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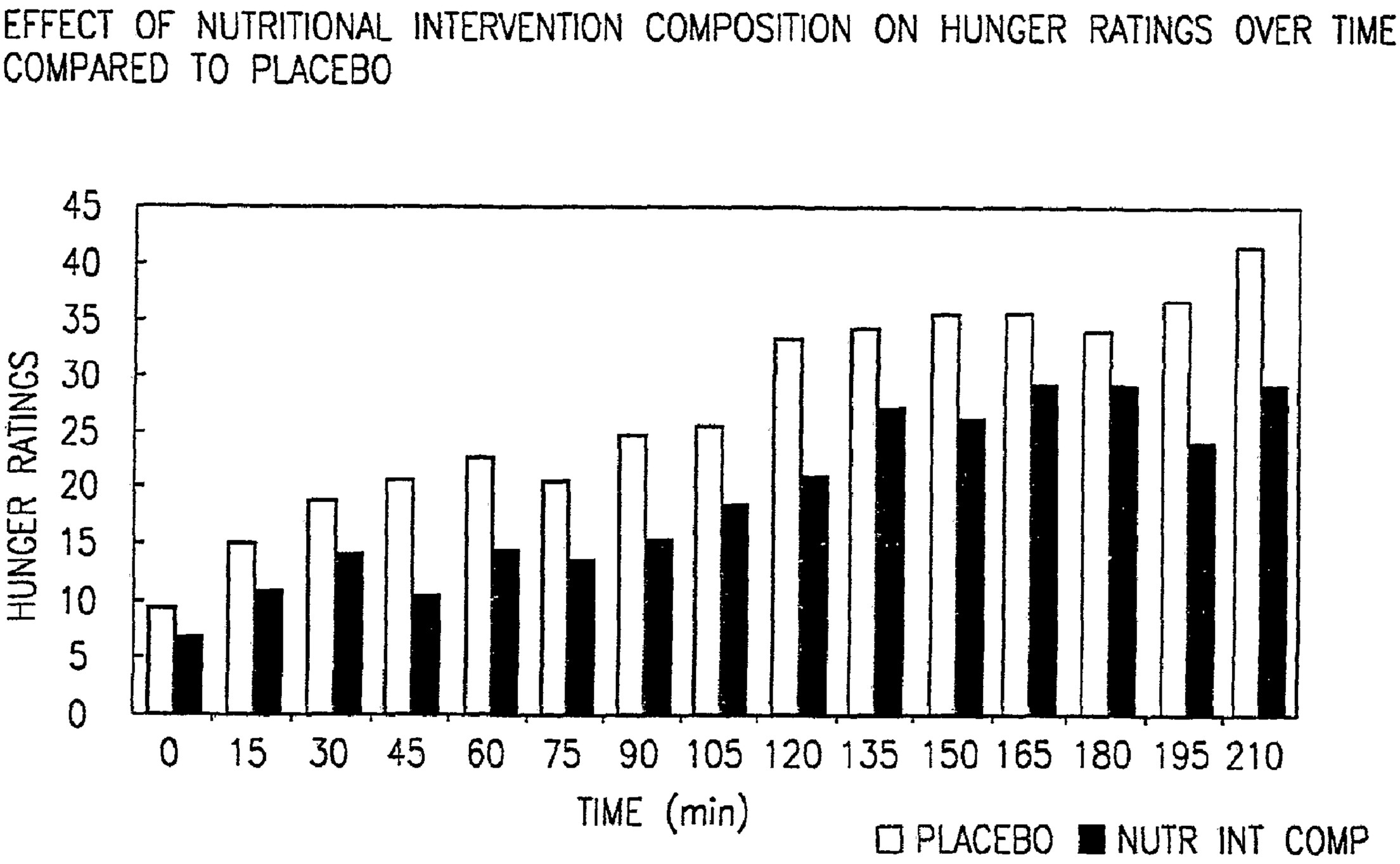
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(54) Titre : COMPOSITION D'INTERVENTION NUTRITIONNELLE DESTINEE A AUGMENTER ET A PROLONGER L'EFFET DE SATIETE

(54) Title: NUTRITIONAL INTERVENTION COMPOSITION FOR ENHANCING AND EXTENDING SATIETY




(57) Abrégé/Abstract:
This invention relates to a nutritional intervention composition in a dry power form for enhancing satiety prior to a meal and extending satiety after a meal in a calorically efficient fashion. The dry nutrional composition includes protein, caseinmacropeptide or glycomacropeptide, long chain fatty acids, soluble and/or insoluble fibers. The dry nutritional composition includes protein in the range of 0.22% to 88.30%, glycomacropeptide in the range of 0.06% to 87.72%, oleic acid in the range of 2.42% to 97.25%,

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(57) Abrégé(suite)/Abstract(continued):
soluble fibers in the range of 0.20% to 79.05%, and insoluble fibers in the range of 0.20% to 79.05%. The composition may also include plant saponins, calcium and cholestyramine.

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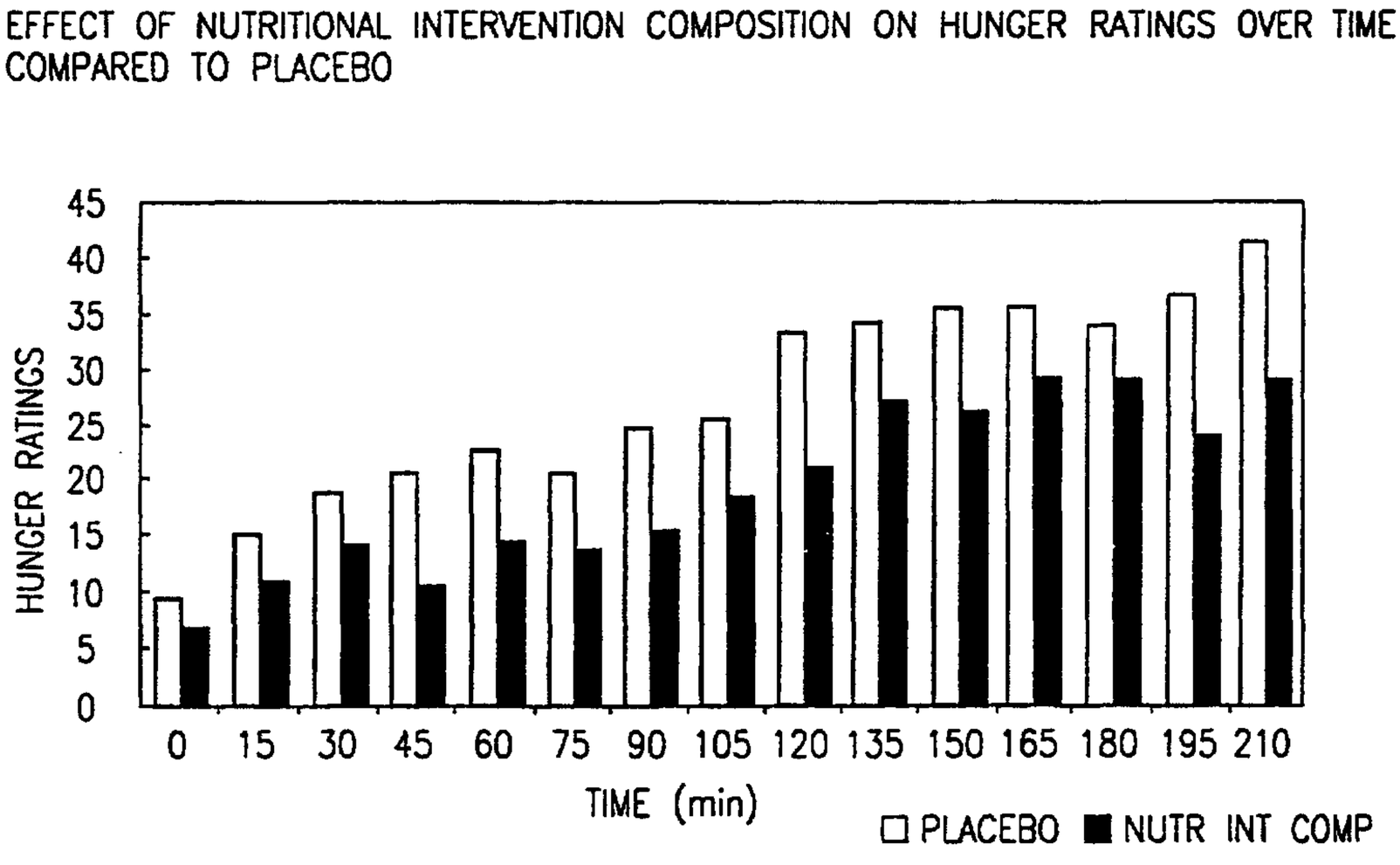
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(54) Title: NUTRITIONAL INTERVENTION COMPOSITION FOR ENHANCING AND EXTENDING SATIETY




