pmol/L to 65.04 ± 33.21 pmol/L during the 14-week investigation. This latter finding confirms that in those individuals who are overweight or obese, baseline and 4 hours post-prandial rates of insulin secretion are higher than those with normal weight. This result is consistent with another study that measured 24-hour profiles of insulin secretion in normal and obese subjects (Polansky, et al., *J. Clin. Investig. 28*(suppl 2):3-6 (1998)).

Moreover, these results also suggests that lifestyle modifications along with VFB granules would be helpful in treating insulin resistance. Obesity plays a key role in insulin resistance, and an increase or decrease in insulin resistance is linked to weight gain or loss, respectively (Lamounier-Zepter, et al., *Best Pract. Res. Clin. Endocrin. Metabol.* 20:355-367 (2006)).

These latter outcomes together suggest that the therapeutic use of VFB is of practical benefit to those suffering with excess weight, obesity and/or metabolic syndrome.

EXAMPLE 16

This Example describes a study with obese non-diabetic and diabetic human subjects exhibiting glycemic volatility demonstrating that the administration of Viscous Fiber Blend (VFB) to these subjects is effective to reduce their glycemic volatility.

Rationale: 12 non-diabetic obese subjects and several diabetic subjects were studied using a continuous glucose monitoring system (MiniMed® CGMS, Medtronic Inc.) and compared to normal weight control subjects. The CGMS is a portable electronic device worn for up to one week that is connected to a microelectronic sensor inserted by a physician into the abdominal adipose tissue. This device is FDA approved for monitoring blood sugar in insulin-dependent diabetics and it is typically used in diabetes specialty centers to obtain a more accurate and around-the-clock look at the diabetic's blood sugar to allow for more precise adjustments of their insulin. Rather than sampling blood sugar a few times per day, as with finger stick glucose monitors, the CGMS samples blood sugar several hundred times per day. After several days, the patient returns to the physician and the blood sugar data is downloaded into the physician's computer. The data can then be displayed graphically and can be quantitatively analyzed to assess such parameters as frequency of hypoglycemic episodes, as well as mean and peak blood sugar values. To our knowledge, as well as the knowledge of the device manufacturer, we are the first group to use the CGMS in the assessment of non-diabetic, obese individuals. We refer to the collective of increased frequency of blood sugar excursions, the rapid nature of the rise and fall of blood sugar, and the amount of time spent above an ideal blood sugar level as *increased glycemic volatility*.

Methods: The glycemic volatility for the 12 obese non-diabetic subjects and several diabetic subjects was assessed at baseline and again after the five-week study using a continuous glucose monitoring system (CGMS MiniMed, Medtronic, Inc.). During the five-week study, each subject consumed from 10-15 g of VFB (konjac/xanthan/alginate (70:13:17)) per day. Subjects were also evaluated for subjective hunger and food cravings during the study period.

In a second study, several obese non-diabetic subjects were treated with a low glycemic index diet (without VFB) for a period of six months, and the glycemic volatility

was assessed at baseline before the low glycemic index diet, and again after the six month diet.

In a third study, several diabetic subjects undergoing insulin treatment were treated with 10-15 g of VFB (konjac/xanthan/alginate (70:13:17)) per day for four weeks. The subjects were assessed at baseline and again after the four week study using a continuous glucose monitoring system (CGMS MiniMed, Medtronic, Inc.).

Results:

Normal Subjects:

FIGURE 15 shows a representative continuous glucose monitoring system (CGMS) graph measuring normal glycemic volatility in a non-obese, non-diabetic subject over a 24-hour period. As shown in FIGURE 15, the blood glucose levels of the normal subject are between the ideal value of 70 to 120 mmol/dL, and the glycemic volatility shows very modest and infrequent excursions from the average blood glucose level of approximately 100 mmol/dl over the 24-hour period, resulting in a fairly flat overall glycemic volatility. The data shown in FIGURE 15 is representative of several normal subjects tested.

Obese, Non-Diabetic Subjects (before and after VFB treatment):

In contrast to the results obtained in the normal subject, it was discovered that obese individuals had rapidly fluctuating blood sugar levels and typically exhibited highly frequent hyperglycemic and hypoglycemic blood sugar excursions as compared to age matched controls, as described in more detail below.

FIGURE 16A shows a CGMS graph for an obese, non-diabetic subject (ID:10) measured over a 24-hour period prior to treatment with VFB (baseline). The results shown in FIGURE 16A are representative of the results measured over 5 consecutive 24-hour time periods in this subject prior to treatment with VFB. As shown in FIGURE 16A, the subject (ID:10) had increased glycemic volatility in comparison to the normal subject (FIGURE 15), with peak blood glucose levels exceeding 180 mg/dL, along with frequent blood glucose excursions, resulting in an overall increased glycemic volatility as compared to a normal individual (see FIGURE 15). FIGURE 16B shows a CGMS graph for the same subject ID:10 shown in FIGURE 16A after 5 weeks of consumption of VFB (10-15 g/day). As shown in FIGURE 16B, a dramatic decrease in glycemic volatility was observed in the subject ID:10 after treatment with VFB, with an

average blood glucose level of approximately 100 mmol/dL maintained over the 24-hour period, similar to that observed in the normal subject (FIGURE 15).

FIGURE 17A shows a CGMS graph for a second obese, non-diabetic subject (ID:90) measured over a 24-hour period prior to treatment with VFB (baseline). The results shown in FIGURE 17A are representative of the results measured over 5 consecutive 24-hour time periods in this subject prior to treatment with VFB. As shown in FIGURE 17A, the subject (ID:90) had increased glycemic volatility in comparison to the normal subject (FIGURE 15), with frequent blood glucose excursions, resulting in an overall increased glycemic volatility as compared to a normal individual (see FIGURE 15). FIGURE 17B shows a CGMS graph for the same subject ID:90 shown in FIGURE 17A after 5 weeks of consumption of VFB (10-15g/day). As shown in FIGURE 17B, a dramatic decrease in glycemic volatility was observed in the subject ID:90 after treatment with VFB, with an average blood glucose level of approximately 100 mmol/dL maintained over the 24-hour period, similar to that observed in the normal subject (FIGURE 15). The results shown in FIGURE 17B are representative of the results measured over 5 consecutive 24-hour time periods in this subject after treatment with VFB.

FIGURE 18A shows a CGMS graph for a third obese, non-diabetic subject (ID:20) measured over a 24-hour period prior to treatment with VFB (baseline). The results shown in FIGURE 18A are representative of the results measured over 5 consecutive 24-hour time periods in this subject prior to treatment with VFB. As shown in FIGURE 18A, the subject (ID:20) had increased glycemic volatility in comparison to the normal subject (FIGURE 15), with frequent blood glucose excursions, resulting in an overall increased glycemic volatility as compared to a normal individual (see FIGURE 15). FIGURE 18B shows a CGMS graph for the same subject ID:20 shown in FIGURE 18A after 5 weeks of consumption of VFB (10-15 g/day). As shown in FIGURE 18B, a dramatic decrease in glycemic volatility was observed in the subject ID:20 after treatment with VFB, with an average blood glucose level of approximately 100 mmol/dL maintained over the 24-hour period, similar to that observed in the normal subject (FIGURE 15). The results shown in FIGURE 18B are representative of the results measured over 5 consecutive 24-hour time periods in this subject after treatment with VFB.

The results of the three subjects (ID:10, 20, 90) described above were representative of the other subjects included in this study (data not shown). These results demonstrate that VFB was effective to significantly reduce the glycemic volatility observed in obese subjects. In addition, it was noted that the obese, non-diabetic subjects in this study reported a significant decrease in subjective hunger and food cravings over the course of the five-week study.

Obese, Non-diabetic Subjects (before and after low glycemic index diet):

CGMS data was obtained from several obese, non-diabetic subjects before and after treatment with a low glycemic index diet (without VFB). Importantly, in contrast to the results observed with VFB, it was observed that the low glycemic index diet did not significantly reduce glycemic volatility in these subjects. FIGURE 19A shows a CGMS graph over a 24-hour period of an obese non-diabetic subject (ID:1098) prior to treatment with a low glycemic index diet (baseline). FIGURE 19B shows a CGMS graph over a 24-hour period (from the same obese non-diabetic subject shown in FIGURE 19A), after a six-month low glycemic index diet. As shown, the glycemic volatility exhibited in the subject prior to the diet (FIGURE 19A) was not significantly reduced by the low glycemic index diet (FIGURE 19B). As another example, FIGURE 19C shows a CGMS graph over a 24-hour period of a second obese, non-diabetic subject (ID:1146) prior to treatment with a low glycemic index diet (baseline). FIGURE 19D shows a CGMS graph over a 24-hour period (from the same obese non-diabetic subject shown in FIGURE 19C), after a six-month low glycemic index diet. As shown, the glycemic volatility exhibited in the subject prior to the diet (FIGURE 19C) was not significantly reduced by the low glycemic index diet (FIGURE 19D). Therefore, these results demonstrate that a low glycemic index diet was not effective to reduce the glycemic volatility observed in obese subjects.

Diabetic Subjects (before and after VFB treatment)

CGMS data was obtained from several diabetic subjects undergoing insulin treatment before and after treatment with VFB (10-15 g/day over a four-week period). FIGURE 20A shows a CGMS graph over a 24-hour period from an obese diabetic subject on insulin (ID:60) prior to treatment with VFB (baseline). As shown in FIGURE 20A, the blood sugar is poorly controlled in this subject, with peak blood glucose levels exceeding 300 mg/dL and low blood glucose levels below 70 mg/dL, along with frequent blood glucose excursions, resulting in an overall increased glycemic volatility as

compared to a normal individual. The results shown in FIGURE 20A are representative of the results measured over 5 consecutive 24-hour time periods in this subject prior to treatment with VFB.

FIGURE 20B shows a CGMS graph over a 24-hour period from the same diabetic subject as shown in FIGURE 20A after treatment with VFB (10-15g/day) for 4 weeks. As shown in FIGURE 20B, the blood sugar levels are much better controlled with VFB treatment, and importantly, the insulin requirements were less than 1/2 the dose previously required before VFB treatment. The results shown in FIGURE 20A are representative of the results measured over 5 consecutive 24-hour time periods in this subject after treatment with VFB. Similar effects have been observed in other diabetic subjects.

Conclusions:

In summary, these results demonstrate the significant and unexpected impact of VFB treatment on glycemic volatility and the superiority of VFB treatment to treatment with a low glycemic index diet alone in obese non-diabetic subjects. All the obese non-diabetic subjects analyzed in this study were observed to have increased glycemic volatility when measured over a 24-hour period prior to the initiation of the study (baseline) in comparison to normal control subjects which was markedly reduced after treatment with VFB. In addition, it was demonstrated that VFB treatment is effective to significantly improve blood sugar regulation in obese, insulin dependent diabetic subjects.

While the preferred embodiment of the invention has been illustrated and described, it will be appreciated that various changes can be made therein without departing from the spirit and scope of the invention.

CLAIMS

1. A method for reducing the glycemic index of a food product, the method comprising adding to the food product prior to consumption a dietary fiber composition in an amount of 2.5 g to 7.5 g of the dietary fiber composition per 50 g available carbohydrate of the food product effective to reduce the glycemic index of the food product by at least 5 glycemic index units, wherein the dietary fiber composition comprises from 48% to 90% (w/w) glucomannan, from 5% to 20% (w/w) xanthan gum, and from 5% to 30% (w/w) alginate.

2. The method of Claim 1, wherein the dietary fiber composition is baked into the food product.

3. The method of Claim 1, wherein the dietary fiber composition is mixed with the food product prior to consumption.

4. The method of Claim 1, wherein the dietary fiber composition is sprinkled onto the food product prior to consumption.

5. The method of any one of Claims 1-4, wherein the food product is a solid food product that is rice, cereal, granola, baked goods, pasta or meat.

6. The method of any one of Claims 1-4, wherein the food product is a dairy product that is milk, yogurt, cheese, butter, or ice cream.

7. The method of any one of Claims 1-6, wherein the dietary fiber composition comprises granules in the size range of from 40 mesh to 60 mesh.

8. The method of Claim 1, wherein the food product is margarine.

9. The method of Claim 5, wherein the meat is poultry, beef, pork, or fish.

10. A food product comprising from 2.5 g to 7.5 g of a dietary fiber composition per 50 g available carbohydrate of the food product, wherein the dietary fiber composition

comprises from 48% to 90% (w/w) glucomannan, from 5% to 20% (w/w) xanthan gum, and from 5% to 30% (w/w) alginate.

11. The food product of Claim 10, wherein the food product is a solid food product that is rice, cereal, granola, baked goods, pasta or meat.

12. The food product of Claim 11, wherein the meat is poultry, beef, pork, and fish.

13. The food product of Claim 10, wherein the food product is a dairy product that is milk, yogurt, cheese, butter, or ice cream.

14. The food product of Claim 10, wherein the food product is margarine.

15. The food product of Claim 10, wherein the food product is a liquid or semi-liquid selected from the group consisting of a meal replacement drink; a smoothie, a dietary supplement, a soup, and a juice.

16. The food product of Claim 10, wherein the dietary fiber composition comprises from 50% to 80% (w/w) glucomannan, from 10% to 20% (w/w) xanthan gum, and from 10% to 20% (w/w) alginate.

17. The food product of Claim 10, wherein the alginate is a medium viscosity alginate.

18. The food product of Claim 10, wherein the dietary fiber composition comprises granules in the size range of from 40 mesh to 60 mesh.

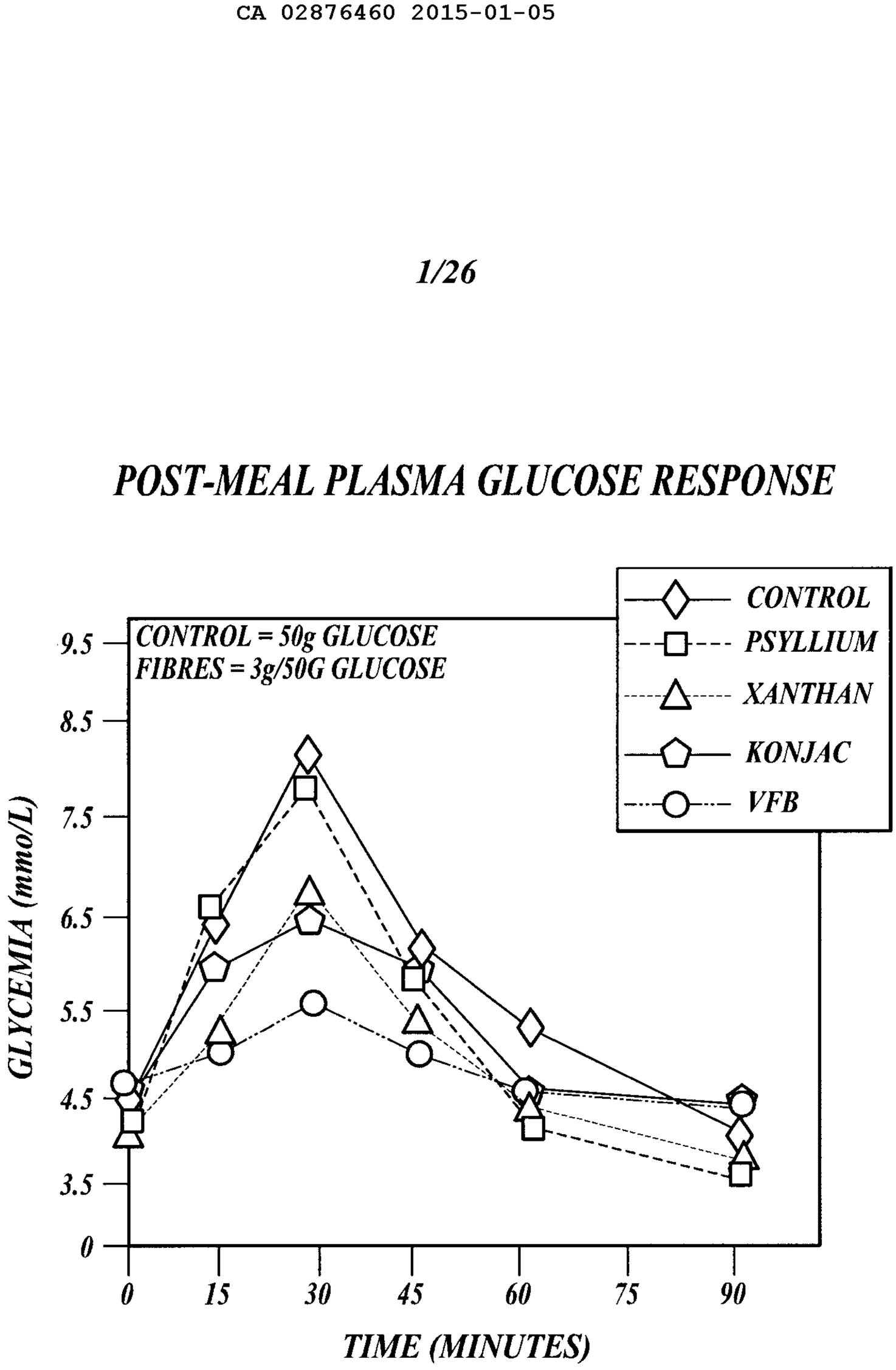

POST-MEAL PLASMA GLUCOSE RESPONSE
CONTROL = 50g GLUCOSE
FIBRES = 3g/50G GLUCOSE
CONTROL
PSYLLIUM
XANTHAN
KONJAC
VFB
GLYCEMIA (mmo/L)
9.5
8.5
7.5
6.5
5.5
4.5
3.5
0
0
15
30
45
60
75
90
TIME (MINUTES)

Fig.1.

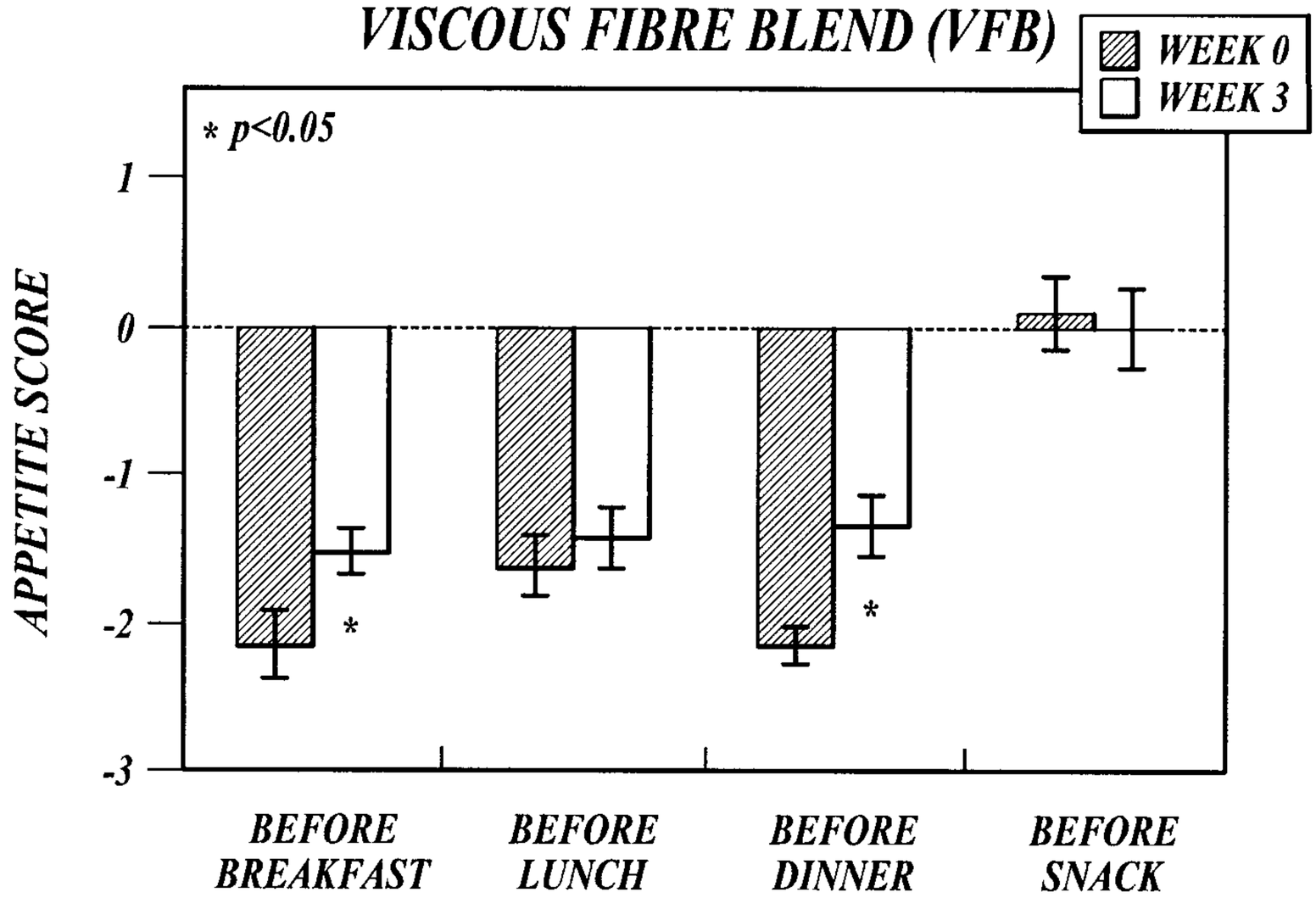

VISCOUS FIBRE BLEND (VFB)
WEEK 0
WEEK 3
* p<0.05
APPETITE SCORE
1
0
-1
-2
-3
*
*
BEFORE BREAKFAST
BEFORE LUNCH
BEFORE DINNER
BEFORE SNACK

Fig.2A.

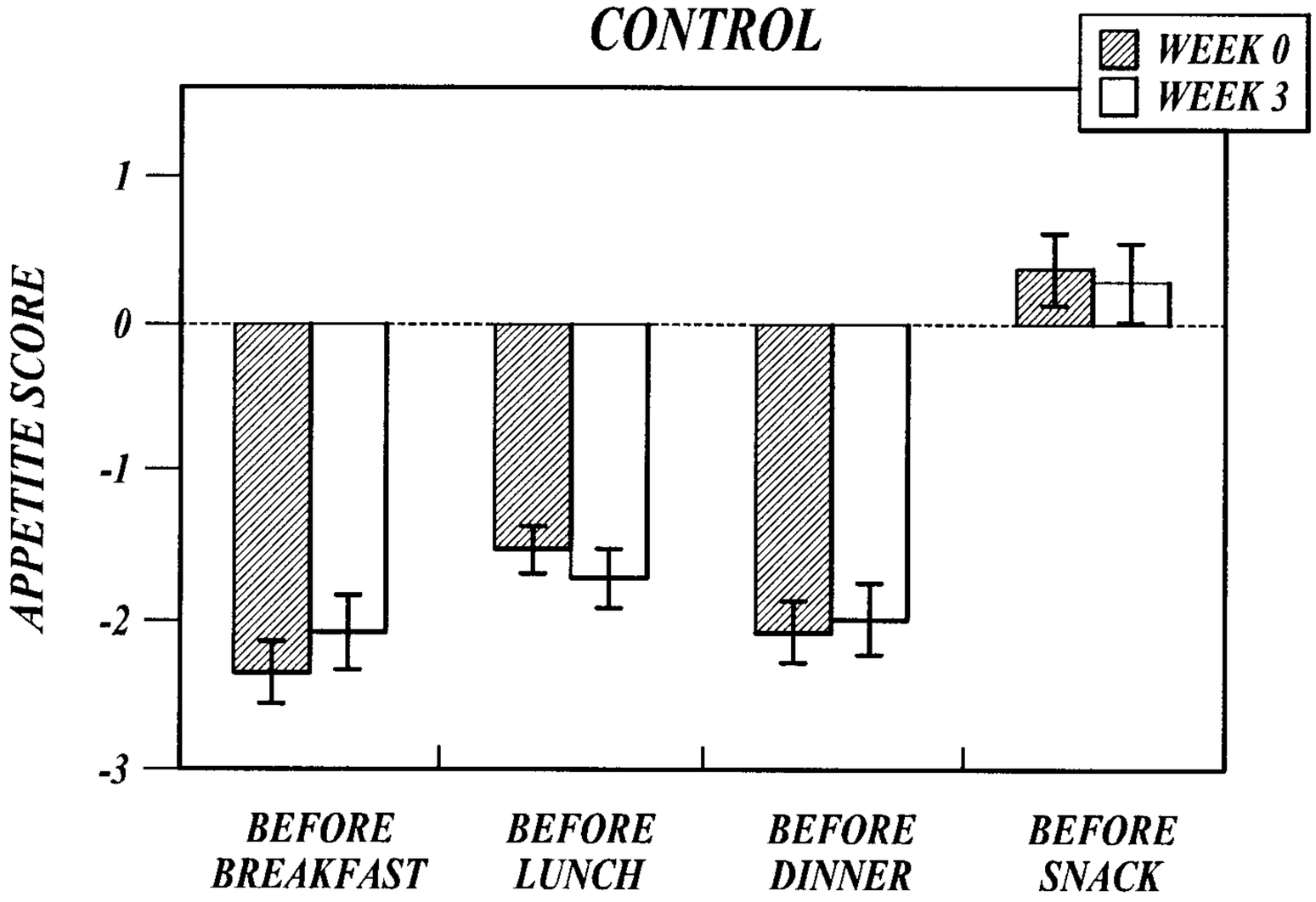

CONTROL
WEEK 0
WEEK 3
APPETITE SCORE
1
0
-1
-2
-3
BEFORE BREAKFAST
BEFORE LUNCH
BEFORE DINNER
BEFORE SNACK

Fig.2B.

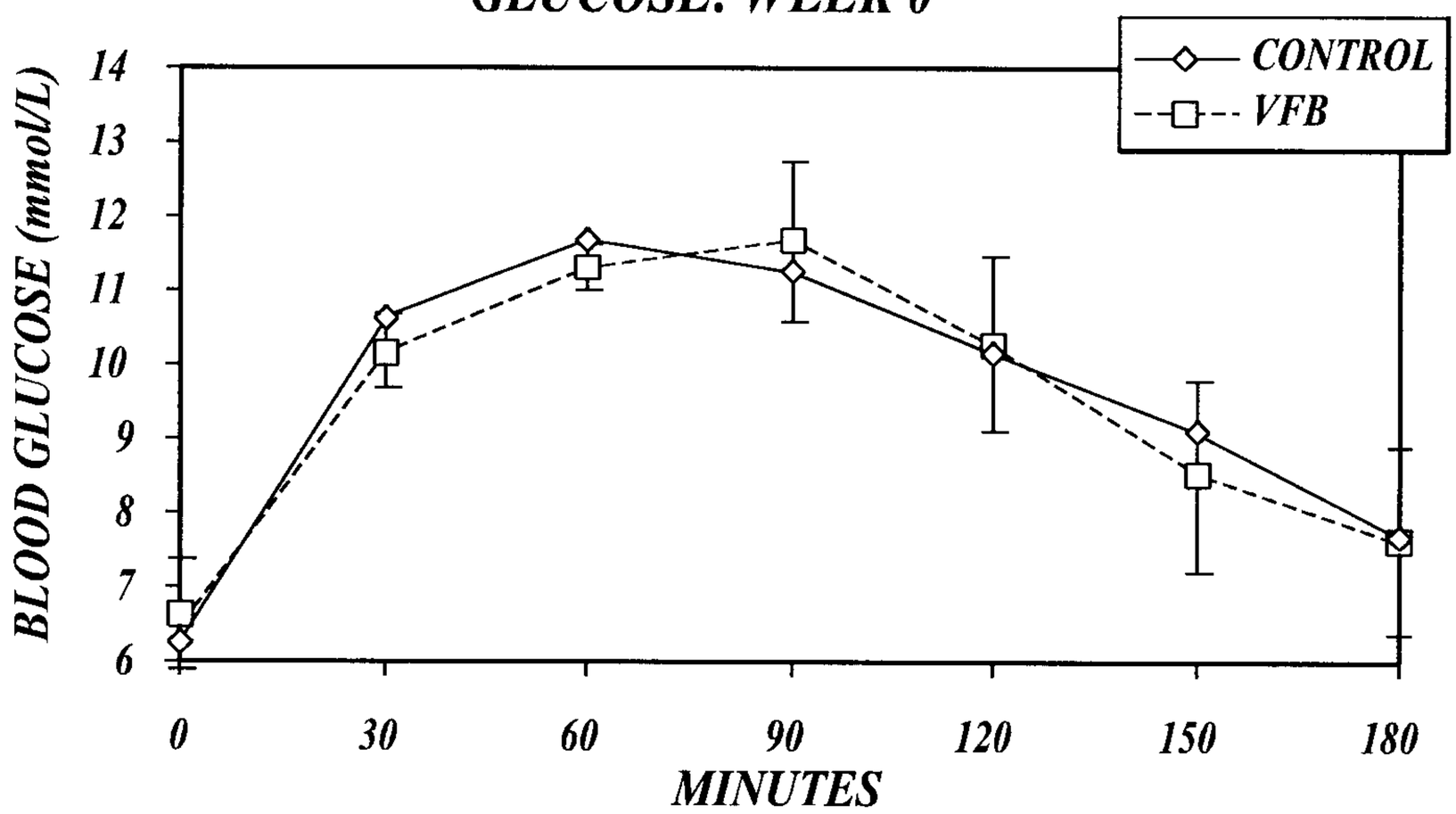

GLUCOSE: WEEK 0
CONTROL
VFB
BLOOD GLUCOSE (mmol/L)
14
13
12
11
10
9
8
7
6
0
30
60
90
120
150
180
MINUTES

Fig.3A.

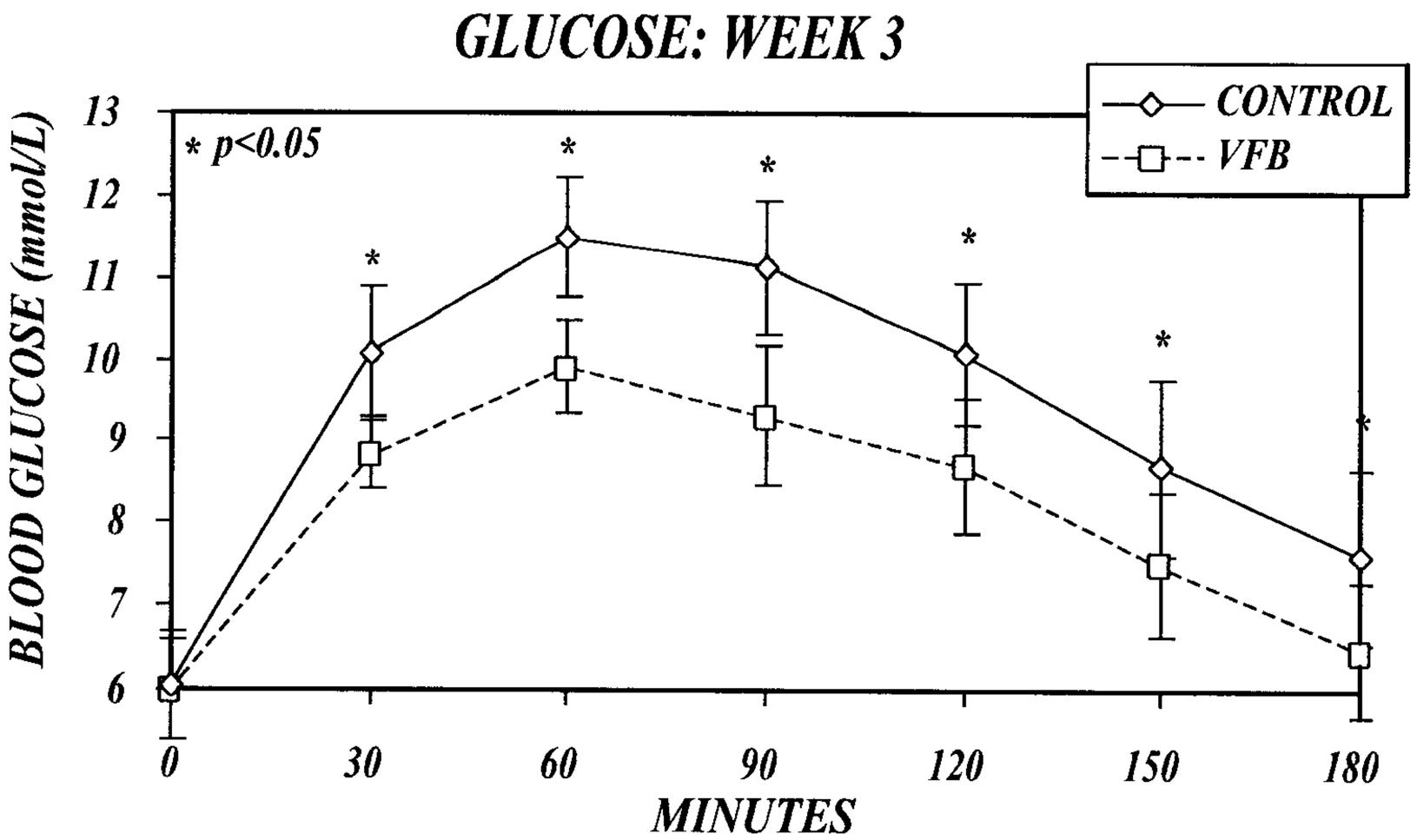

GLUCOSE: WEEK 3
* p<0.05
CONTROL
VFB
BLOOD GLUCOSE (mmol/L)
13
12
11
10
9
8
7
6
0
30
60
90
120
150
180
MINUTES

Fig.3B.

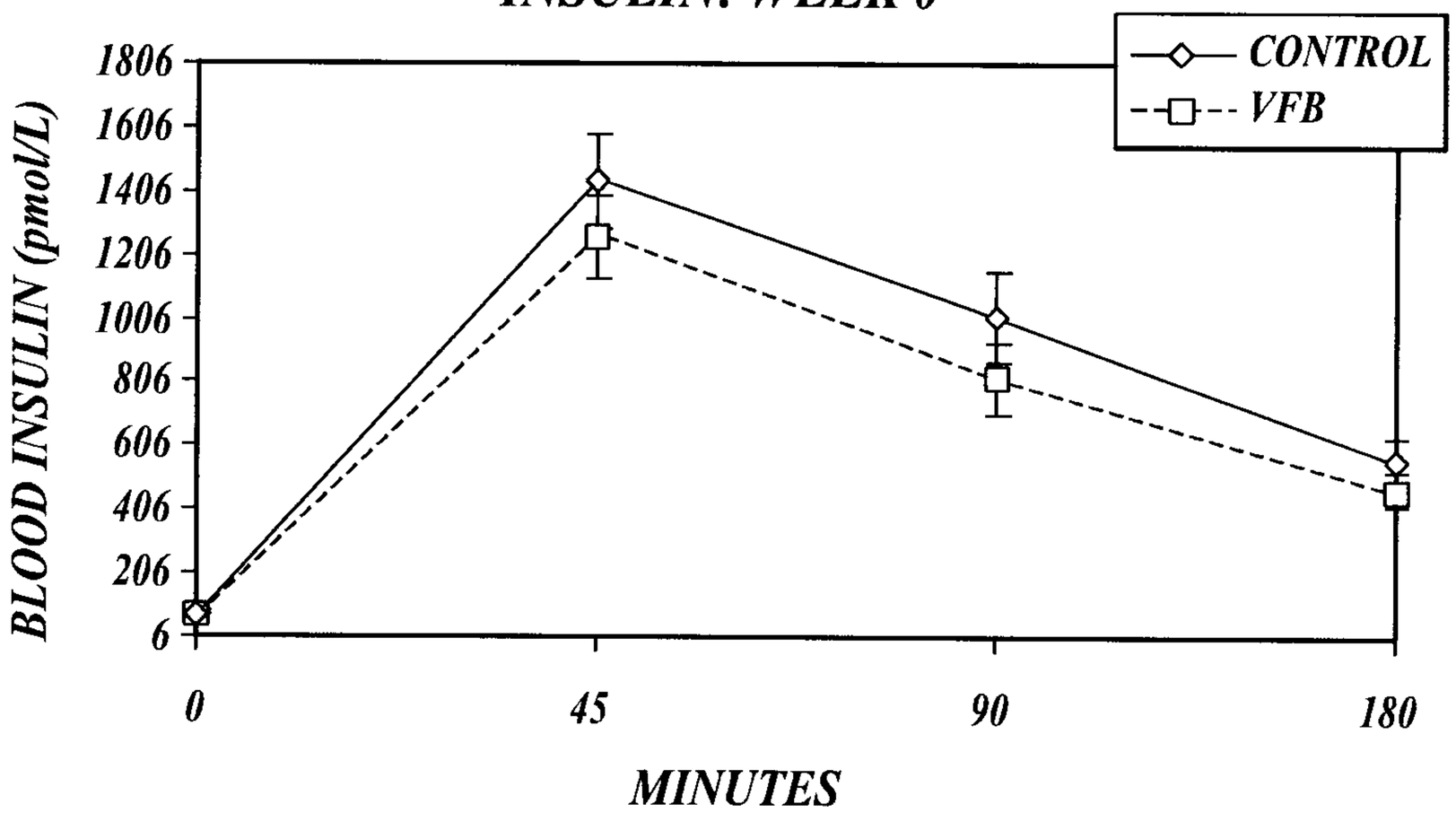

INSULIN: WEEK 0
CONTROL
VFB
BLOOD INSULIN (pmol/L)
1806
1606
1406
1206
1006
806
606
406
206
6
0
45
90
180
MINUTES

Fig.3C.