(57) Abstract: This invention relates to a nutritional intervention composition in a dry power form for enhancing satiety prior to a meal and extending satiety after a meal in a calorically efficient fashion. The dry nutrional composition includes protein, casein-macropeptide or glycomacropeptide, long chain fatty acids, soluble and/or insoluble fibers. The dry nutritional composition includes protein in the range of 0.22% to 88.30%, glycomacropeptide in the range of 0.06% to 87.72%, oleic acid in the range of 2.42% to 97.25%, soluble fibers in the range of 0.20% to 79.05%, and insoluble fibers in the range of 0.20% to 79.05%. The composition may also include plant saponins, calcium and cholestyramine.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# NUTRITIONAL INTERVENTION COMPOSITION FOR ENHANCING AND EXTENDING SATIETY

## FIELD OF THE INVENTION

The present invention relates to a nutritional intervention composition for enhancing satiety prior to the consumption of a meal resulting in reduced caloric intake during the meal, and lengthening the inter-meal interval by extending satiety for up to three hours following the meal. More particularly, the nutritional intervention composition includes a protein source, long chain fatty acids, and calcium to stimulate the release of cholecystokinin (CCK). Further, the nutritional composition includes soluble and insoluble fibers to bind bile acids and bile salts that inhibit the release of CCK. By extending the feeling of satiety, the nutritional intervention composition decreases food intake producing weight loss over time. The composition can be taken prior to a meal or can be mixed with food to extend the satiation effect of that food.

The present invention also relates to a nutritional intervention composition to help individuals with Type II diabetes maintain glycemic control and extend satiety. By extending the feeling of satiety, the nutritional intervention composition decreases food intake resulting in a decrease in body weight over time while providing better regulation of glucose and insulin levels following consumption of a meal. Furthermore, since CCK causes a delay in stomach emptying, the nutritional intervention composition can slow the absorption of glucose by the small intestine further improving glycemic control.

The present invention also relates to a nutritional intervention composition designed as an adjunct to treat patients with bulimia and eating disorders who have been shown to have a defect in their satiety control mechanisms. By stimulating satiety before a meal and extending satiety after a meal, the present invention reduces binge eating in bulimic patients.

## BACKGROUND OF THE INVENTION

SATIETY

Cholecystokinin (CCK) is a peptide released following the consumption of food. The literature demonstrates an injection of CCK in animals elicited the total range of satiety behavior. When injected CCK levels peak quickly and usually return to baseline with an hour. The drop in CCK levels is associated with a decline in the characteristic satiety behavior.

Release of cholecystokinin has also been shown to be a satiety signal in humans. In 1981, researchers showed that an injection of CCK decreased food intake by 16 percent. The subjects did not alter their rate of eating but rather stopped eating earlier, which would be the expected results if cholecystokinin were a satiety signal. The results in humans confirmed the results in the laboratory that CCK is an important agent in terminating the meal. CCK levels in man peak within 20 minutes following a meal and usually returns to baseline in one hour. Although the full mechanism wherebyCCK exerts its effect on satiety is not known, there appears to be two components, a central component involving CCK receptors in the brain and a peripheral component involving the stomach and small intestine..

When food is consumed, CCK releasing protein (CCKRP) is released in the small intestine. CCKRP stimulates CCK release from intestinal cells. The release of CCK generates the behavioral symptoms associated with satiety and at the same time activates a number of negative feedback mechanisms to turn off the CCK response. There are primarily two negative feedback mechanisms, one involving proteases secreted by the pancreas and the second bile from the gallbladder. CCK stimulates the pancreas to secrete a number of proteases, specifically trypsin and chymotrypsin, which inactivate CCKRP. CCK also stimulates gallbladder contraction causing bile acids to be released into the intestinal lumen. Bile acids are powerful regulators of CCK, inhibiting its release.

The literature has also shown that CCK release can be stimulated by protein such as whey and casein, hydrolysis products of casein including glycomacropeptide, phenylalanine, calcium and long chain fatty acids. All of the literature to date has shown that regardless of how CCK is stimulated or what intervention is taken to prevent its breakdown, its reported effect is on the termination of the meal.

It has been well documented that some soluble and insoluble fibers as well as plant saponins bind bile salts. In fact, it is the binding of bile salts by fiber, which is believed partly responsible for the hypocholestrolemic effect of these agents. Different fibers have different binding capacities to the various bile acids and salts. For instance, cellulose has been shown to bind bile acids poorly.

The ability of CCK to reduce appetite would appear to make it an extremely useful agent in treating obesity. In a weight management program, stimulation of CCK would result in less food consumed and reduction of hunger cravings between meals. These effects would enable an overweight individual to better comply with a diet that has a reduced caloric intake. The major limitation in the use of CCK, as an appetite control agent, is that it must be given by injection. Additionally, CCK release initiates a number of negative feedback mechanisms described above involving the pancreas and gallbladder that terminate the CCK response.

There is a definite need in the art for a nutritional intervention composition that can be taken orally to permit a subject to be satiated with a lower caloric intake. There is also a definite need in the art for a nutritional intervention composition that not only can be taken prior to a meal to stimulate satiety before the meal but whose properties extend satiety following the meal thereby lengthening the inter-meal interval.

There is also a definite need in the art for a nutritional intervention composition that can be taken orally and that with a total caloric value of only 80 calories can strongly provoke satiety.

GLYCEMIC CONTROL

It is well known the art that slowing gastric emptying can blunt the post-prandial rise in glucose and insulin. Most persons with Type II diabetes are obese and have an inability to respond normally to insulin. Obesity is a major contributing factor to the development of Type II diabetes. The primary treatment for Type II diabetics is diet and a weight loss program. Dietary guidelines for Type II diabetics include

consumption of fiber. Fiber has been shown to slow gastric emptying. One of the prominent effects of cholecystokinin is also to delay gastric emptying. The ability of fiber and cholecystokinin to delay gastric emptying are well known in the art and the result of delayed gastric emptying is to slow the absorption of glucose.

There is a definite need in the art for a nutritional intervention composition that can be taken orally by Type II diabetics that stimulates the release of CCK in a calorically efficient way, and that permits Type II diabetics to be satiated with a lower caloric intake and offers a better degree of glycemic control.

There is a definite need in the art for a nutritional intervention composition that not only can be taken prior to a meal to stimulate satiety before the meal but whose properties extend satiety following the meal thereby lengthening the intermeal interval in order to help the Type II diabetic lose weight.

BULIMIA

Bulimia is an eating disorder that usually effects females. A major characteristic of bulimia is an inability to become satiated by food. As a result bulimics tend to binge on food and regurgitate it to prevent weight gain. This disorder is classically treated with psychotherapy. Studies have shown that bulimics have a defect in their normal satiety mechanisms. They release less CCK following a meal.

There is a definite need in the art for a nutritional intervention composition that can be taken orally by bulimics, and is a calorically efficient stimulator of CCK to permit bulimics to be satiated. An important element of this invention is the design of a product that not only can be taken prior to a meal to stimulate satiety before the meal but whose properties extend satiety following the meal thereby lengthening the inter-meal interval.

## DESCRIPTION OF THE PRIOR ART

SATIETY

US Patent No 4833128 discloses the oral administration of phenylalanine in conjunction with protein, carbohydrate and fat to stimulate satiety. This invention teaches that when a dietary supplement containing phenylalanine is consumed fifteen minutes prior to a meal, it generates a feeling of satiety resulting in less food consumption at the subsequent meal. The CCK release slows gastric emptying and the fiber in the invention provides an additional effect by slowing gastric emptying. The nutritional supplement in this patent contains 140 calories and it is recommended that it be taken three times a day. At a dose of three times a day this dietary supplement would provide almost 25% of the total calories suggested in a reduced caloric program (1600 calories) to lose weight. Furthermore, the addition of phenylalanine limits its use in patients with phenylketonuria. The invention also teaches that cellulose should be added. Cellulose has been shown to be one of the poorest binders of bile acids and therefore would not stimulate satiety by blocking the effect of bile acids and salts on cholecystokinin release. Finally, the invention does not have any effect on extending the duration of action of CCK. In fact, the invention teaches that the appetite suppression of CCK may be merely temporary resulting in a limited satiety effect.

US Patent No. 4,491,578 discloses the oral administration of a trypsin inhibitor to enhance satiety by stimulating the release of CCK. This patent teaches that the negative feedback signal for cholecystokinin secretion results from the release of trypsin from the pancreas. The administration of a therapeutically effective quantity of trypsin inhibitor blocks the trypsin released from the pancreas thereby interfering with a negative feedback mechanism. The nutritional intervention composition

described in this application does not depend on trypsin inhibition for its effect on satiety.

U.S. Patent 5,932,561 teaches that dietary supplements that bind lipids can aid in weight loss and reduce cholesterol. The patent also teaches that a dietary supplement composition that contains saponins from aloe increase the capacity of chitosan to bind fat. The saponins also act as a laxative to off set the constipating effects of chitosan. This patent does not teach that either chitosan or saponins can be used to stimulate cholecystokinin. The weight management characteristics of this invention are to primarily combine fat and cholesterol and remove it from the body.

U.S. Patent 5,703,052 teaches that saponins are useful in controlling hypercholesterolemia. This patent does not describe the use of saponins as a stimulator of CCK.

GLYCEMIC CONTROL

U.S. Patent No 5187154 teaches that Type II diabetics exhibit more rapid gastric emptying than normal controls in the early stages of their diagnosis and that an invention that can slow gastric emptying will improve glycemic control. The patent also teaches that the invention is useful for assessing the risk of diabetes in subjects who do not show any abnormalities in glucose metabolism. The patent utilizes a therapeutic dose of trypsin inhibitor to stimulate CCK release and thereby slow gastric emptying which in turn results in improved glycemic control. The nutritional intervention described in the present invention does not depend on trypsin inhibition for its effect on glycemic control.

None of the prior art patents disclose the nutritional composition of the present invention for enhancing and extending satiety with a calorically efficient preparation.

## OBJECTS

Accordingly it is an object of the present invention to provide a nutrition intervention composition for enhancing satiety before a meal.

Another object of the present invention is to provide a nutrition intervention composition to extend satiety after a meal.

Another object of the present invention is to provide a nutrition intervention composition that can be consumed prior to a meal to enhance satiety.

Another object of the present invention is to provide a nutrition intervention composition that can be added to food to extend the satiating effect of the food to which it is added.

Another object of the present invention is to provide a nutrition intervention composition to stimulate cholecystokinin release in a calorically efficient manner.

Another object of the present invention is to provide a nutrition intervention composition to increase cholecystokinin by stimulating its release through a combination of nutritional agents.

Another object of the present invention is to provide a nutrition intervention composition to stimulate cholecystokinin release by binding to bile acids and to bile salts.

Another object of the present invention is to provide a nutrition intervention composition to cause weight loss resulting from a reduced caloric intake.

Another object of the present invention is to provide a nutrition intervention composition to provide better glycemic control for Type II diabetics.

Another object of the present invention is to provide a nutrition intervention composition to help Type II diabetics enhance and extend satiety in a calorically efficient fashion.

Another object of the present invention is to provide a nutrition intervention composition to increase satiety in bulimics who have a defect in their normal CCK release mechanism.

Another object of the present invention is to provide a nutrition intervention composition to help in the management of the bulimic patients.

Another object of the present invention is to provide a nutrition intervention composition that is palatable, well tolerated and without side effects to individuals.

## SUMMARY OF THE INVENTION

In brief this invention relates to a nutritional intervention composition in a dry power form for enhancing satiety prior to a meal and extending satiety after a meal in a calorically efficient fashion. The dry nutritional composition includes protein, caseinmacropeptide or glycomacropeptide, long chain fatty acids, soluble and/or insoluble fibers. The dry nutritional composition includes protein in the range of 0.22% to 88.30%, glycomacropeptide in the range of 0.06% to 87.72%, oleic acid in the range of 2.42% to 97.25%, soluble fibers in the range of 0.20% to 79.05%, and insoluble fibers in the range of 0.20% to 79.05%. The composition may also include plant saponins, calcium and cholestyramine.