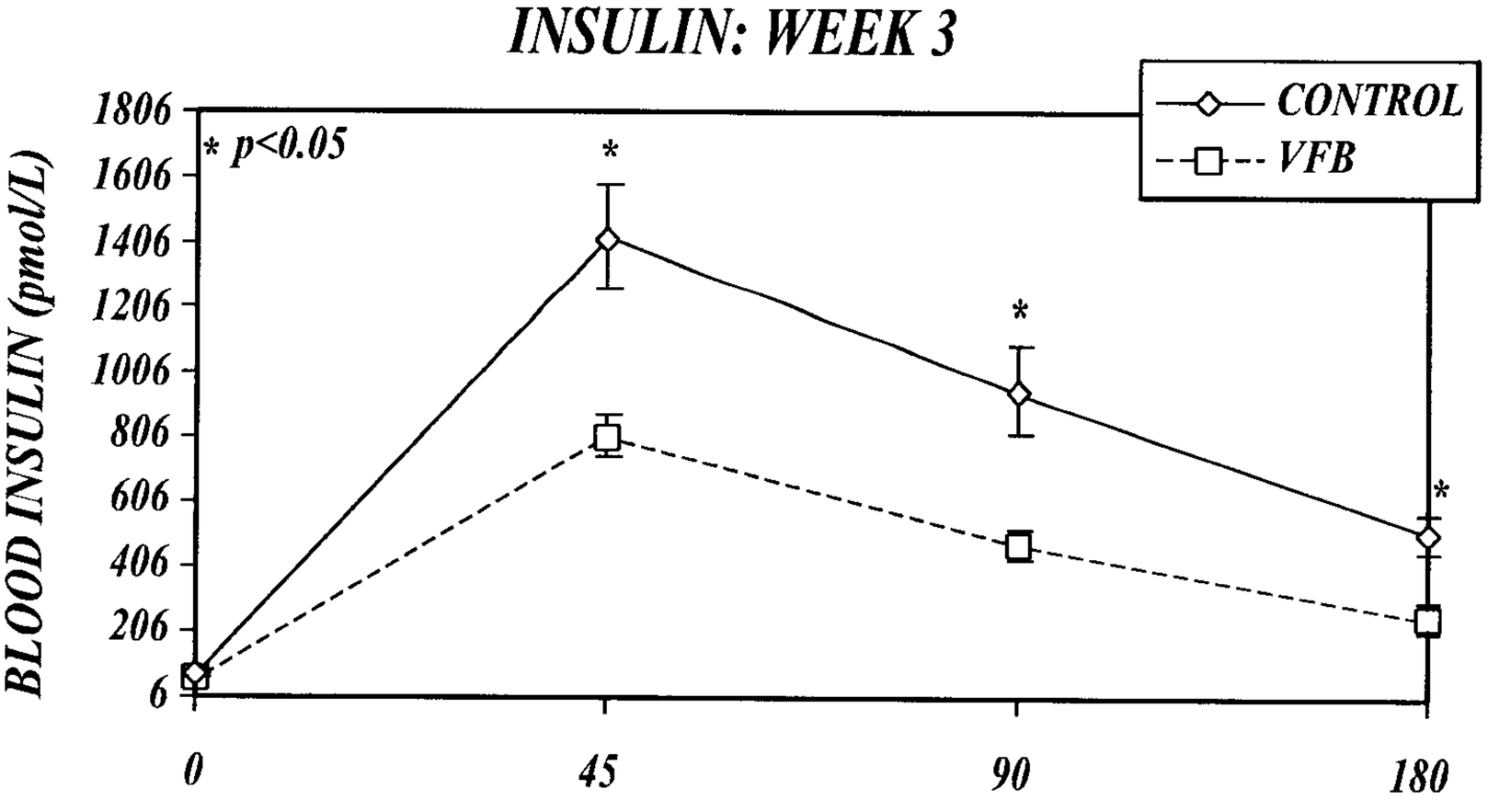

INSULIN: WEEK 3
CONTROL
VFB
* p<0.05
BLOOD INSULIN (pmol/L)
1806
1606
1406
1206
1006
806
606
406
206
6
0
45
90
180
MINUTES

Fig.3D.

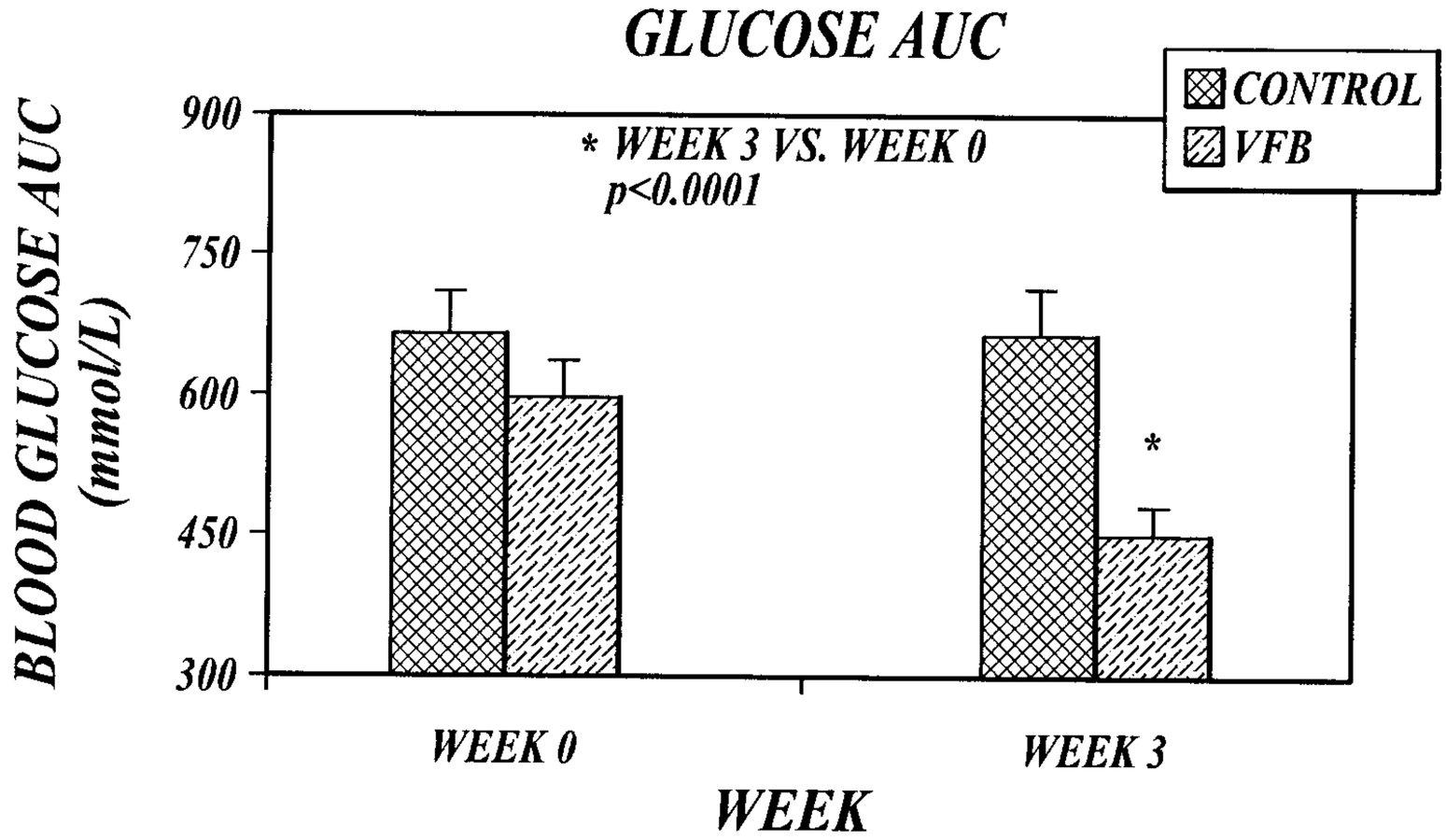

GLUCOSE AUC
CONTROL
VFB
* WEEK 3 VS. WEEK 0
p<0.0001
BLOOD GLUCOSE AUC
(mmol/L)
900
750
600
450
300
*
WEEK 0
WEEK 3
WEEK

Fig.4.

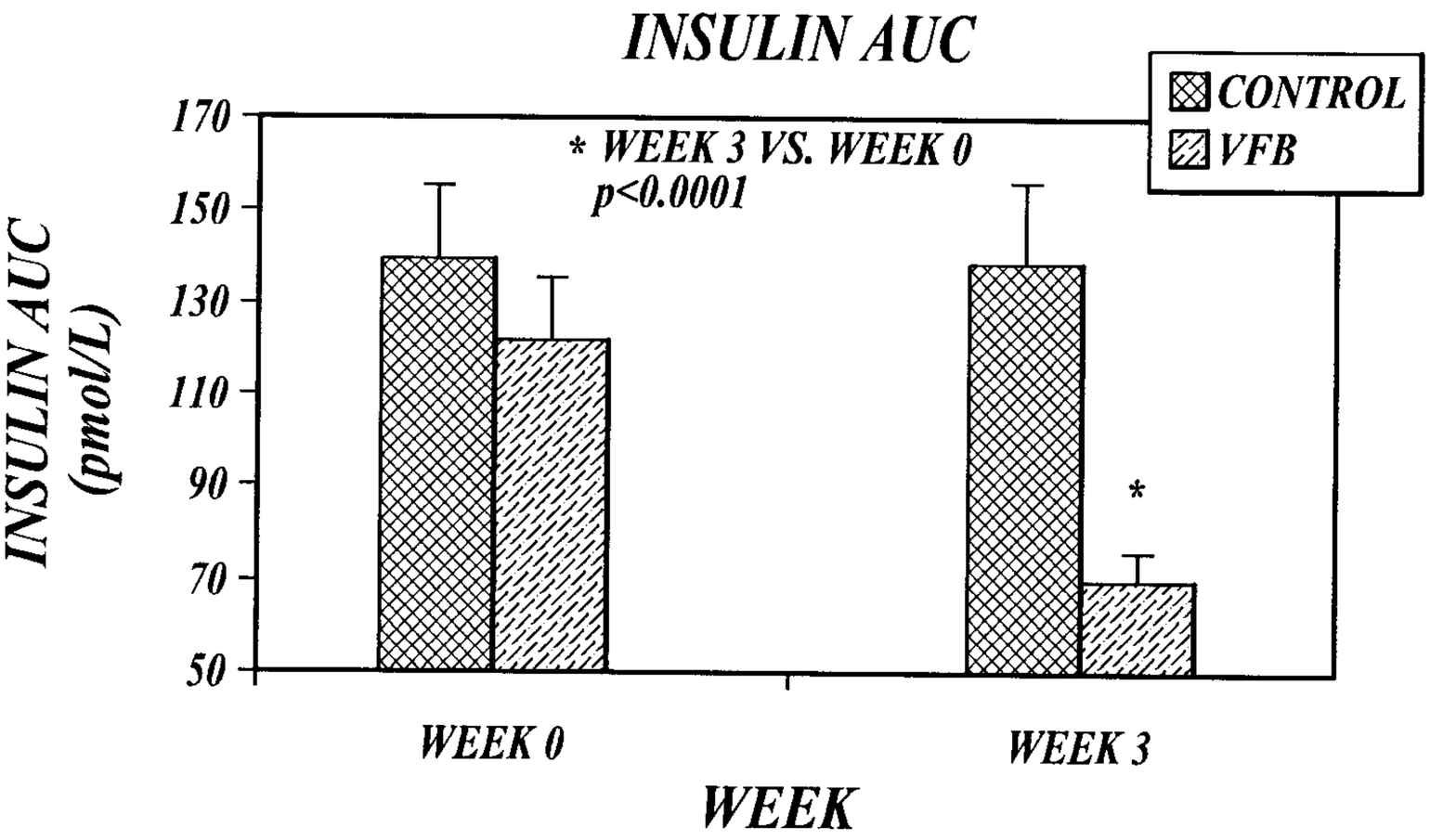

INSULIN AUC
CONTROL
VFB
* WEEK 3 VS. WEEK 0
p<0.0001
INSULIN AUC
(pmol/L)
170
150
130
110
90
70
50
*
WEEK 0
WEEK 3
WEEK

Fig.5.

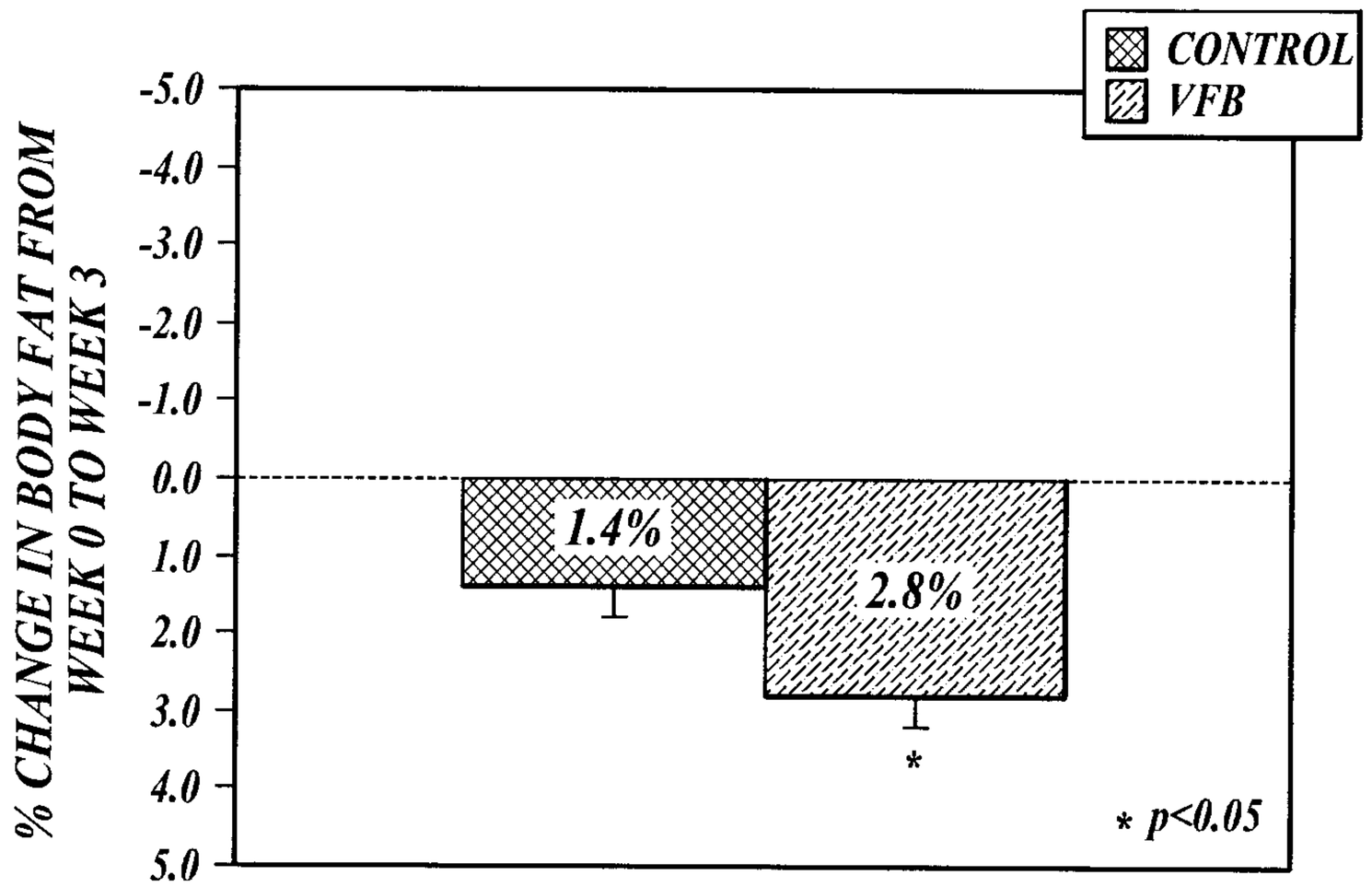

CONTROL
VFB
% CHANGE IN BODY FAT FROM WEEK 0 TO WEEK 3
-5.0
-4.0
-3.0
-2.0
-1.0
0.0
1.0
2.0
3.0
4.0
5.0
1.4%
2.8%
*
* p<0.05

Fig. 6.