## BRIEF DESCRIPTION OF THE DRAWINGS

Further objects, features, and advantages of the present invention will become apparent upon the consideration of the following detailed description of the presently preferred embodiment when taken in conjunction with the accompanying drawings, wherein:

Figure 1 is a graph showing a comparison of hunger ratings between a placebo group and the nutritional intervention composition of the present invention.

Figure 2 is a graph showing a comparison of food consumption ratings between a placebo group and the nutritional intervention composition of the present invention.

Figure 3 is a graph showing a comparison of hunger ratings following consumption of two forms of low fat yogurt, one containing a placebo mixture and the other containing the nutritional intervention composition of the present invention.

Figure 4 is a graph showing a comparison of the change in hunger ratings over time following consumption of two forms of low fat yogurt, one containing a placebo mixture and the other containing the nutritional intervention composition of the present invention.

Figure 5 is a graph showing a comparison of food consumption ratings following consumption of two forms of low fat yogurt, one containing a placebo mixture and the other containing the nutritional intervention composition of the present invention.

Figure 6 is a graph showing the effect of the nutritional intervention composition on appetite change over six weeks.

Figure 7 is a graph showing the effect of the nutritional intervention composition on food cravings over six weeks.

Figure 8 is a graph showing the effect of the nutritional intervention composition on appetite over six weeks.

Figure 9 is a graph showing the effect of the nutritional intervention composition on weight loss over six weeks.

Figure 10 is a table showing the effect of the nutritional intervention composition on mean satiety ratings over six weeks.

## DETAILED DESCRIPTION OF THE INVENTION

The invention is based on the unexpected and surprising discovery that by providing a nutritional intervention composition to stimulate CCK release and block the negative feedback mechanisms that inhibit CCK release, satiety is enhanced with the consumption of fewer calories and satiation effects can be extended for up to three and one half hours following the meal.

A second unexpected and surprising discovery is that by consuming as little as 80 calories of the nutritional composition, one can produce a significant and extended satiation effect with the consumption of a meal of only 385 calories.

A third unexpected and surprising discovery is that by combining specific soluble and/or insoluble fibers with plant saponins one can bind specific bile salts thereby removing powerful inhibitors of cholecystokinin release.

A fourth unexpected and surprising discovery is that by consuming glycomacropeptides (GMP) or caseinmacropeptides (CMP) one can stimulate CCK and enhance satiety.

The nutritional intervention composition of the invention comprises glycomacropeptides (GMP) or caseinmacropeptide (CMP), long chain fatty acids C12-C18 in length, and soluble and/or insoluble fibers. The composition may further include protein, calcium and/or plant saponins. The nutritional intervention composition can be taken fifteen minutes before a meal, during a meal or incorporated into food to produce an extended effect on satiation.

The nutritional intervention composition is designed to achieve multiple effects leading to the increase in satiety by stimulating and maintaining levels of CCK. According to the present invention, stimulation of CCK by meals not only produces satiety but also stimulates negative feedback mechanisms, involving the gall bladder's release of bile salts which inhibit CCK release, resulting in a decrease in satiety. An important aspect of the invention is that a combination of elements are used to stimulate CCK and at the same time reduce the level of bile salts in the intestine so that CCK release is not inhibited.

In one of the preferred embodiments, the source of protein is casein, whey or soy. The preferred range for the protein is in the range of 1.0 to 4.0 grams by weight of the composition, or in the range of 3.89% to 44.97% by weight of the composition. The broad range for the protein is in the range of 0.10 to 10.0 grams by weight of the composition, or in the range of 0.22% to 88.30% by weight of the composition.

In the preferred embodiment, the source of glycomacropeptide (GMP) or caseinmacropeptide (CMP) is whey protein concentrate. Glycomacropeptide (GMP) is the glyosilated form of caseinmacropeptide (CMP), the first hydrolysis product resulting from the action of gastric proteases on kappa casein. The preferred range for glycomacropeptide or caseinmacropeptide (CMP) is in the range of 0.03 to 1.0 grams by weight of the composition, or in the range of 0.11% to 14.57% by weight of the composition. The broad range for the glycomacropeptide or caseinmacropeptide is in the range of 0.25 to 10.0 grams by weight of the composition, or in the range of 0.06% to 87.72% by weight of the composition.

The most effective fatty acids in stimulating CCK are long chain fatty acids between C12-C18 in length. In the preferred embodiment, C18 oleic acid is used. Sources of oleic acid are babassu oil, butter oil, chicken fat, cocoa butter, coconut oil, corn oil, cottonseed oil, lard, olive oil, palm oil, palm kernel oil, peanut oil, rapeseed oil, safflower oil, soybean oil, sunflower oil, tallow or tucum oil. The preferred range for the long chain fatty acids are in the range of 2.0 to 9.0 grams by weight of the composition, or in the range of 9.22% to 69.79% by weight of the composition. The broad range for the long chain fatty acids are in the range of 1.0 to 15.00 grams by weight of the composition, or in the range of 2.42% to 97.25% by weight of the composition. The preferred range for oleic acid is in the range of 1.0 to 4.0 grams by weight of the composition, or in the range of 3.89% to 44.97% by weight of the composition.

The source of the soluble fibers are guar, glucomannan, potato, methyl cellulose, phyllium, pectin, oat fiber and sugar beet. The source of the insoluble fibers are cellulose, potato, lignin, hemicelluloses, and insoluble pectins. The preferred range for the soluble and/or insoluble fibers are in the range of 1.5 to 7.0 grams by weight

of the composition, or in the range of 6.47% to 61.40% by weight of the composition. The broad range for the soluble and/or insoluble fibers are in the range of 0.20 to 10.0 grams by weight of the composition, or in the range of 0.44% to 89.09% by weight of the composition. The preferred range for the soluble fibers are in the range of 1.0 to 4.0 grams by weight of the composition, or in the range of 3.89% to 44.97% by weight of the composition. The broad range for the soluble fibers are in the range of 0.10 to 5.0 grams by weight of the composition, or in the range of 0.20% to 79.05% by weight of the composition. The preferred range for the insoluble fibers are in the range of 0.50 to 3.0 grams by weight of the composition, or in the range of 1.91% to 35.74% by weight of the composition. The broad range for the insoluble fibers are in the range of 0.10 to 5.0 grams by weight by the composition, or in the range of 0.20% to 79.05% by weight of the composition.

The soluble fibers, as well as the insoluble fibers, bind those specific bile salts in the intestinal lumen which are the strongest inhibitors of CCK release. At least one soluble fiber, or at least one insoluble fiber, or a mixture thereof, may be used in the composition for the release of CCK.

GMP has been shown to be more calorically efficient in stimulating CCK release than protein. In addition, GMP may also effect the pancreatic feedback mechanism by serving as a substrate source for the released proteases. This may lower the amount of available proteases to inactivate CCKRP.

The composition of the present invention may also include calcium. Calcium has been shown to stimulate CCK release. The source of the calcium may be calcium salts selected from the group consisting of calcium carbonate, calcium lactate, calcium citrate, calcium malate and equivalents thereof. The range of calcium is 0.05 to 0.30 grams by weight of the composition.

The composition may also include plant saponins. The source may be alfalfa. The range of plant saponins is 0.05 to 10.0 grams by weight of the composition.

The composition may also include bile acid sequestering resins, such as cholestyramine in the range of 0.10 to 5.0 grams by weight of the composition.

One specific example of the composition of the present invention is 0.50 grams of GMP, 2.40 grams of oleic acid, and 3.06 grams of guar or glucomannan (soluble fibers).

Another specific example of the composition is 0.50 grams of GMP, 2.40 grams of oleic acid, 3.06 grams of guar or glucommannan, and 2.81 grams of whey protein.

Another specific example of the composition is 0.50 grams of GMP, 2.40 grams of oleic acid, 3.06 grams of guar or glucomman, 2.81 grams of whey protein, and 0.19 grams of calcium lactate.

The present invention provides for a nutritional intervention composition in a dry powder form for enhancing satiety before a meal and extending satiety following a meal. It is therefore useful in treatment of weight loss.

The following charts show additional examples of the present invention and caloric contents of different examples:

# EXAMPLE ONE

| | | | | Range (gm) | | Per Cent | |
|---|---|---|---|---|---|---|---|
| Ingredient | Source | grams | % | Lower | Upper | Lower | Upper |
| Protein | Casein, whey, soy | 2.81 | 24.67% | 1.00 | 4.00 | 3.89% | 44.97% |
| GMP | Whey Protein | 0.50 | 4.39% | 0.03 | 1.00 | 0.11% | 14.57% |
| Oleic acid | Sunflower Oil | 2.40 | 21.07% | 2.00 | 9.00 | 9.22% | 69.79% |
| Soluble Fiber | Guar, potato, glucomannan, methyl cellulose | 1.92 | 16.86% | 1.00 | 4.00 | 3.89% | 44.97% |
| Insoluble Fiber | Cellulose, potato | 1.14 | 10.01% | 0.50 | 3.00 | 1.91% | 35.74% |
| Calcium | Lactate, Carbonate, Citrate, Malate | 0.019 | 1.67% | 0.05 | 0.30 | 0.18% | 4.88% |
| Flavors | | 2.20 | 19.32% | 1.10 | 3.00 | 4.10% | 34.11% |
| Emulsifiers | Lecithin | 0.20 | 1.76% | 0.20 | 0.40 | 0.70% | 6.56% |
| Sweeteners | Aspartame, Sucrose | 0.03 | 0.25% | 0.015 | 4.00 | 0.06% | 40.49% |
| Totals | | 11.39 | 100.00% | 5.895 | 28.70 | | |
| Total Soluble and/or Insoluble Fibers | | | | 1.50 | 7.00 | 6.47% | 61.40% |

## EXAMPLE TWO

| | | | | Range (gm) | | Per Cent | |
|---|---|---|---|---|---|---|---|
| Ingredient | Source | grams | % | Lower | Upper | Lower | Upper |
| Protein | Casein, whey, soy | 2.81 | 31.02% | 0.10 | 10.00 | 0.22% | 88.30% |
| GMP | Whey Protein | 0.50 | 5.52% | 0.025 | 10.00 | 0.06% | 87.72% |
| Oleic acid | Sunflower Oil | 2.40 | 26.49% | 1.00 | 15.00 | 2.42% | 97.25% |
| Soluble Fiber | Guar, potato, glucomannan, methyl cellulose | 1.92 | 21.19% | 0.10 | 5.00 | 0.20% | 79.05% |
| Insoluble Fiber | Cellulose, potato | 1.14 | 12.58% | 0.10 | 5.00 | 0.20% | 79.05% |
| Calcium | Lactate, Carbonate, Citrate, Malate | 0.19 | 2.10% | 0.05 | 0.30 | 0.09% | 17.91% |
| Plant Saponins | Alfalfa | 0.10 | 1.10% | 0.05 | 10.00 | 0.11% | 87.91% |
| Totals | | 9.06 | 100.00% | 1.425 | 55.30 | | |
| Total Soluble and/or Insoluble Fibers | | | | 0.20 | 10.00 | 0.44% | 89.09% |

## EXAMPLE THREE

| | | | | Range (gm) | | Per Cent | |
|---|---|---|---|---|---|---|---|
| Ingredient | Source | grams | % | Lower | Upper | Lower | Upper |
| GMP | Whey Protein | 0.50 | 8.39% | 0.025 | 10.00 | 0.18% | 89.29% |
| Oleic acid | Sunflower Oil | 2.40 | 40.27% | 1.00 | 4.00 | 4.76% | 94.67% |
| Soluble Fiber | Guar, glucomannan, methyl cell | 1.92 | 32.21% | 0.10 | 5.00 | 0.52% | 81.63% |
| Insoluble Fiber | Cellulose, potato | 1.14 | 19.13% | 0.10 | 5.00 | 0.52% | 81.63% |
| Totals | | 5.96 | 100.00 | 1.225 | 24.00 | | |
| Total Soluble and/or Insoluble Fibers | | | | 0.20 | 10.00 | 1.41% | 90.70% |

## TABLE ONE - CALORIC CONTENT

| Item | gms Lower | gms Upper | Cals/gm | Cals Lower | Cals Upper |
|---|---|---|---|---|---|
| Protein | 1.00 | 4.00 | 4.0 | 4.00 | 16.00 |
| GMP | 0.03 | 1.00 | 4.0 | 0.12 | 4.00 |
| Oleic Acid | 3.00 | 9.00 | 9.0 | 27.00 | 81.00 |
| Soluble or Insoluble Fibers | 1.50 | 7.00 | 0 | 0 | 0 |
| Total | 5.53 | 21.00 | | 31.12 | 101.00 |

## TABLE TWO - CALORIC CONTENT

| Item | gms Lower | gms Upper | Cals/gm | Cals Lower | Cals Upper |
|---|---|---|---|---|---|
| Protein | 0.10 | 10.0 | 4.0 | 0.40 | 40.00 |
| GMP | 0.025 | 10.0 | 4.0 | 0.10 | 40.00 |
| Oleic Acid | 1.05 | 15.0 | 9.0 | 9.45 | 135.00 |
| Soluble or Insoluble Fibers | 0.20 | 10.00 | 0 | 0 | 0 |
| Total | 1.425 | 45.15 | | 9.95 | 215.00 |

## TABLE THREE - CALORIC CONTENT

| Item | gms Lower | gms Upper | Cals/gm | Cals Lower | Cals Upper |
|---|---|---|---|---|---|
| GMP | 0.025 | 10.00 | 4.0 | 0.10 | 40.00 |
| Oleic Acid | 1.05 | 15.00 | 9.0 | 9.45 | 135.00 |
| Soluble or Insoluble Fibers | 0.20 | 10.00 | 0 | 0 | 0 |
| Total | 1.325 | 35.15 | | 9.55 | 175.00 |

The nutritional intervention composition includes a flavor component for imparting a characteristic taste to the nutritional intervention composition selected from the group consisting of water soluble, natural or artificial extracts that include apple, banana, cherry, cinnamon, cranberry, grape, honeydew, honey, kiwi, lemon, lime, orange, peach, peppermint, pineapple, raspberry tangerine, watermelon, wild cherry and equivalents thereof; being in the range of 1.10 to 3.00 grams by weight of the composition.