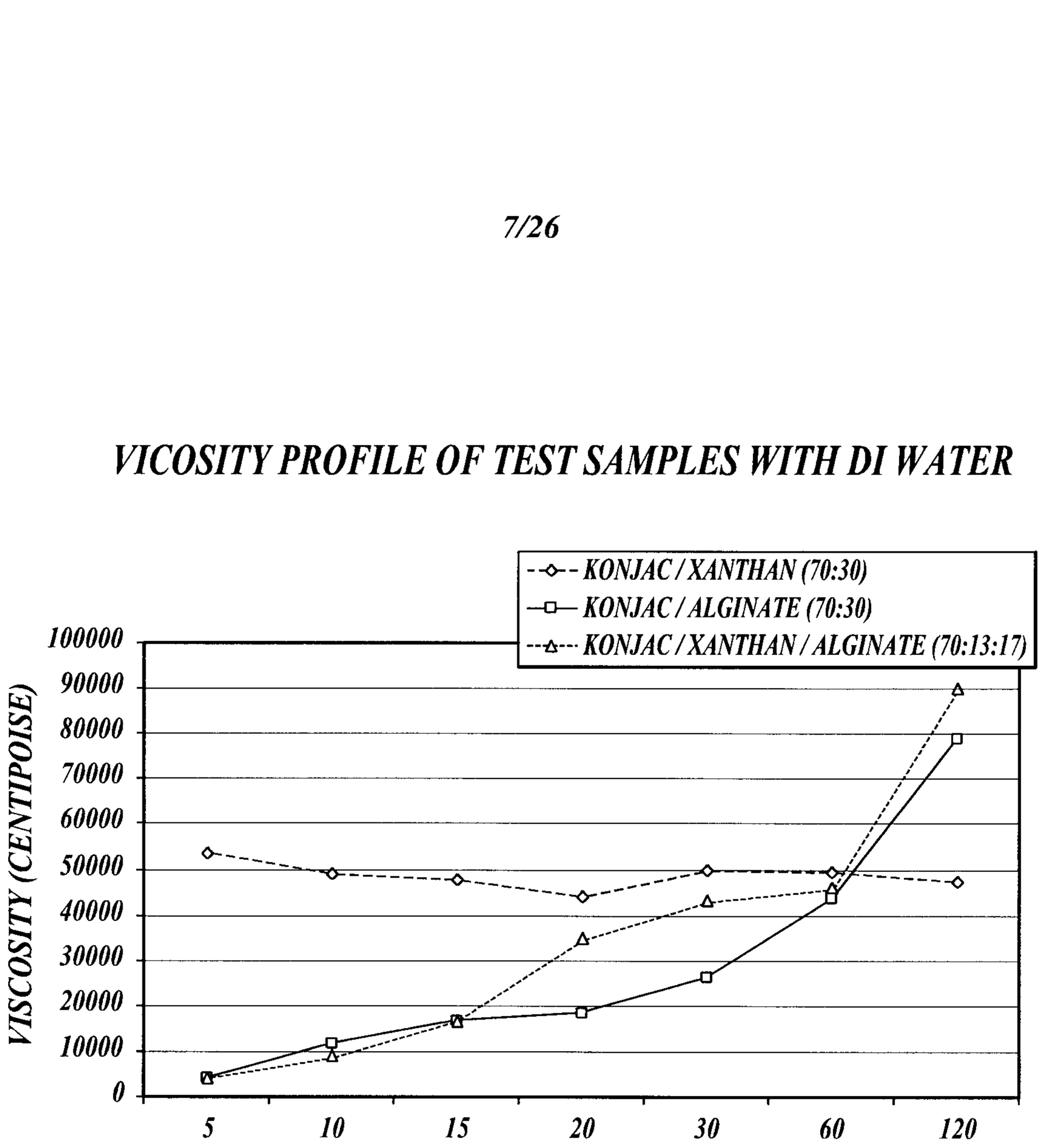

VICOSITY PROFILE OF TEST SAMPLES WITH DI WATER
KONJAC / XANTHAN (70:30)
KONJAC / ALGINATE (70:30)
KONJAC / XANTHAN / ALGINATE (70:13:17)
VISCOSITY (CENTIPOISE)
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
5
10
15
20
30
60
120
TIME (MINUTES)

Fig. 7.

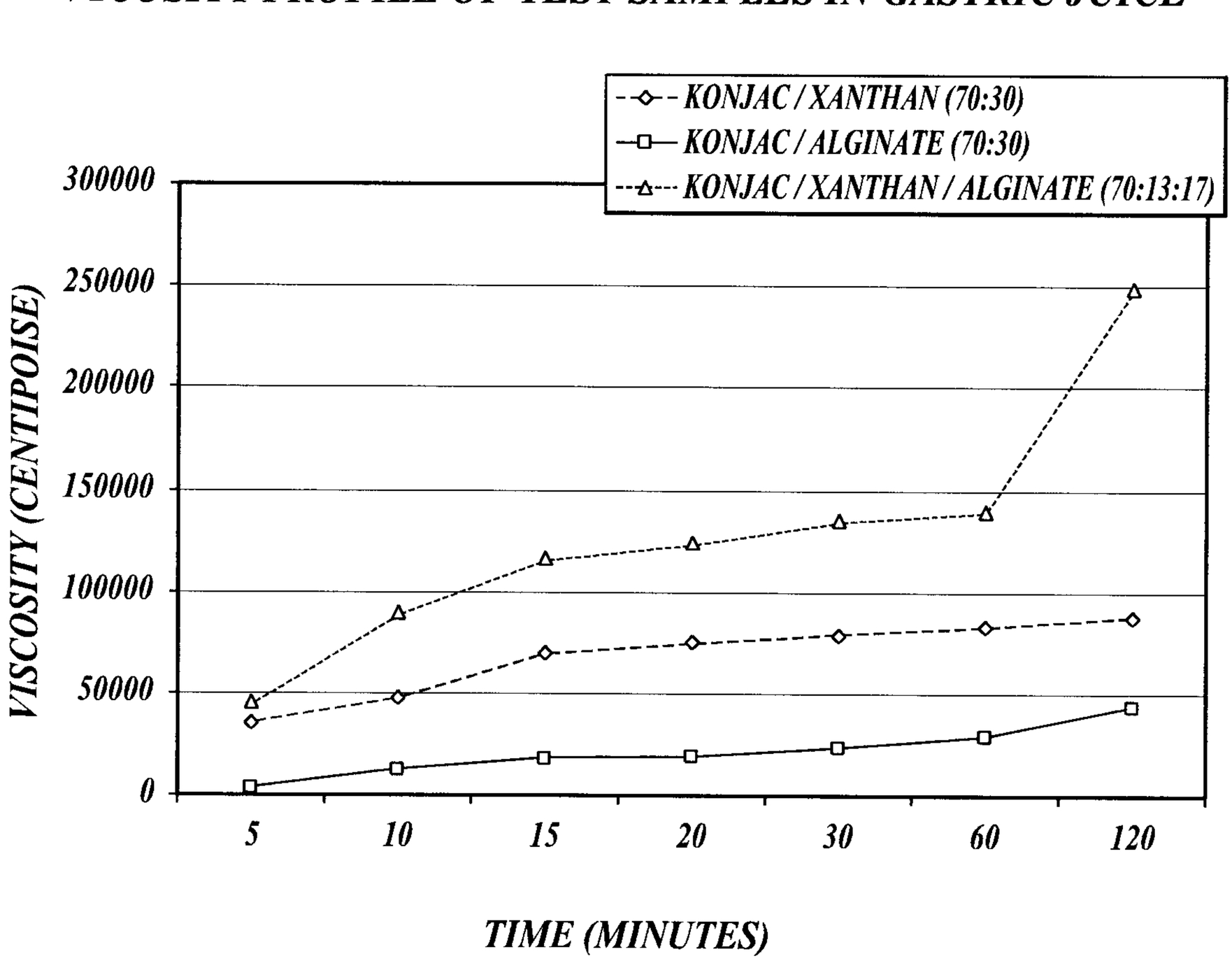

VICOSITY PROFILE OF TEST SAMPLES IN GASTRIC JUICE
KONJAC / XANTHAN (70:30)
KONJAC / ALGINATE (70:30)
KONJAC / XANTHAN / ALGINATE (70:13:17)
VISCOSITY (CENTIPOISE)
300000
250000
200000
150000
100000
50000
0
5
10
15
20
30
60
120
TIME (MINUTES)

Fig. 8.

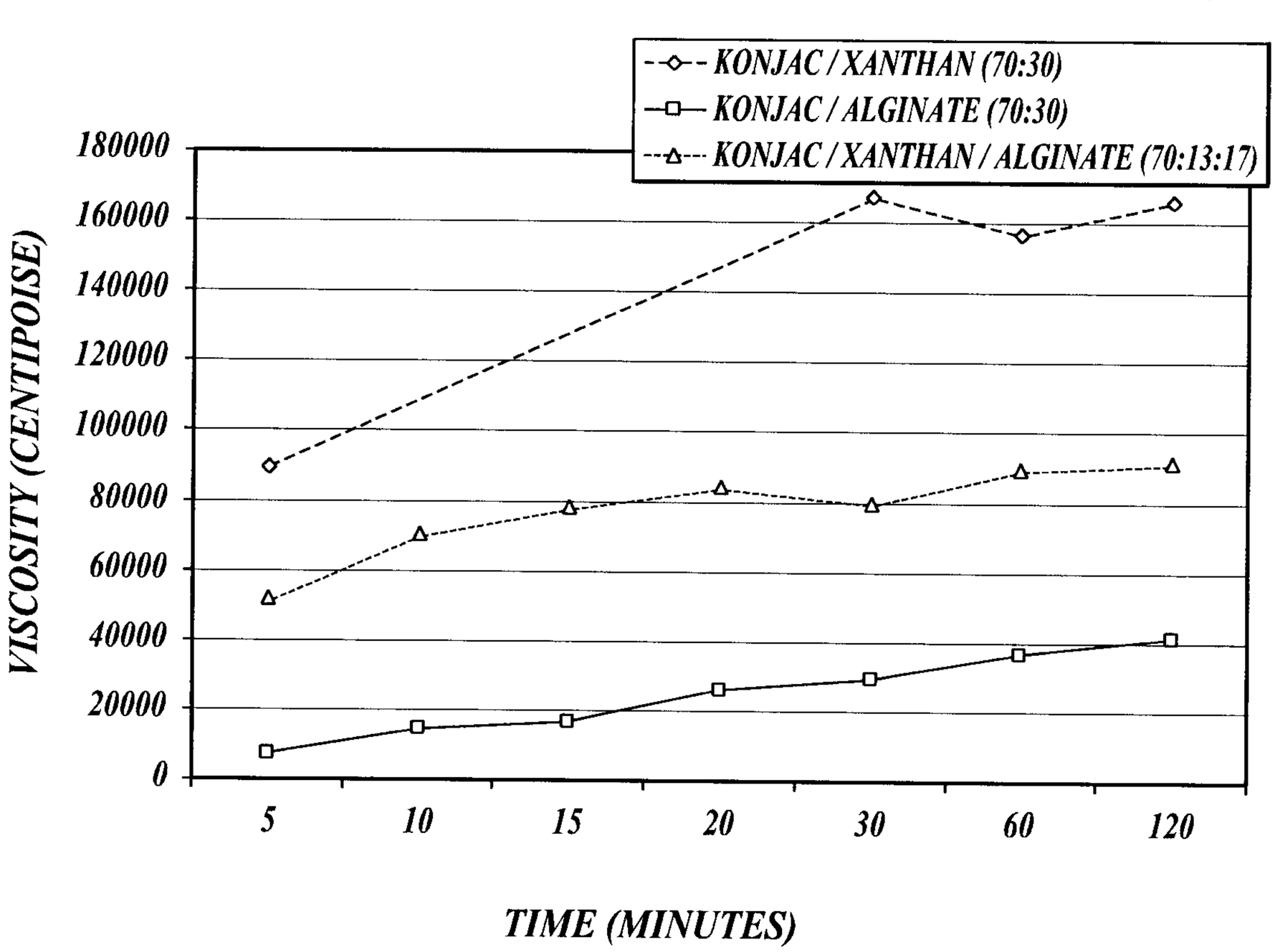

VICOSITY PROFILE OF TEST SAMPLES IN INTESTINAL JUICE
KONJAC / XANTHAN (70:30)
KONJAC / ALGINATE (70:30)
KONJAC / XANTHAN / ALGINATE (70:13:17)
VISCOSITY (CENTIPOISE)
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
5
10
15
20
30
60
120
TIME (MINUTES)

Fig.9.

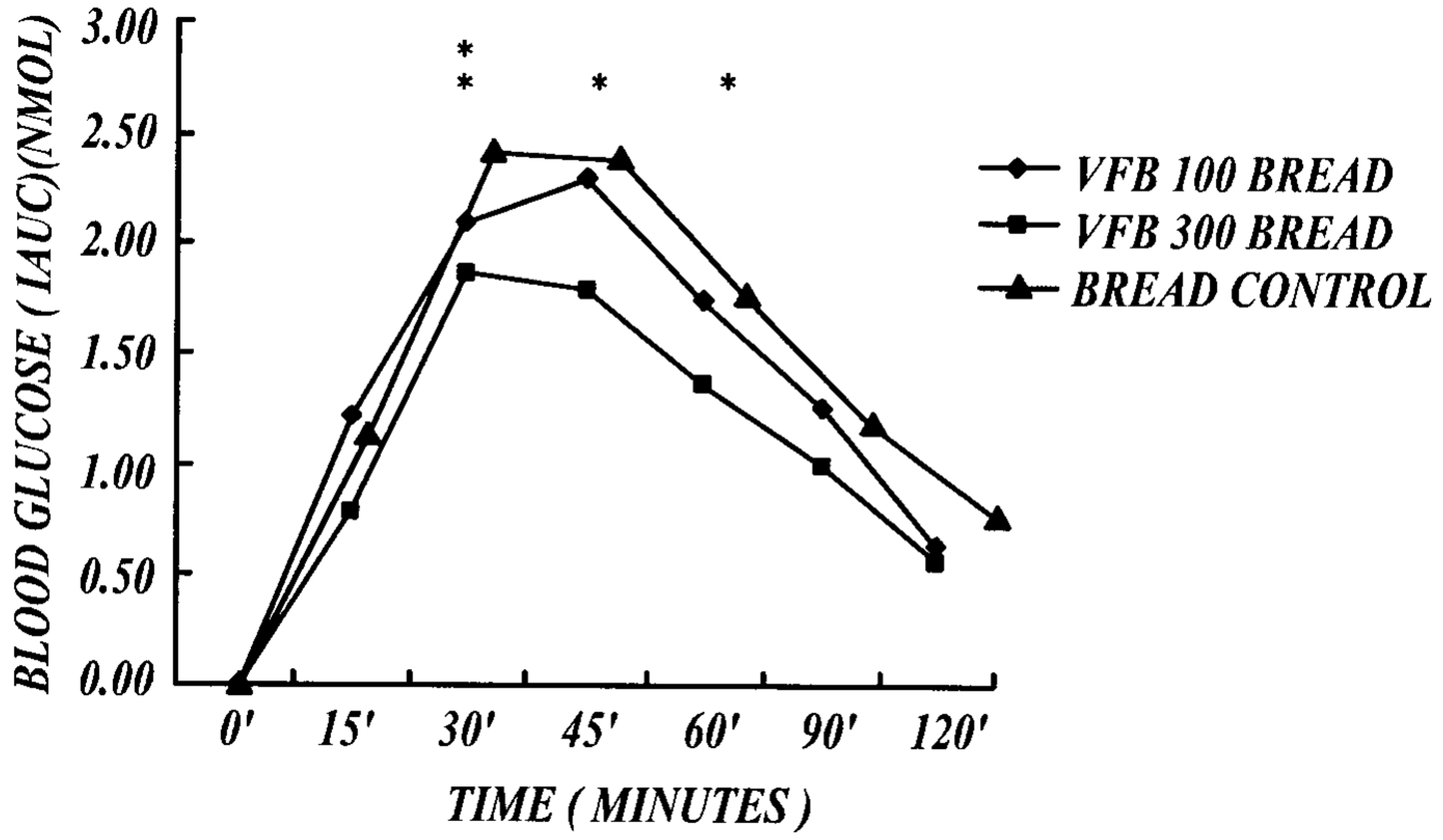


Fig.10A.

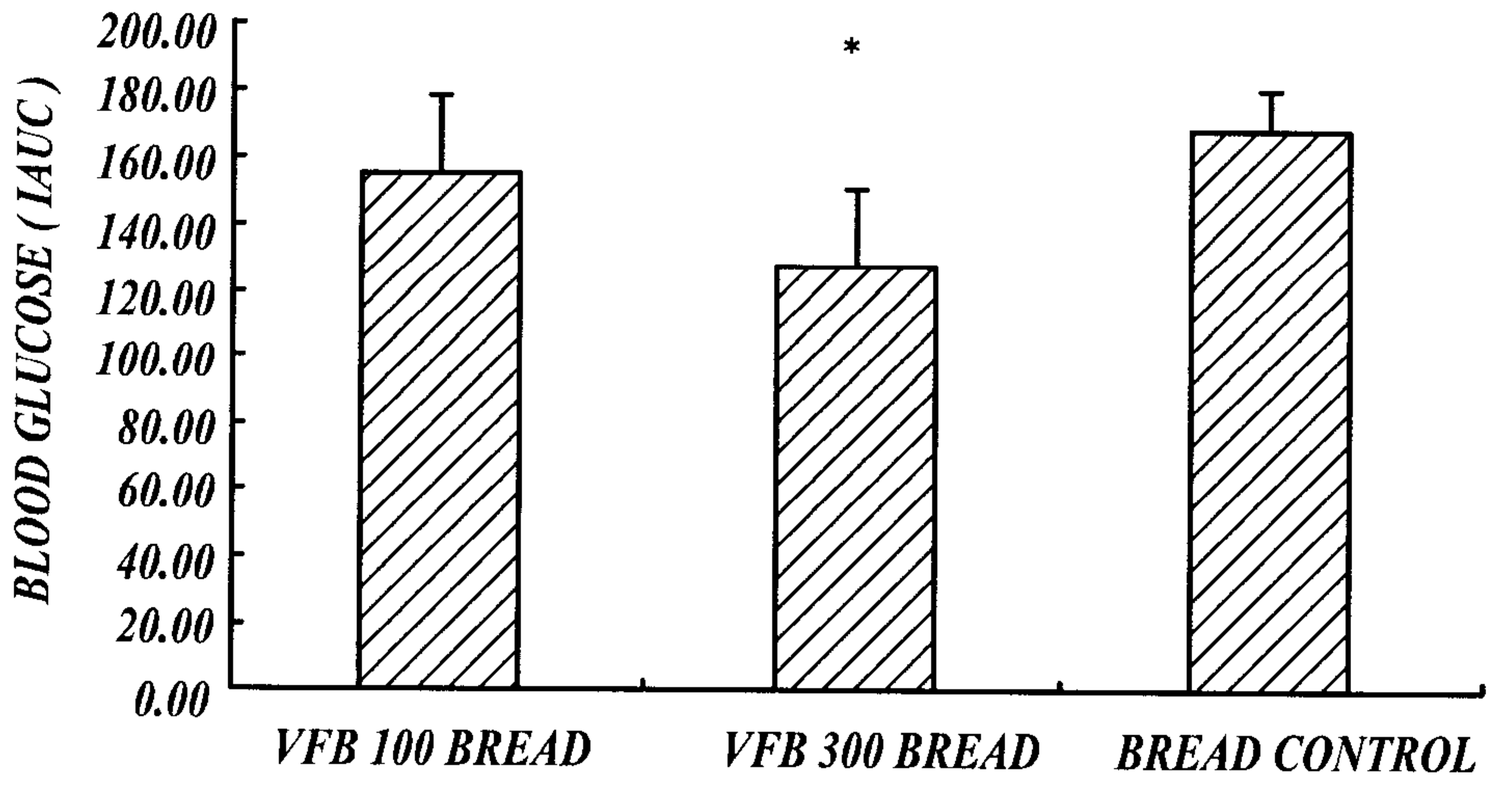


Fig.10B.