The nutritional intervention composition may be used as a food additive added to foods selected from the group consisting of yogurt, jello, apple sauce, cottage cheese, cereal, bread, and candy bars.

The nutritional intervention composition maybe used as a food additive added to drinks selected from the group consisting of apple juice, orange juice, grape juice, grapefruit juice, cranberry juice, coffee, tea, milk, milkshakes, broth, and soup consomme

Experiment One-Consumption Of the Nutritional Intervention Composition of the Present Invention Prior To A Meal

Ten normal weight subjects (Body Mass Index = 24) were administered either a placebo containing polydextrose or one containing the nutritional intervention composition of the present invention. Both the placebo and the nutritional intervention composition of the present invention were mixed with 8 oz of water. Both drinks contain 80 calories. Following consumption of either drink subjects consumed a meal consisting of 350 g (385 cal) of Stouffers macaroni and beef casserole. Two satiety tests were performed. On one occasion subjects drank 8 oz of the beverage containing the nutritional intervention composition of the present invention and the placebo beverage on the other occasion. Subjects were permitted

fifteen minutes to consume their meal. Subjects rated hunger and other questions using a computer before and after drinking the beverage, before and after eating the meal and every fifteen minutes for three and one half hours after the meal. A two way repeated measure analysis of variance was used to evaluate the effect of the nutritional intervention composition of the present invention. The subjects were asked to give their ratings to the following questions:

1. How hungry do you feel right now?
2. How thirsty do you feel right now?
3. How much food would you like to eat right now?

The results showed there was no difference between the groups with regards to thirst but there was significant difference ($p<0.05$) with regard to hunger and how much food the subjects felt they could eat. At two hours there was a significant difference in hunger ratings and this difference continued to the end of the experiment. Similar results were seen in response to subjects' subjective ratings to the question, how much food could they eat.

Experiment Two-Addition Of the Nutritional Intervention Composition of the Present Invention to Food

Ten normal weight subjects (Body Mass Index = 24) were administered either a placebo yogurt containing polydextrose or the nutritional intervention composition of the present invention in low fat yogurt.

Subjects received both formulations three days apart in a crossover double blind designed protocol. Following consumption of the yogurt containing either the placebo or the nutritional intervention composition of the present invention, subjects measured hunger and thirst sensations using a visual analog scale. Measurements were taken every fifteen minutes for three and a half hours. The results showed there

was no difference in thirst sensation, however there was a significant difference in hunger ratings. At 45 minutes subjects receiving a yogurt that contained the nutritional intervention composition of the present invention had significant less hunger and this decreased hunger was extended for almost two hours and ten minutes. An analysis of variance showed a significant treatment effect with a p value less than 0.05. When subjects were asked to rate "how much food they could eat" over the duration of the test there was a significant difference between subjects taking the placebo yogurt and subjects taking yogurt containing the nutritional composition of the present invention. Subjects taking the nutritional intervention composition of the present invention had a significantly less desire to eat. An analysis of variance showed a significant treatment effect with a p value less than 0.05.

Experiment Three-Effect of the Nutritional Intervention Composition of the Present Invention on weight loss and appetite over six weeks

In an open trial 113 overweight subjects (Body Mass Index=27-32) between the ages of 22-55 were administered the nutrition composition of the present invention three times a day 15 minutes prior to their breakfast, lunch and dinner meals for a period of six weeks. Subjects were asked to maintain a 1740 calorie per day diet and materials were given to them to assist in their meal planning.

Each week subjects were asked to fill out a questionnaire measuring global satiety. They were asked whether they agreed or disagreed with the following statements:

1. I have experienced changes in my appetite.
2. I crave food all the time.
3. I have no appetite at all.

The results showed there was a mean weight loss of 8.82 lbs. In addition, the subjects experienced a significant change in mean satiety scores when their subjective feelings of hunger, fullness and appetite were compared to the pre-study readings.

- At the end of the study 49% of the respondents Agreed/Strongly Agreed with the statement "I have experienced changes in my appetite" compared to 28% prior to the study.
- At the end of the study 11% of the respondents Agreed/Strongly Agreed with the statement "I crave food all the time" compared to 33% prior to the study.
- At the end of the study 8% of the respondents Agreed/Strongly Agreed with the statement "I have no appetite at all" compared to 4% prior to the study.
- Respondents who lost more than 5 lbs had a greater change in mean satiety ratings over the course of the study.

The results of this open trial show that the nutritional composition of the present invention increased satiety and reduced hunger cravings in subjects that were on a calorically restricted diet. In addition the nutritional composition of the present invention produced a mean weight loss of 8.82 lbs.

## ADVANTAGES OF THE PRESENT INVENTION

Accordingly an advantage of the present invention is that it provides a nutrition intervention composition for enhancing satiety before a meal.

Another advantage of the present invention is that it provides a nutrition intervention composition to extend satiety after a meal.

Another advantage of the present invention is that it provides a nutrition intervention composition that can be consumed prior to a meal to enhance satiety.

Another advantage of the present invention is to provide a nutrition intervention composition that can be added to food to extend the satiating effect of the food to which it is added.

Another advantage of the present invention is that it provides a nutrition intervention composition that it stimulates cholecystokinin release in a calorically efficient manner.

Another advantage of the present invention is that it provides a nutrition intervention composition that increases cholecystokinin by stimulating its release through a combination of nutritional agents.

Another advantage of the present invention is that it provides a nutrition intervention composition that blocks the inhibition of cholecystokinin release by binding soluble and insoluble fibers to bile acids and to bile salts.

Another advantage of the present invention is that it provides a nutrition intervention composition to cause weight loss resulting from a reduced caloric intake.

Another advantage of the present invention is that it provides a nutrition intervention composition to provide better glycemic control for Type II diabetics.

Another advantage of the present invention is that it provides a nutrition intervention composition to help Type II diabetics enhance and extend satiety in a calorically efficient fashion.

Another advantage of the present invention is that it provides a nutrition intervention composition to increase satiety in bulimics who have a defect in their normal CCK release mechanism.

Another advantage of the present invention is that it provides a nutrition intervention composition to help in the management of the bulimic patients.

Another advantage of the present invention is that it provides a nutrition intervention composition that is palatable, well tolerated and without side effects to individuals.