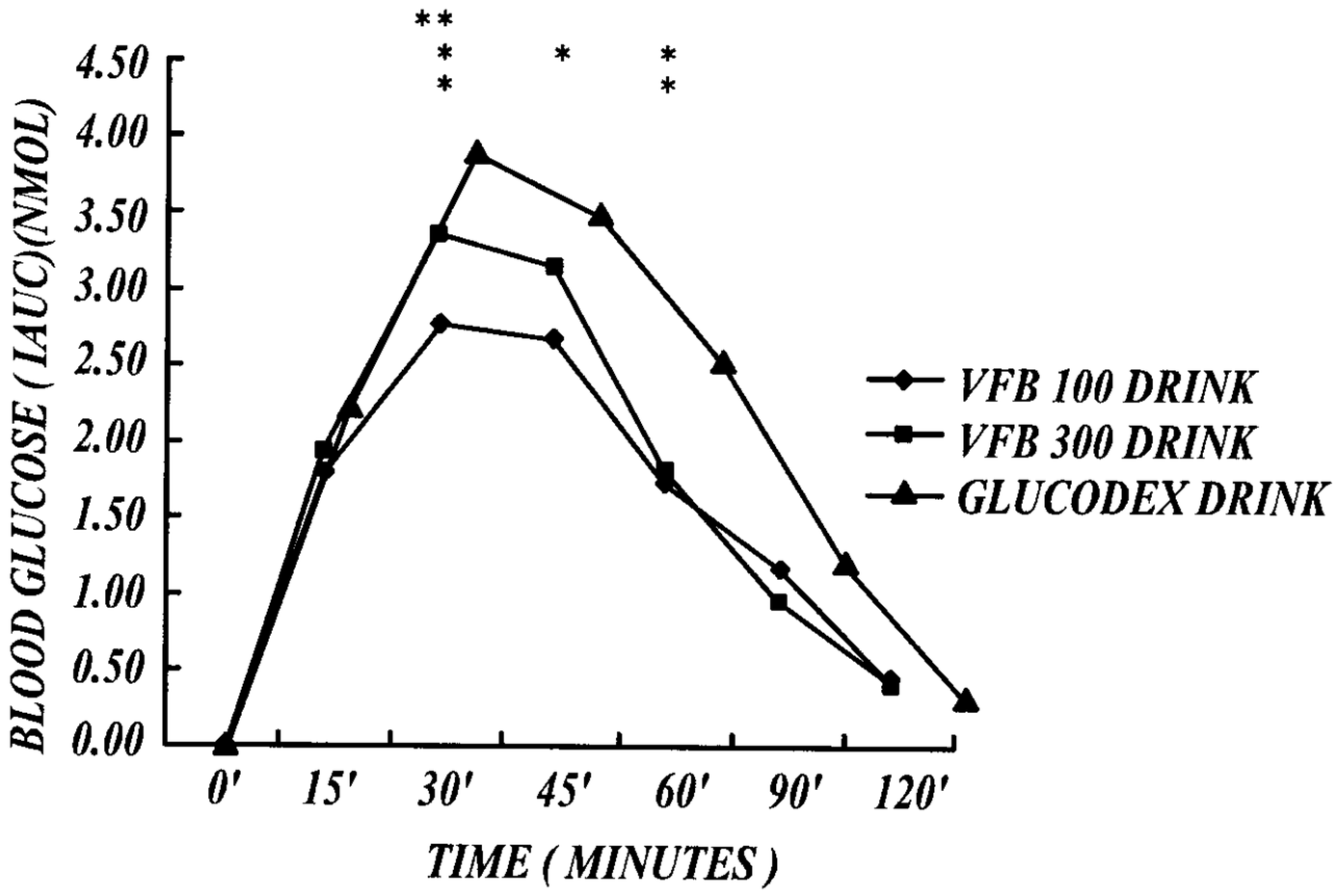


Fig.11A.

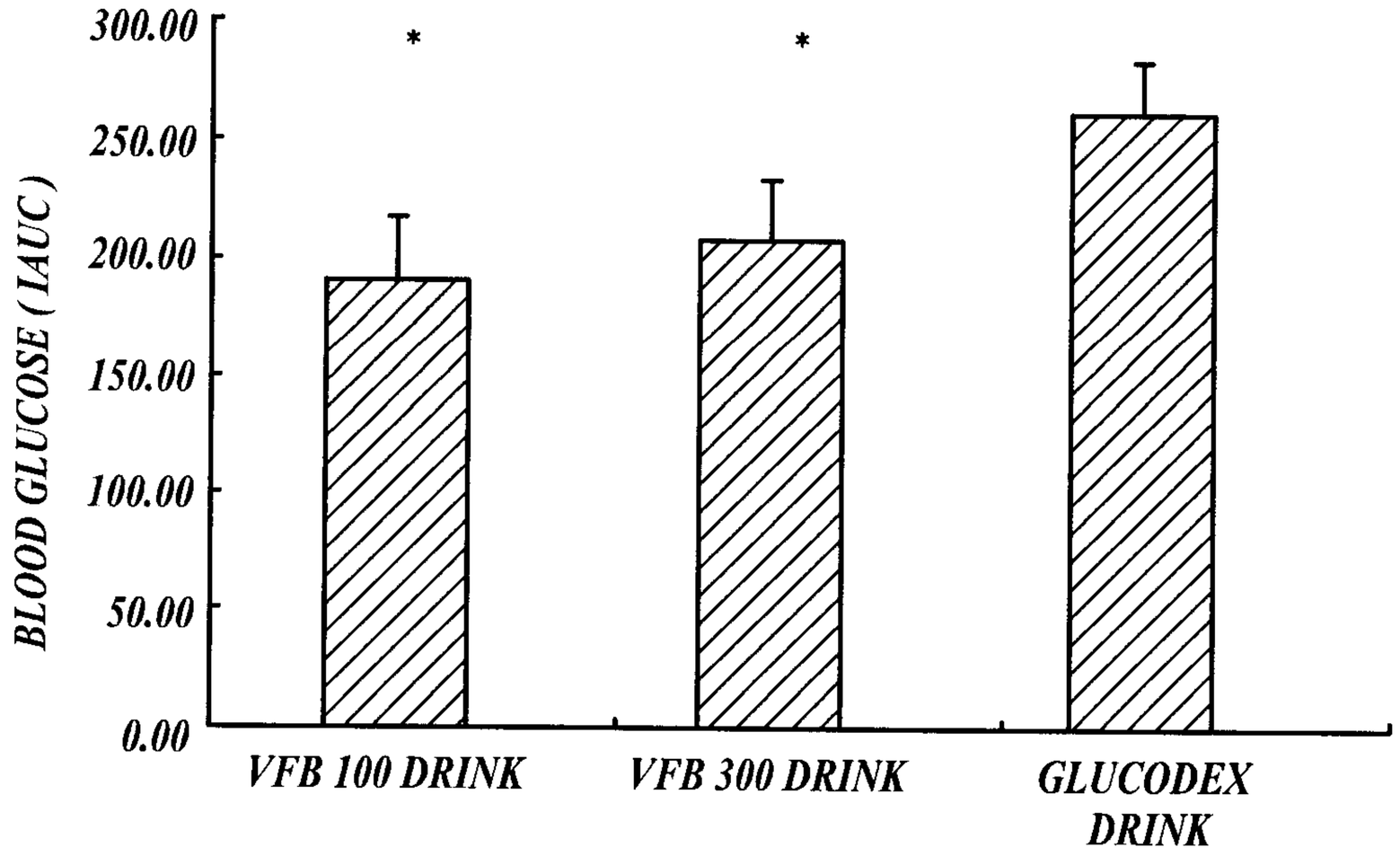


Fig.11B.

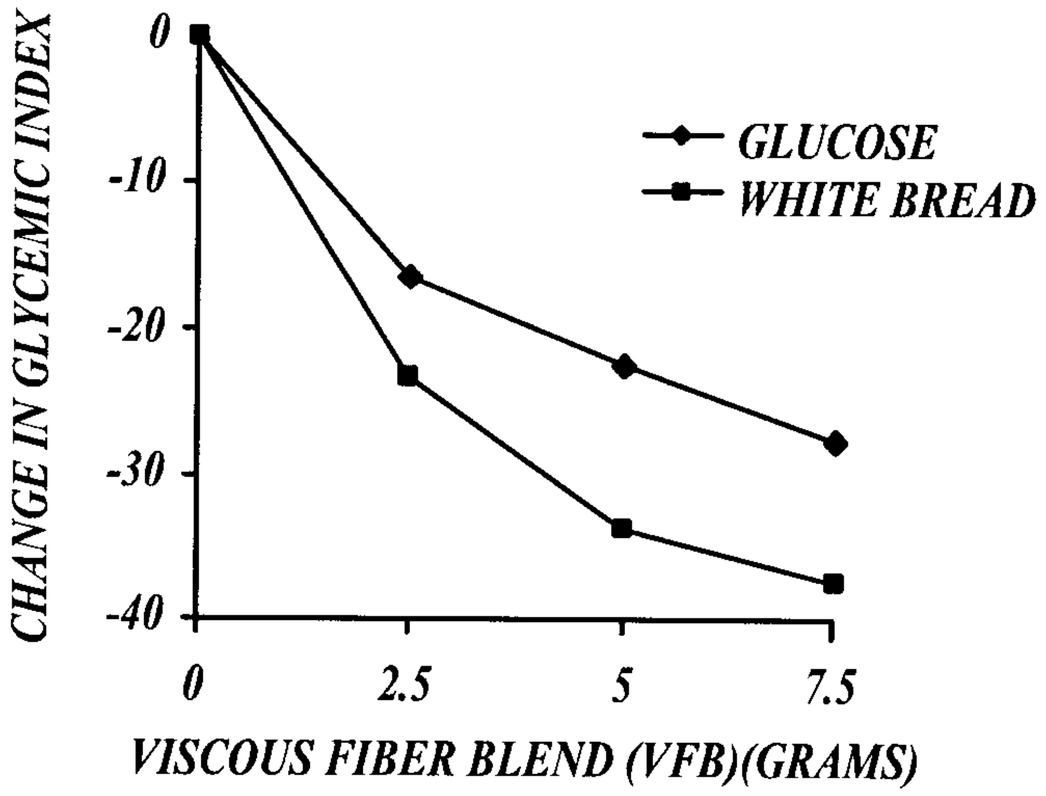

CHANGE IN GLYCEMIC INDEX
0
-10
-20
-30
-40
0
2.5
5
7.5
VISCOUS FIBER BLEND (VFB)(GRAMS)
GLUCOSE
WHITE BREAD

Fig.12.

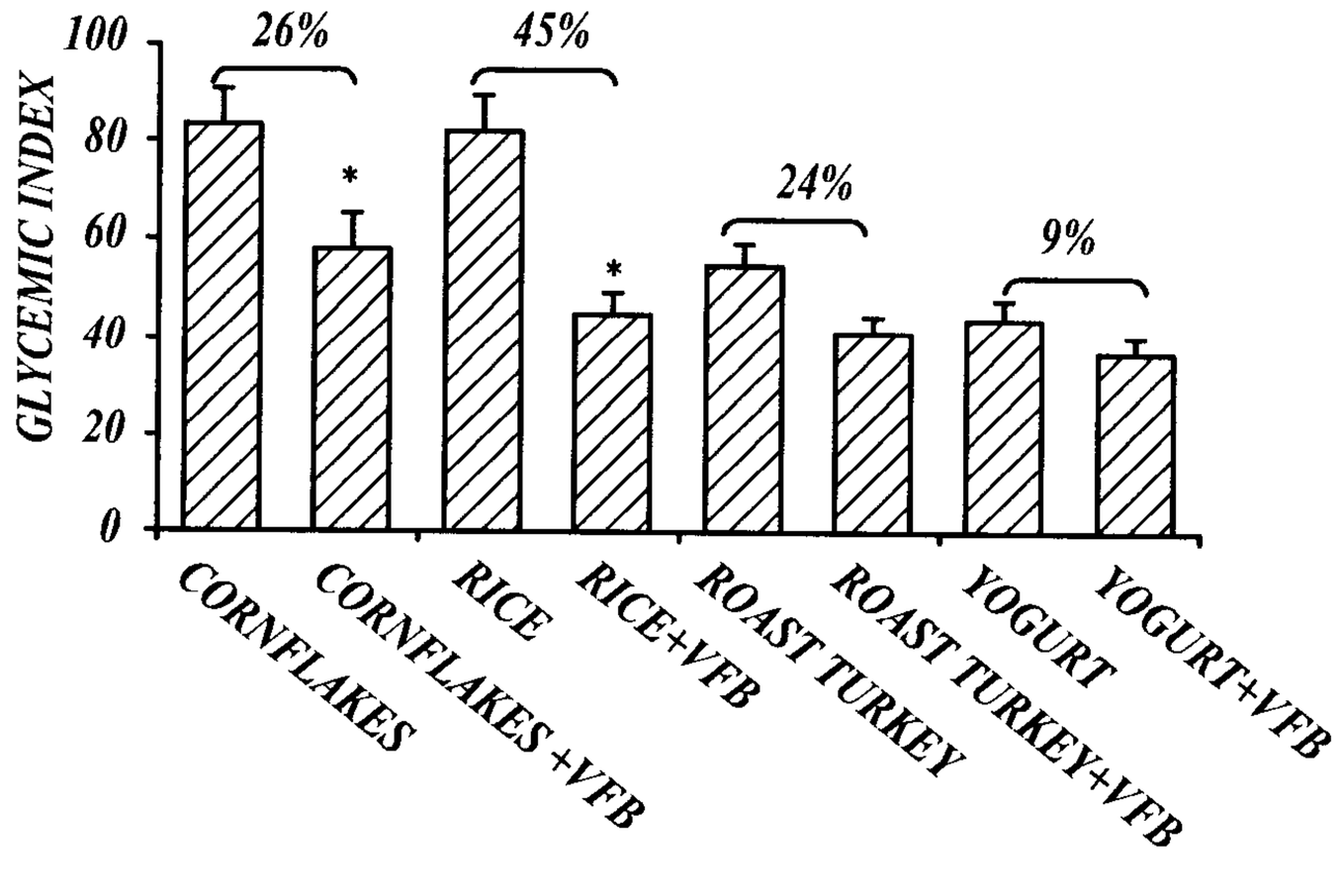

GLYCEMIC INDEX
100
80
60
40
20
0
26%
45%
24%
9%
*
*
CORNFLAKES
CORNFLAKES +VFB
RICE
RICE+VFB
ROAST TURKEY
ROAST TURKEY+VFB
YOGURT
YOGURT+VFB

Fig.13.

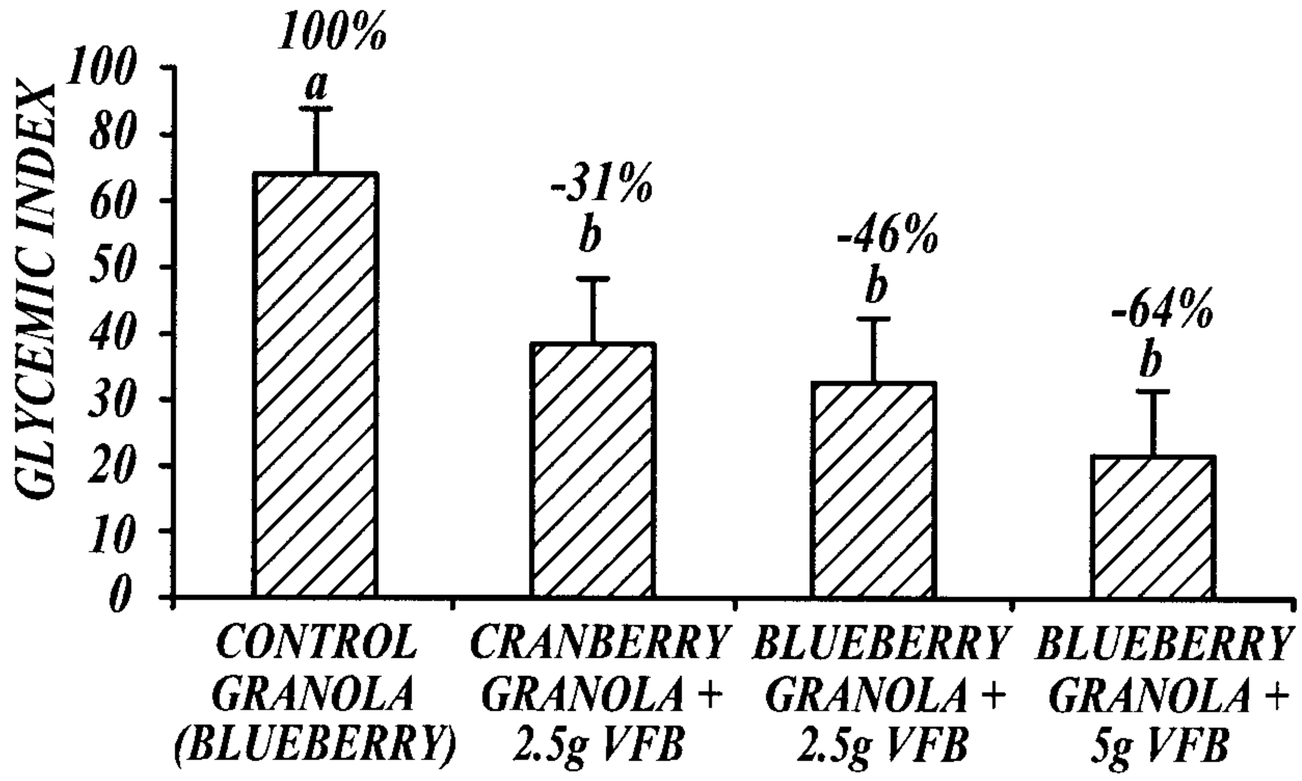

GLYCEMIC INDEX
100
80
60
50
40
30
20
10
0
100%
a
-31%
b
-46%
b
-64%
b
CONTROL GRANOLA (BLUEBERRY)
CRANBERRY GRANOLA + 2.5g VFB
BLUEBERRY GRANOLA + 2.5g VFB
BLUEBERRY GRANOLA + 5g VFB

Fig.14.

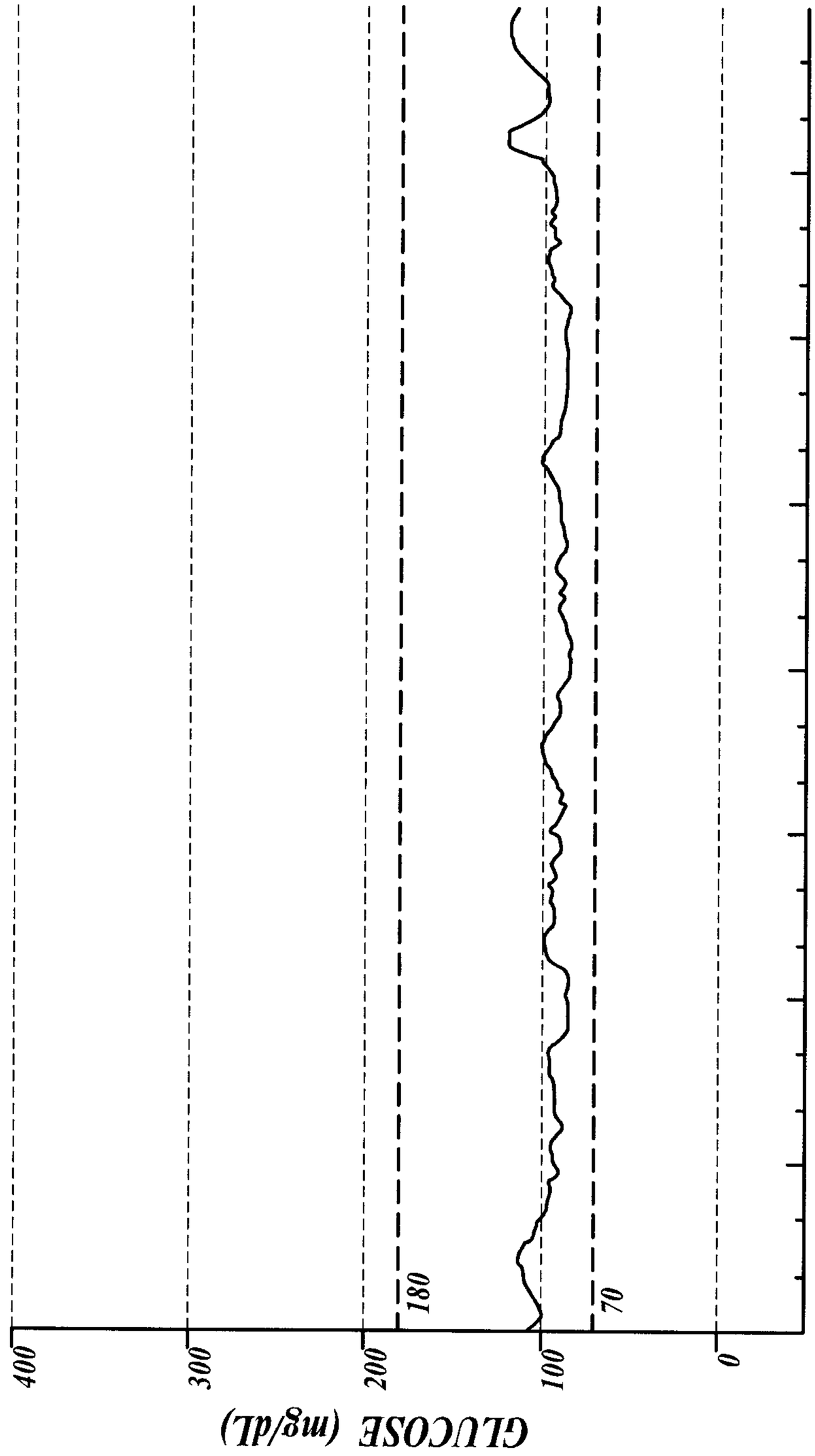

GLUCOSE (mg/dL)
400
300
200
100
0
180
70
3:00 AM
6:00 AM
9:00 AM
12:00 AM
3:00 PM
6:00 PM
9:00 PM
TIME OF DAY

Fig.15.

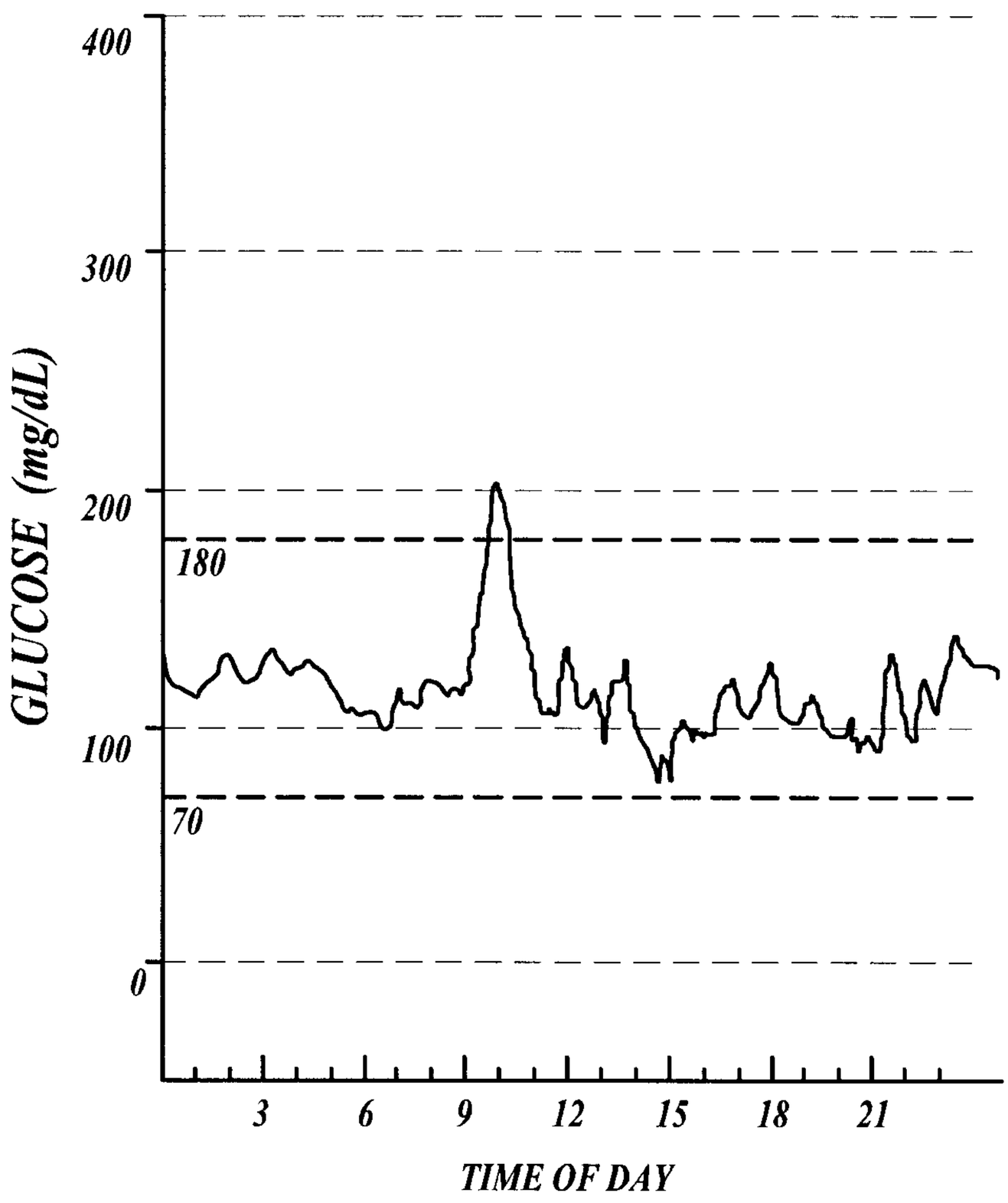


Fig.16A.

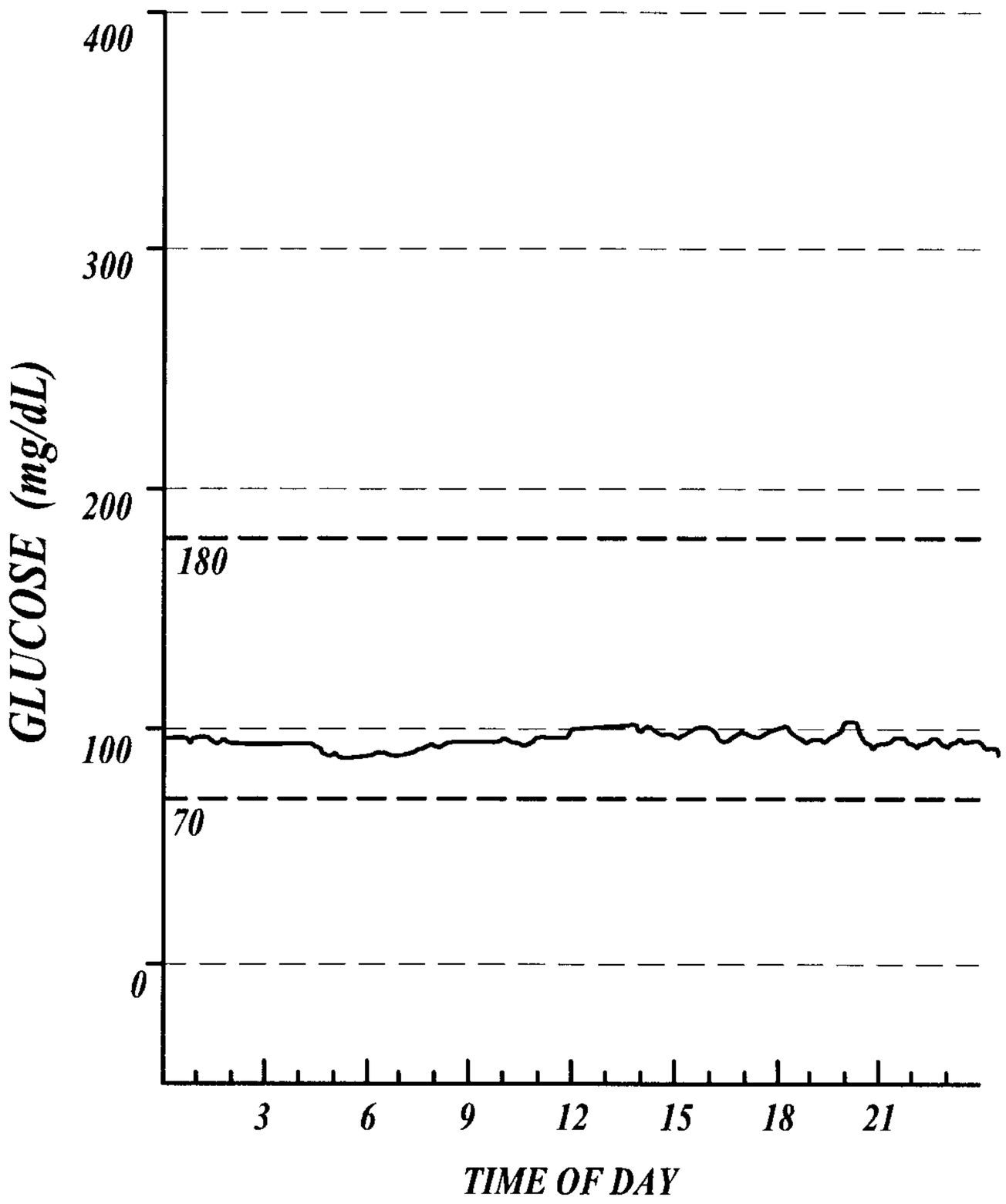


Fig.16B.

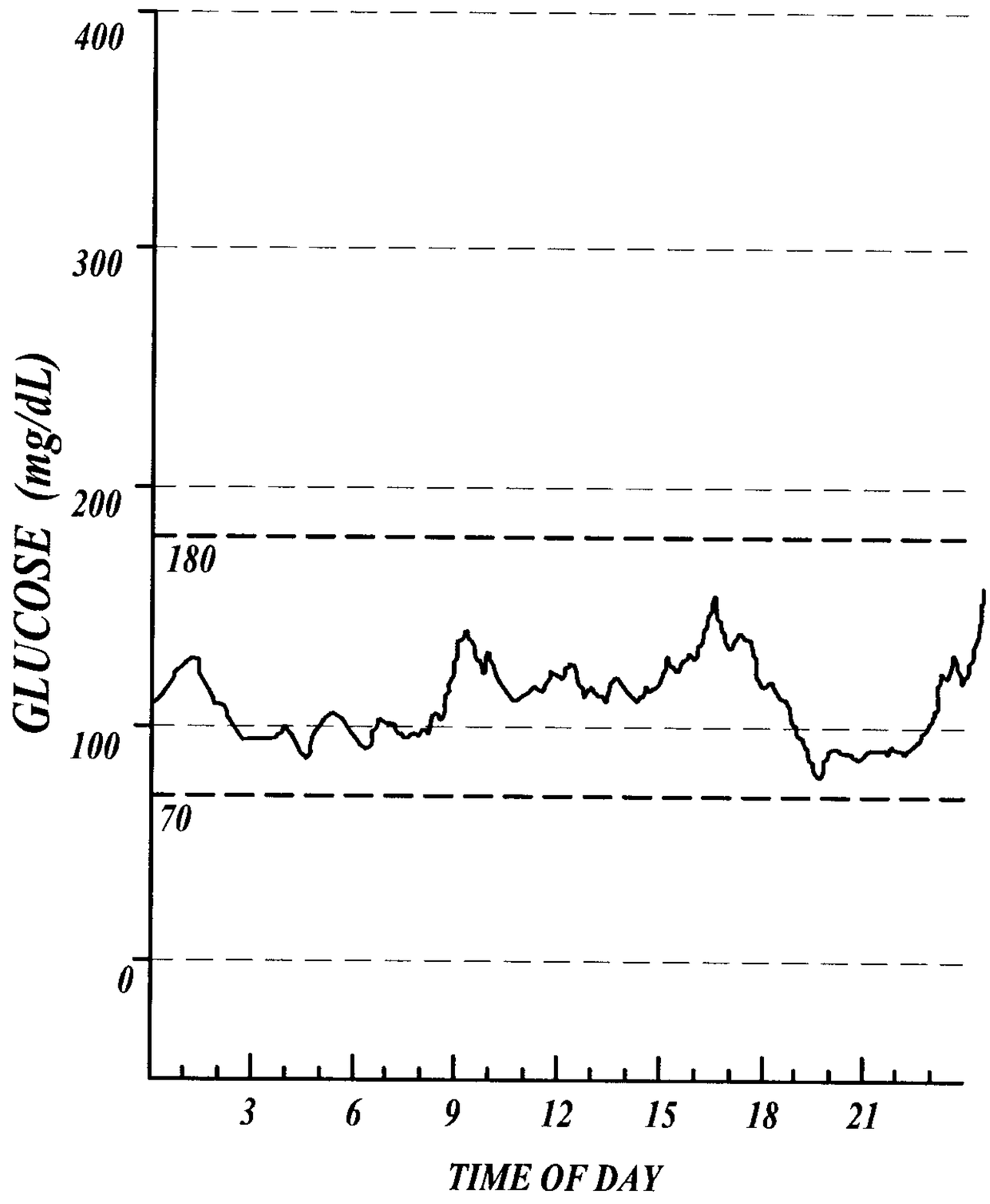


Fig.17A.

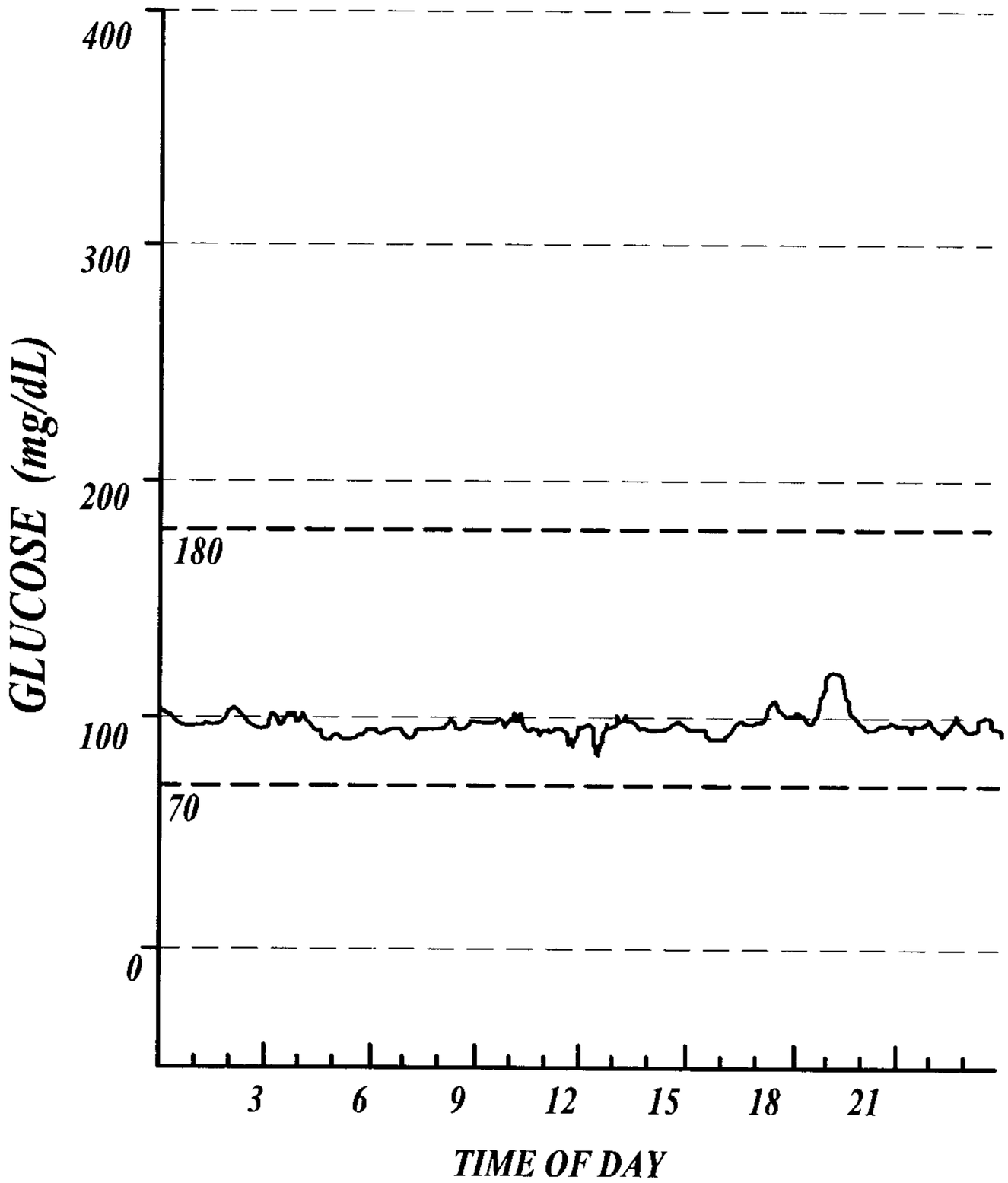


Fig.17B.