## WHAT IS CLAIMED IS:

1. A nutritional intervention composition to be taken before or during consumption of a meal for enhancing and extending post meal satiety for reducing weight, comprising:

a) a protein selected from the group consisting of casein, whey and soy being in the range of 0.22% to 88.30% by weight of said composition;

b) a glycomacropeptide or caseinmacropeptide being in the range of 0.06% to 87.72% by weight of said composition;

c) at least one long chain fatty acid between $C_{12}$ and $C_{18}$ in length being in the range of 2.42% to 97.25% by weight of said composition; and

d) at least one member selected from the group consisting of: at least one soluble fiber, at least one insoluble fiber and mixtures thereof for binding bile salts being in the range of 0.44% to 89.09% by weight of said composition, wherein said composition is in a dry powder form.

2. A nutritional intervention composition in accordance with Claim 1, wherein said composition additionally contains at least one of: a flavoring component; an emulsifier; plant saponins; a sweetener; calcium; and a bile acid sequestering agent.

3. A nutritional intervention composition in accordance with Claims 1 or 2, wherein said at least one soluble fiber is selected from the group consisting of guar, glucomannan, potato, methyl cellulose, psyllium and sugar beet, said at least one insoluble fiber is selected from the group consisting of cellulose and potato, said at least one long chain fatty acid between $C_{12}$ and $C_{18}$ in length is oleic acid, said emulsifier is lecithin and said bile acid sequestering agent is cholestyramine.

4. A nutritional intervention composition to be taken before or during a meal for enhancing and extending post meal satiety for reducing weight, comprising:

a) a glycomacropeptide or caseinmacropeptide being in the range of 0.18% to 89.29% by weight of said composition;

b) at least one long chain fatty acid between $C_{12}$ and $C_{18}$ in length being in the range of 4.76% to 94.67% by weight of said composition; and

c) at least one member selected from the group consisting of: at least one soluble fiber, at least one insoluble fiber and mixtures thereof for binding bile salts being in the range of 1.41% to 90.70% by weight of said composition, wherein said composition is in dry powder form.

5. A nutritional intervention composition in accordance with Claim 4, wherein said composition additionally contains at least one of: a flavoring component; an emulsifier; plant saponins; a sweetener; calcium; protein and a bile acid sequestering agent.

6. A nutritional intervention composition in accordance with Claims 4 or 5, wherein said at least one soluble fiber is selected from the group consisting of guar, glucomannan, potato, methyl cellulose, psyllium and sugar beet, said at least one insoluble fiber is selected from the group consisting of cellulose and potato, said at least one long chain fatty acid between $C_{12}$ and $C_{18}$ in length is oleic acid, said emulsifier is lecithin, said protein is selected from the group consisting of casein, whey and soy, and said bile acid sequestering agent is cholestyramine.

7. A nutritional intervention composition to be taken before or during a meal for enhancing and extending post meal for reducing weight, comprising:

a) a protein selected from the group consisting of casein, whey and soy being in the range of 3.89% to 44.97% by weight of said composition;

b) a glycomacropeptide or caseinmacropeptide being in the range of 0.11% to14.57% by weight of said composition;

c) long chain fatty acids between $C_{12}$ and $C_{18}$ in length being in the range of 9.22% to 69.79% by weight of said composition; and

d) a combination of soluble fibers and insoluble fibers for binding bile salts being in the range of 6.47% to 61.40% by weight of said composition, wherein said composition is in dry powder form.

8. A nutritional intervention composition in accordance with Claim 7, wherein said composition additionally contains at least one of: a flavoring component; an emulsifier; plant saponins; a sweetener; calcium; and a bile acid sequestering agent.

9. A nutritional intervention composition in accordance with Claims 7 or 8, wherein: said at least one soluble fiber is selected from the group consisting of guar, glucomannan, potato, methyl cellulose, psyllium and sugar beet; said at least one insoluble fiber is selected from the group consisting of cellulose and potato; said at least one long chain fatty acid between $C_{12}$ and $C_{18}$ in length includes oleic acid being in the range of 3.89% to 44.97% by weight of said composition; said emulsifier is lecithin; said sweetener is aspartame; said calcium comprises calcium lactate, calcium carbonate, calcium citrate and calcium maleate; and said bile acid sequestering agent is cholestyramine.

10. A nutritional intervention composition to be taken before or during a meal for enhancing and extending post meal for reducing weight, comprising:

a) a protein selected from the group consisting of casein, whey and soy being in the range of 3.89% to 44.97% by weight of said composition;

b) a glycomacropeptide or caseinmacropeptide being in the range of 0.11% to 14.57% by weight of said composition;

c) long chain fatty acids between $C_{12}$ and $C_{18}$ in length being in the range of 8.46% to 48.10% by weight of said composition;

d) oleic acid being in the range of 3.89% to 44.97% by weight of said composition; and

e) soluble fibers for binding bile salts being in the range of 3.89% to 44.97% by weight of said composition; and

f) insoluble fibers for binding bile salts being in the range of 1.91% to 35.74% by weight of said composition, wherein said composition is in dry powder form.

11. A nutritional intervention composition in accordance with Claim 10, wherein said composition additionally contains at least one of: a flavoring component; an emulsifier; plant saponins; a sweetener; calcium; and a bile acid sequestering agent.

12. A nutritional intervention composition in accordance with any one of Claims 1 through 11, wherein said composition is added to a liquid to form a liquid drink or is added to other foods.

13. The use of a nutritional intervention composition in accordance with any one of Claims 1 through 11 for enhancing post-meal satiety for reducing weight.

14. The use of a nutritional intervention composition in accordance with any one of Claims 1 through 11 for stimulating cholecystokin (CCK) levels in a calorically efficient manner for reducing weight.

15. The use in accordance with Claim 14, wherein the nutritional intervention composition is added to a liquid to form a liquid drink or is added to other foods.

16. The use of a nutritional intervention composition in accordance with any one of Claims 1 through 11 wherein the composition is formulated to be added to a liquid to form a liquid drink or to be added to other foods.