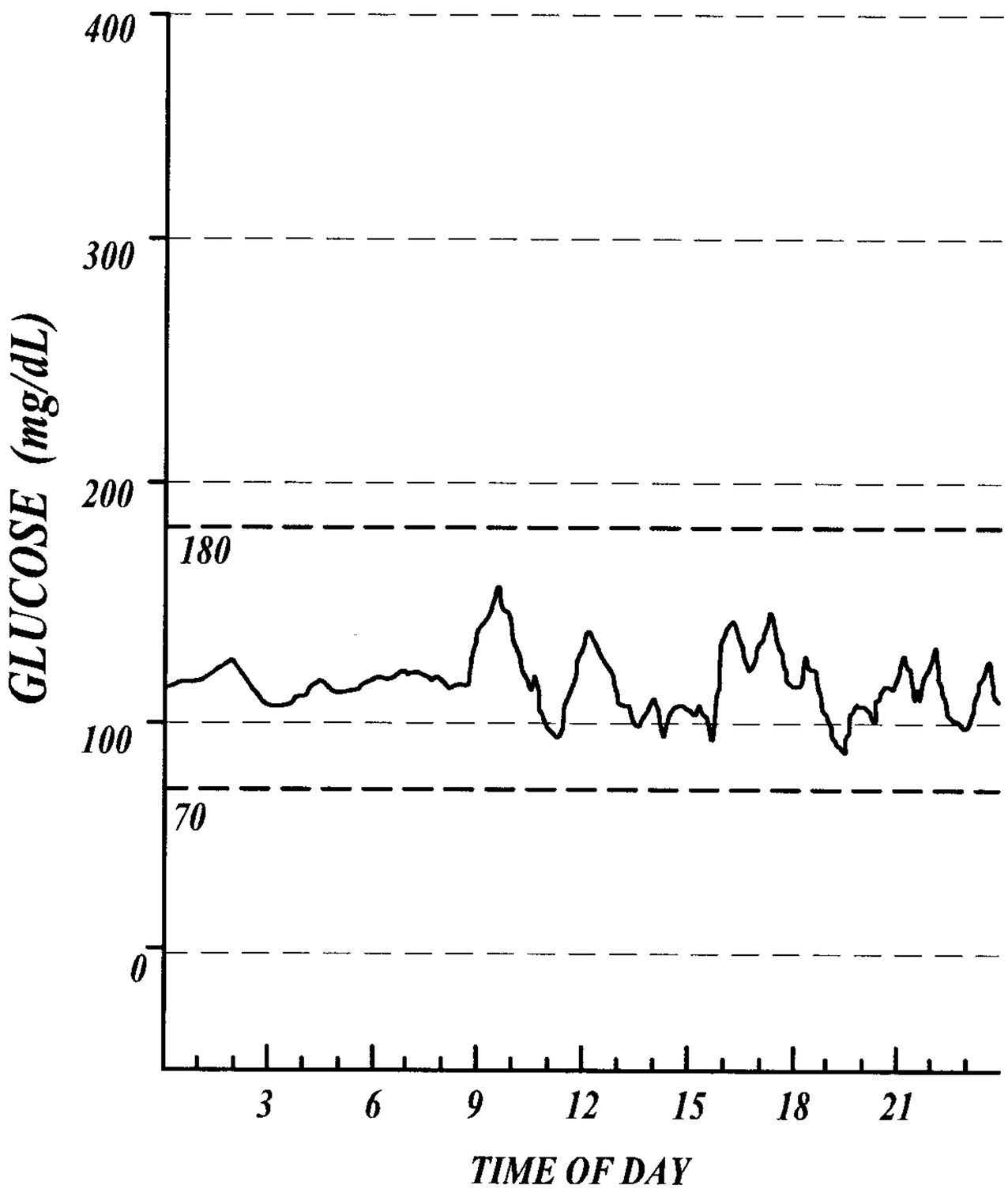


Fig.18A.

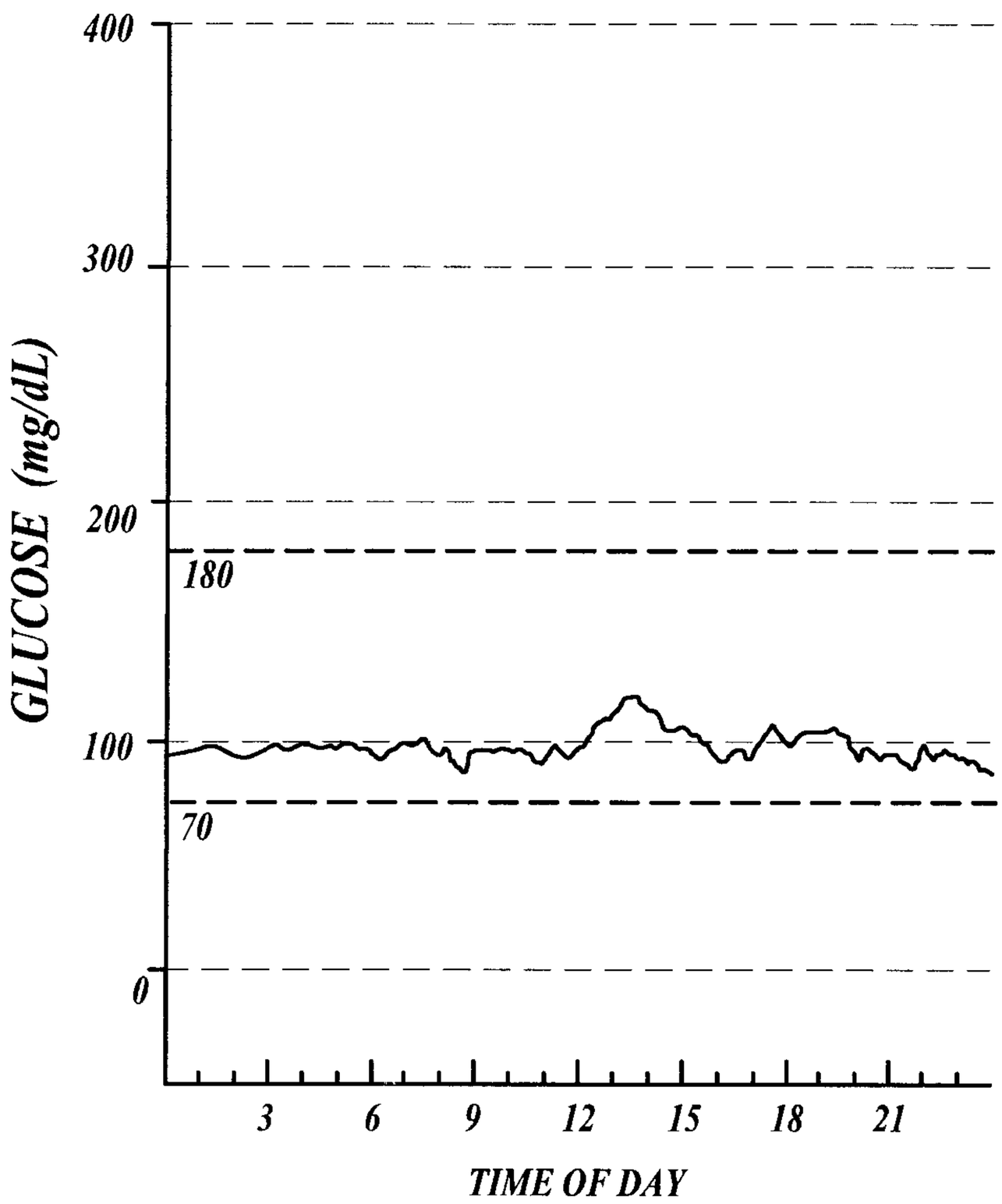


Fig.18B.

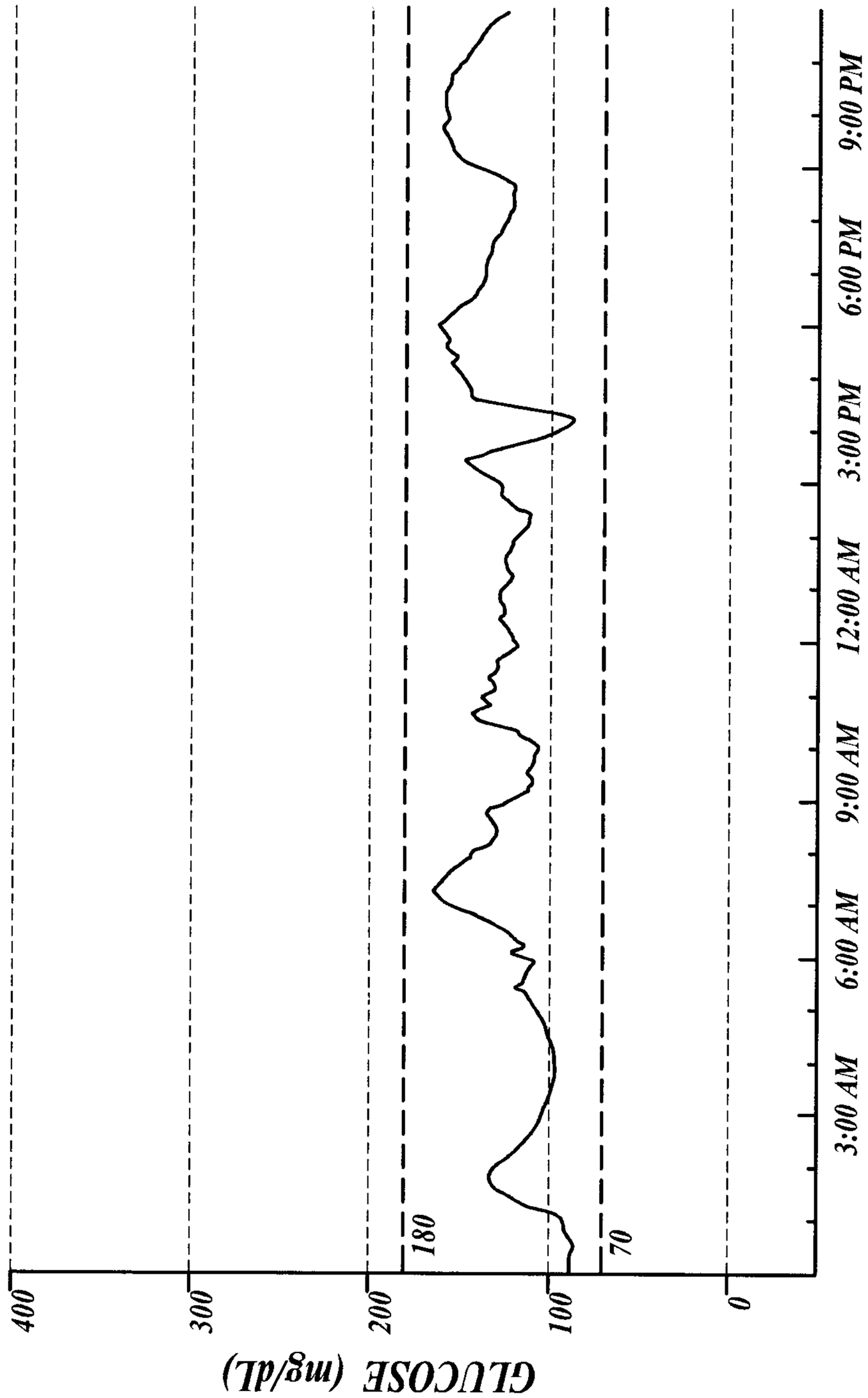

GLUCOSE (mg/dL)
400
300
200
100
0
180
70
3:00 AM
6:00 AM
9:00 AM
12:00 AM
3:00 PM
6:00 PM
9:00 PM
TIME OF DAY

Fig.19A.

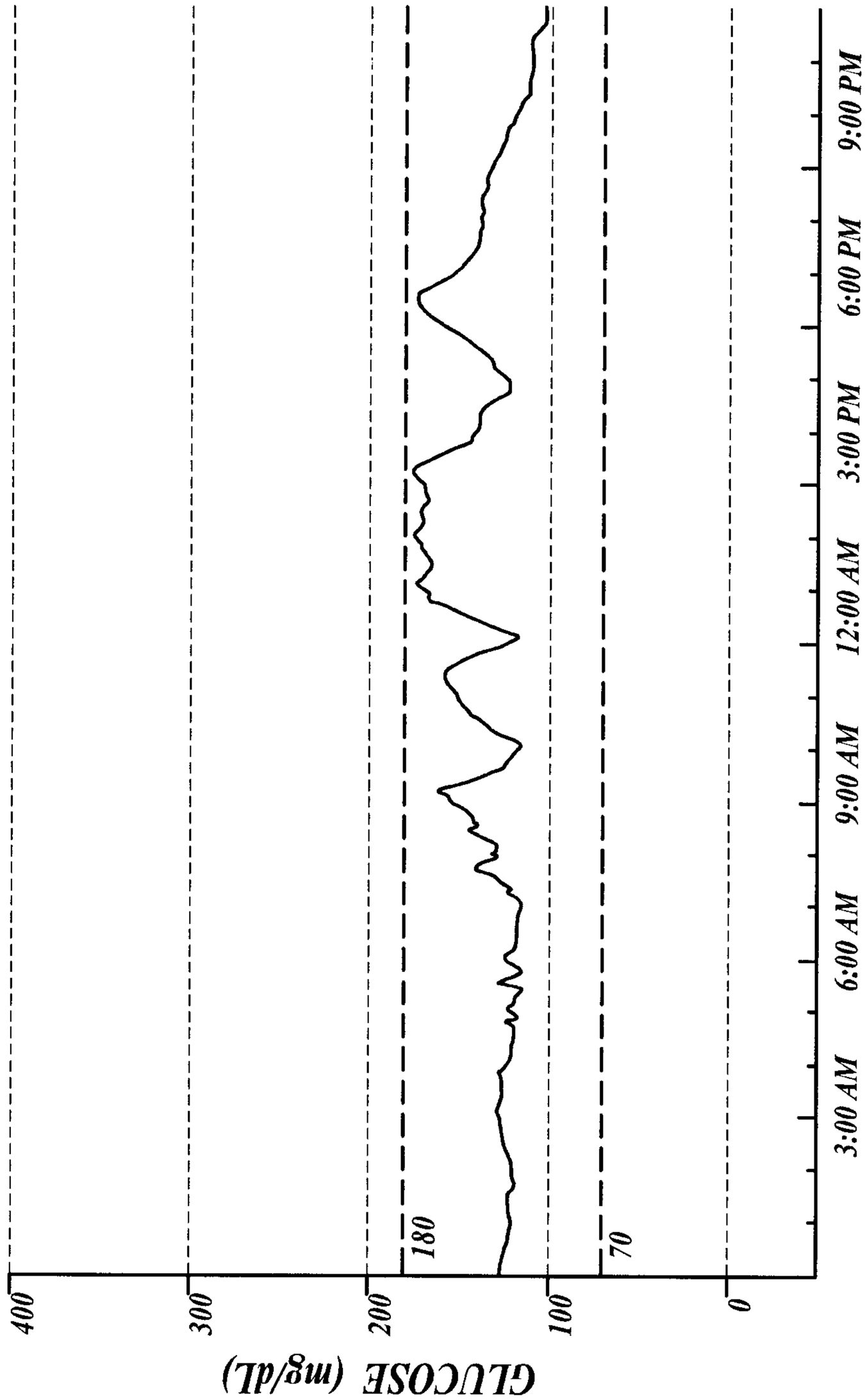

400
300
200
100
0
180
70
GLUCOSE (mg/dL)
3:00 AM
6:00 AM
9:00 AM
12:00 AM
3:00 PM
6:00 PM
9:00 PM
TIME OF DAY

Fig.19B.

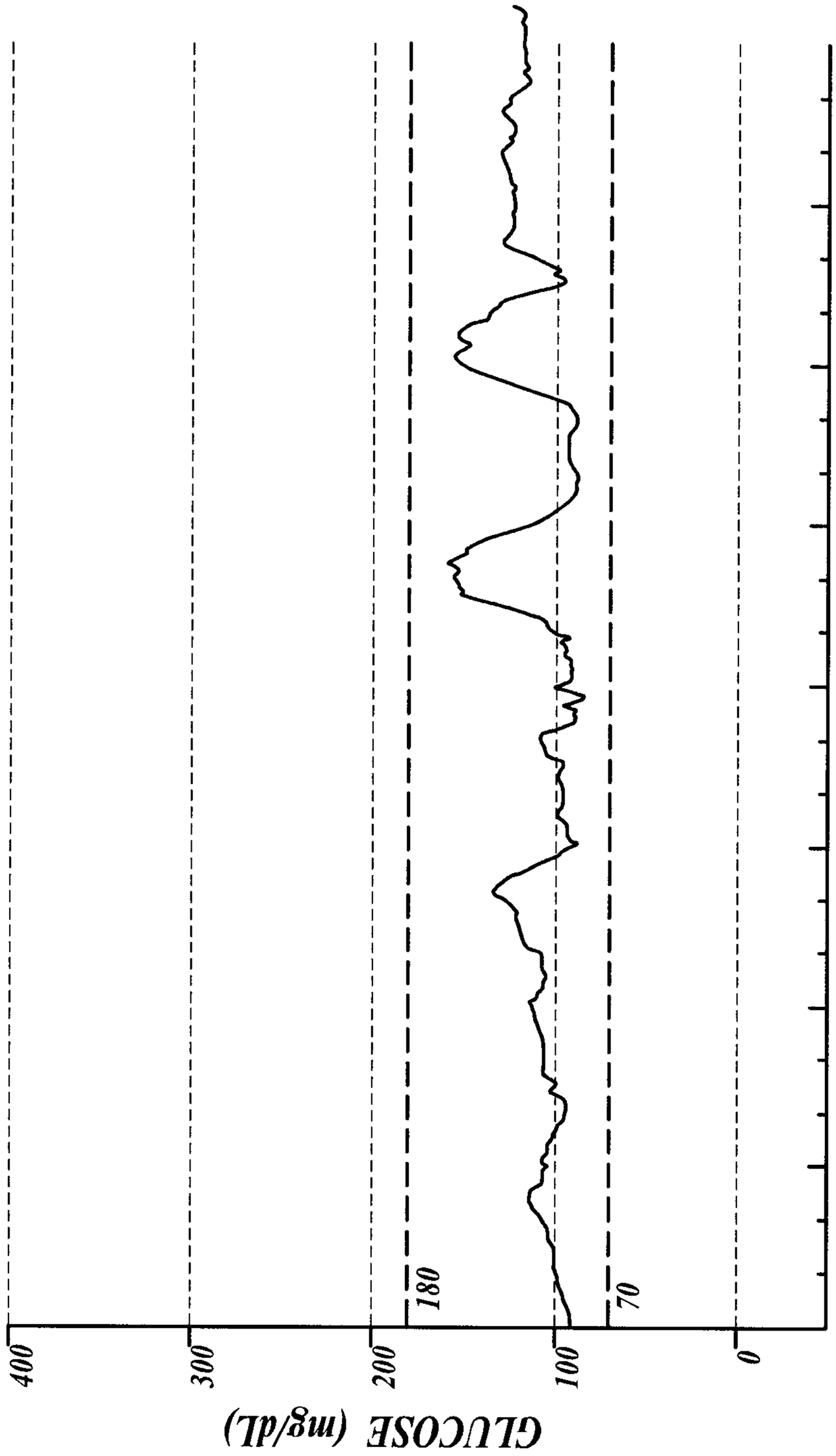

GLUCOSE (mg/dL)
400
300
200
180
100
70
0
3:00 AM
6:00 AM
9:00 AM
12:00 AM
3:00 PM
6:00 PM
9:00 PM
TIME OF DAY

Fig.19C.

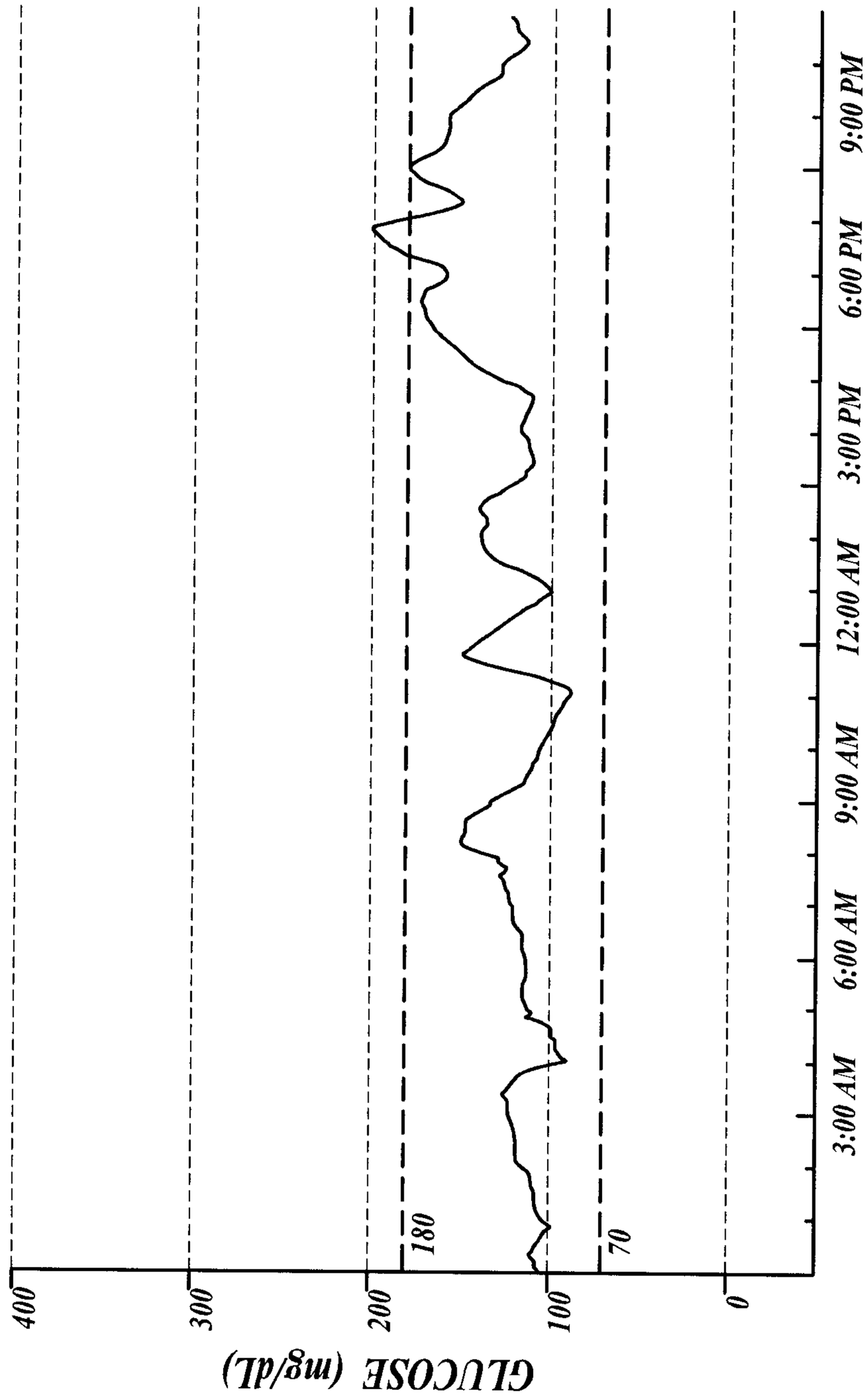

GLUCOSE (mg/dL)
400
300
200
180
100
70
0
3:00 AM
6:00 AM
9:00 AM
12:00 AM
3:00 PM
6:00 PM
9:00 PM
TIME OF DAY

Fig.19D.

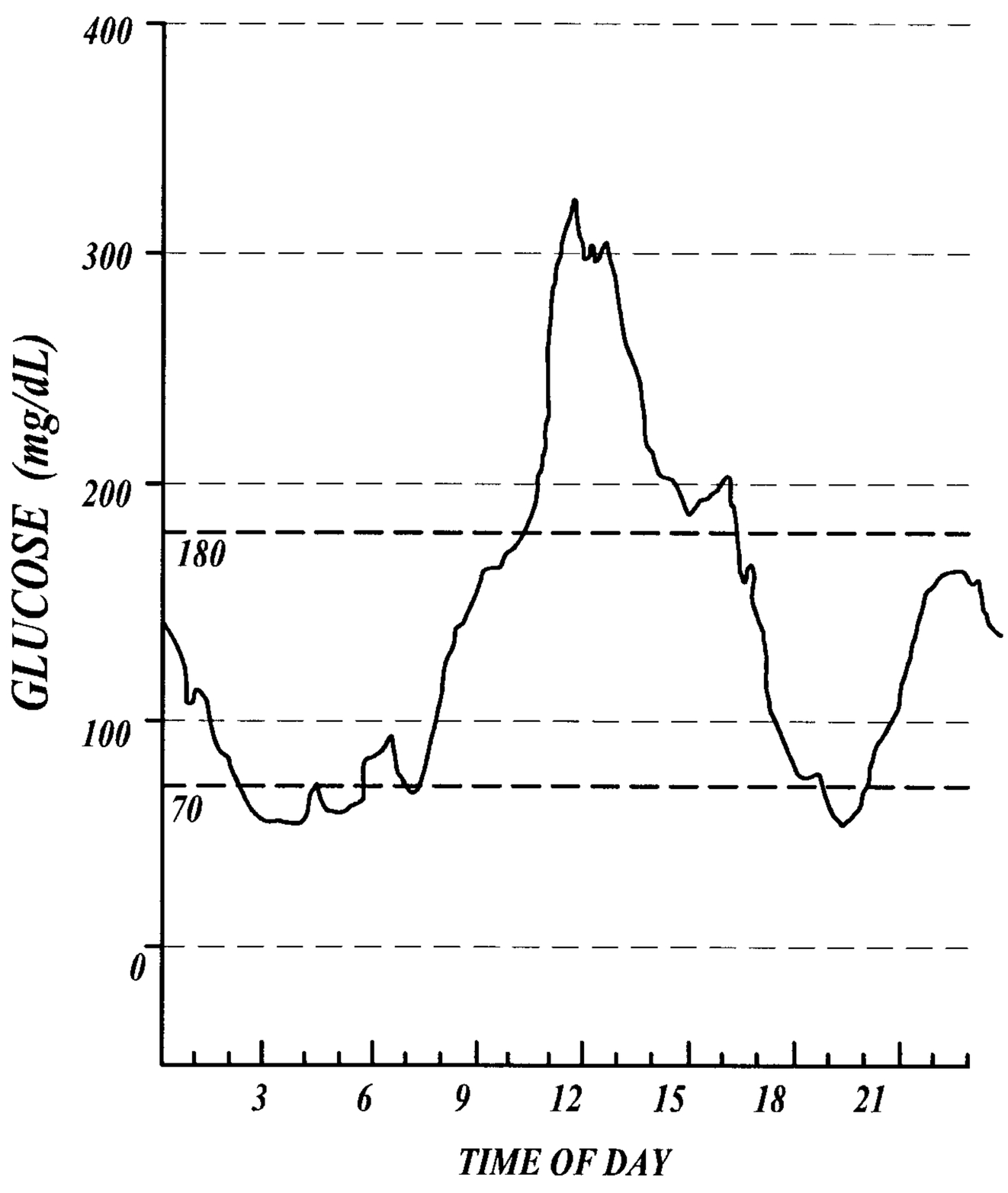


Fig.20A.

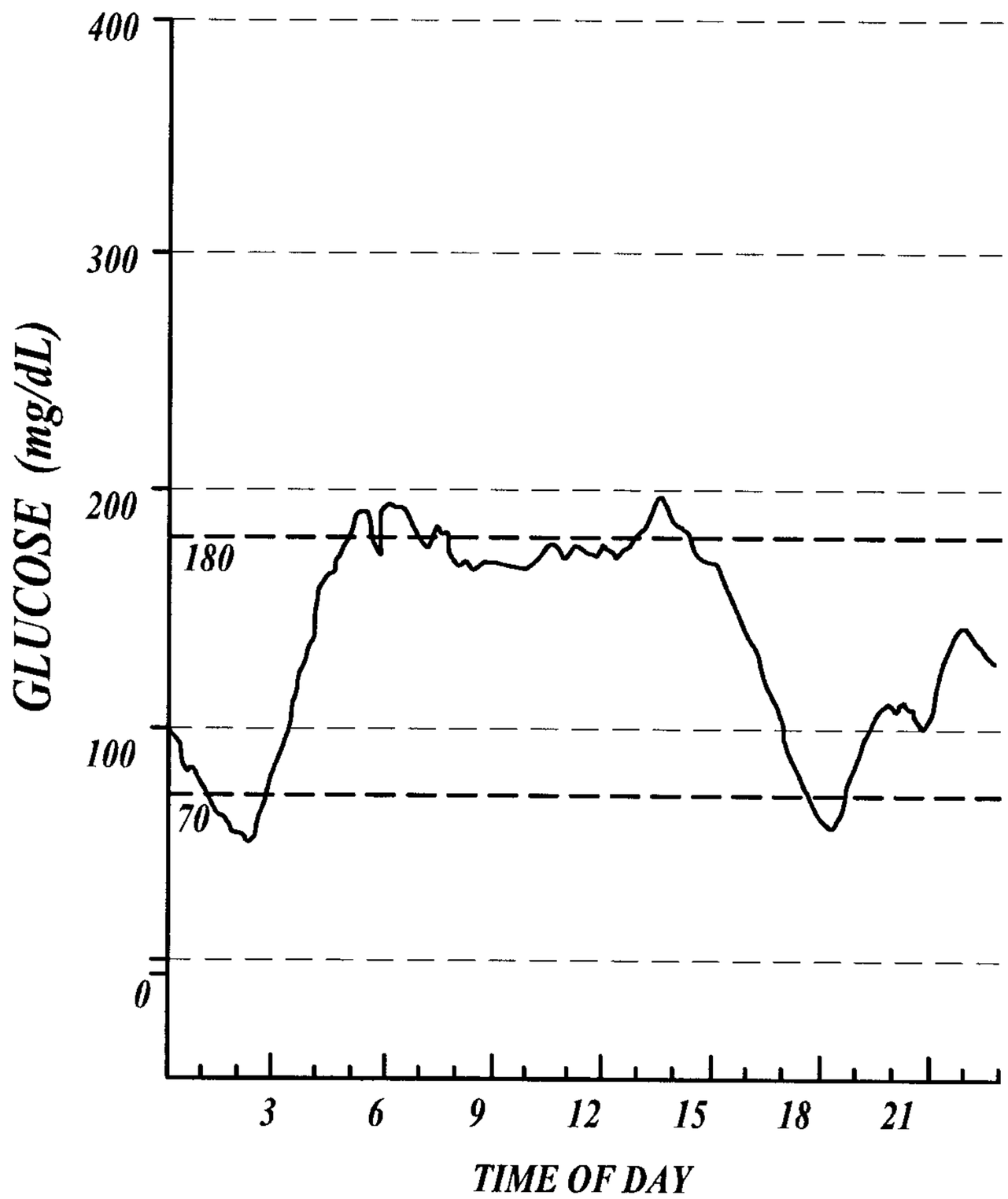
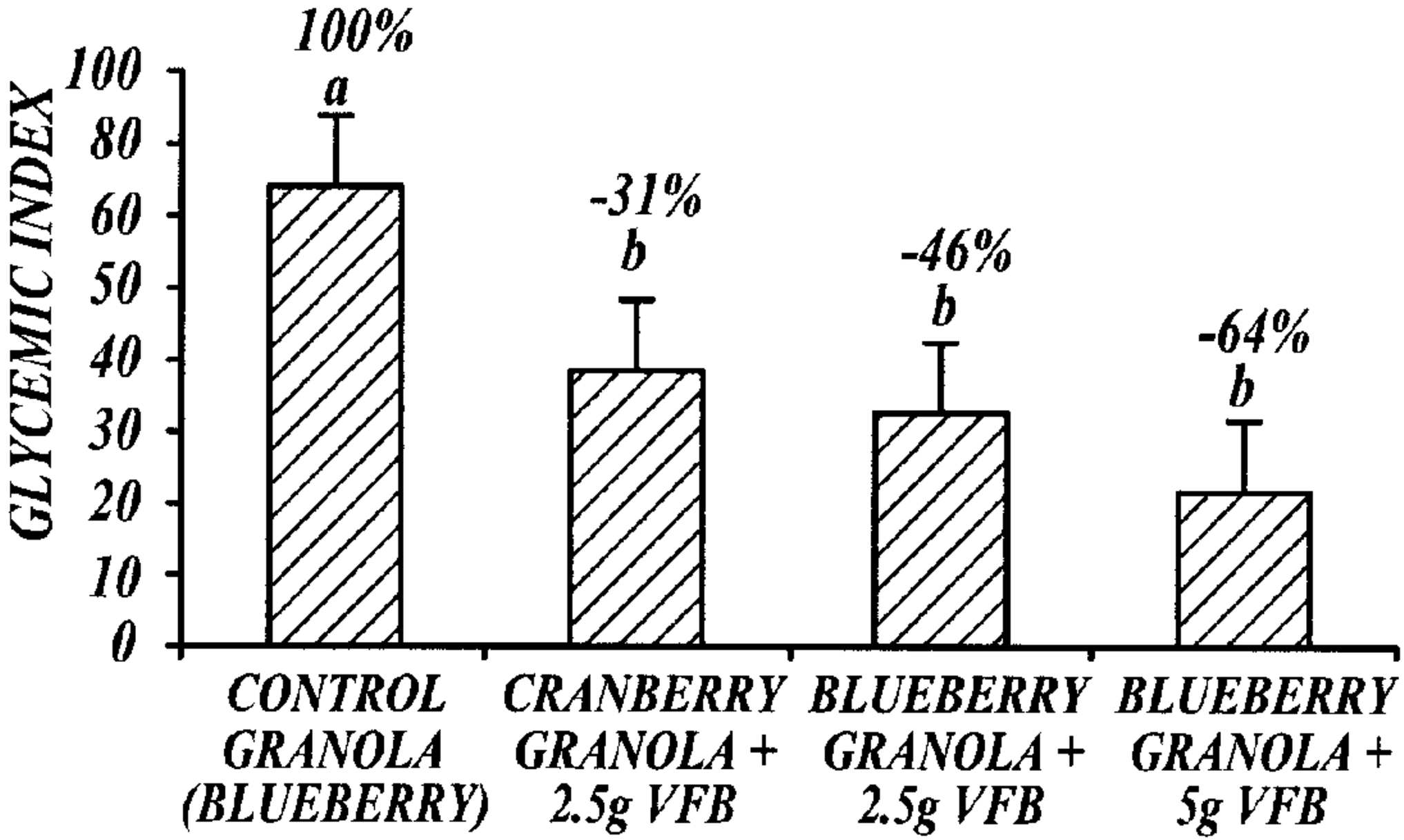


Fig.20B.


GLYCEMIC INDEX
100
80
60
50
40
30
20
10
0
100%
a
-31%
b
-46%
b
-64%
b
CONTROL GRANOLA (BLUEBERRY)
CRANBERRY GRANOLA + 2.5g VFB
BLUEBERRY GRANOLA + 2.5g VFB
BLUEBERRY GRANOLA + 5g VFB