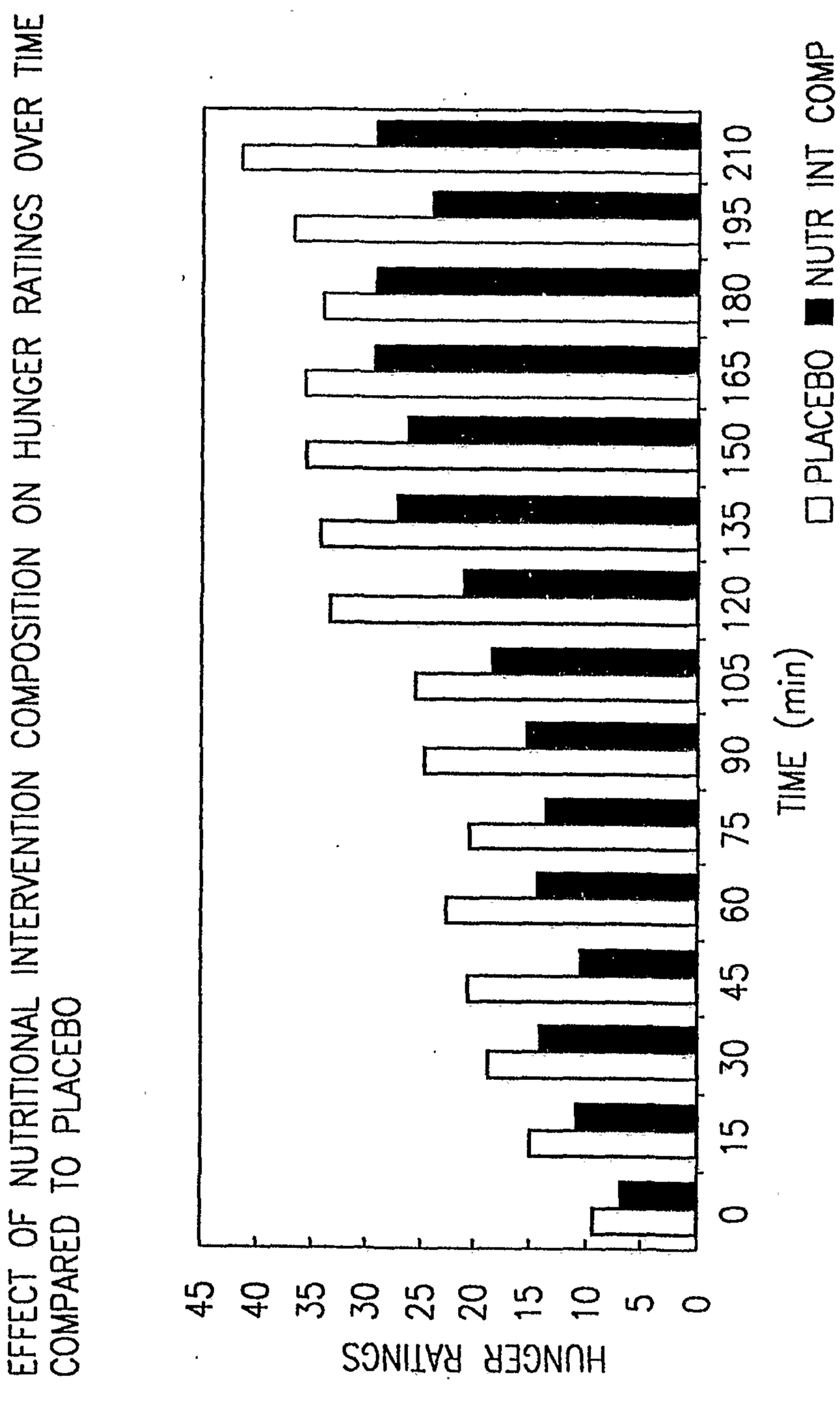

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON HUNGER RATINGS OVER TIME
COMPARED TO PLACEBO
HUNGER RATINGS
0
5
10
15
20
25
30
35
40
45
0
15
30
45
60
75
90
105
120
135
150
165
180
195
210
TIME (min)
□ PLACEBO ■ NUTR INT COMP

*FIG. 1*

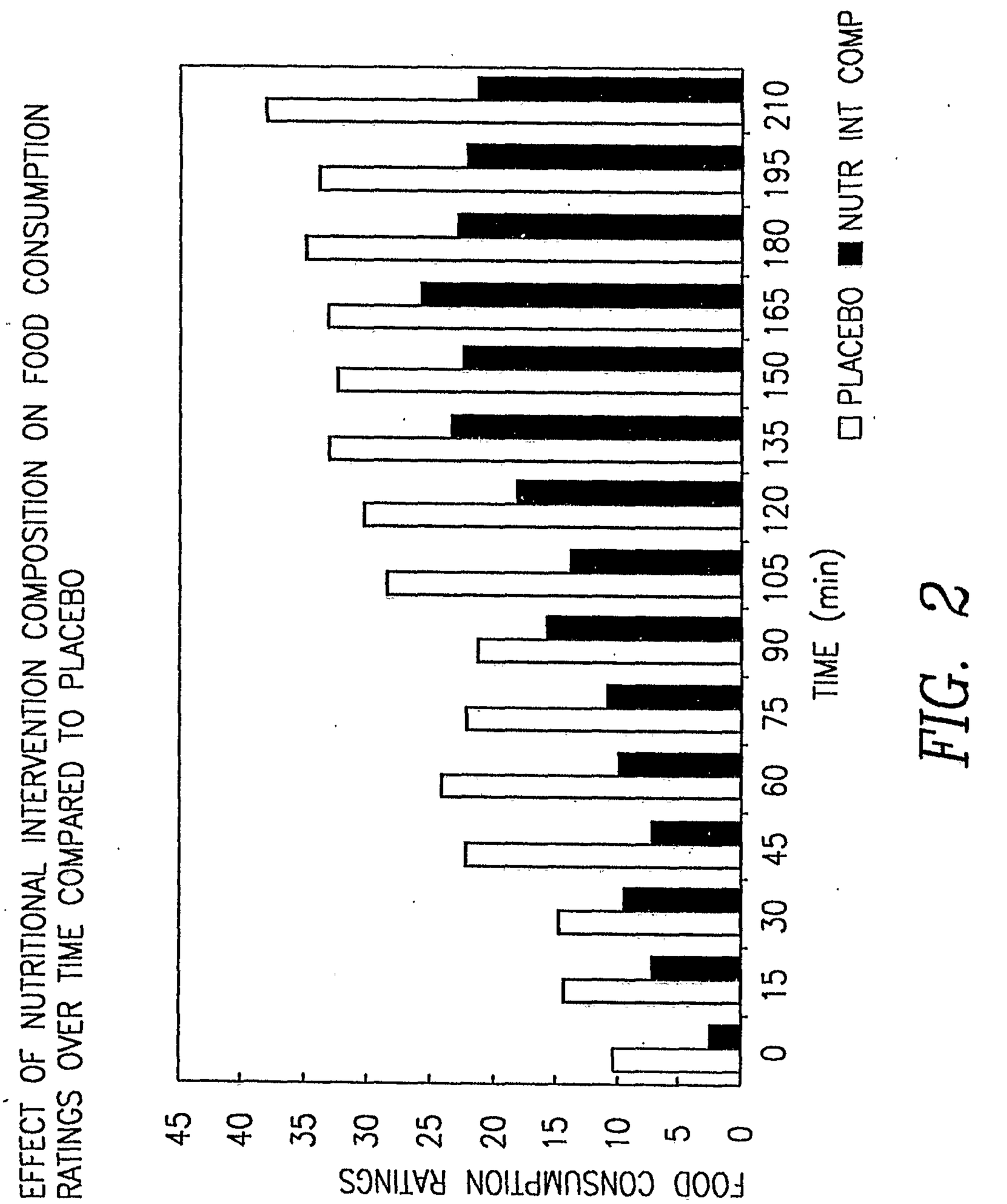

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON FOOD CONSUMPTION
RATINGS OVER TIME COMPARED TO PLACEBO
FOOD CONSUMPTION RATINGS
0
5
10
15
20
25
30
35
40
45
0
15
30
45
60
75
90
105
120
135
150
165
180
195
210
TIME (min)
□ PLACEBO ■ NUTR INT COMP

FIG. 2

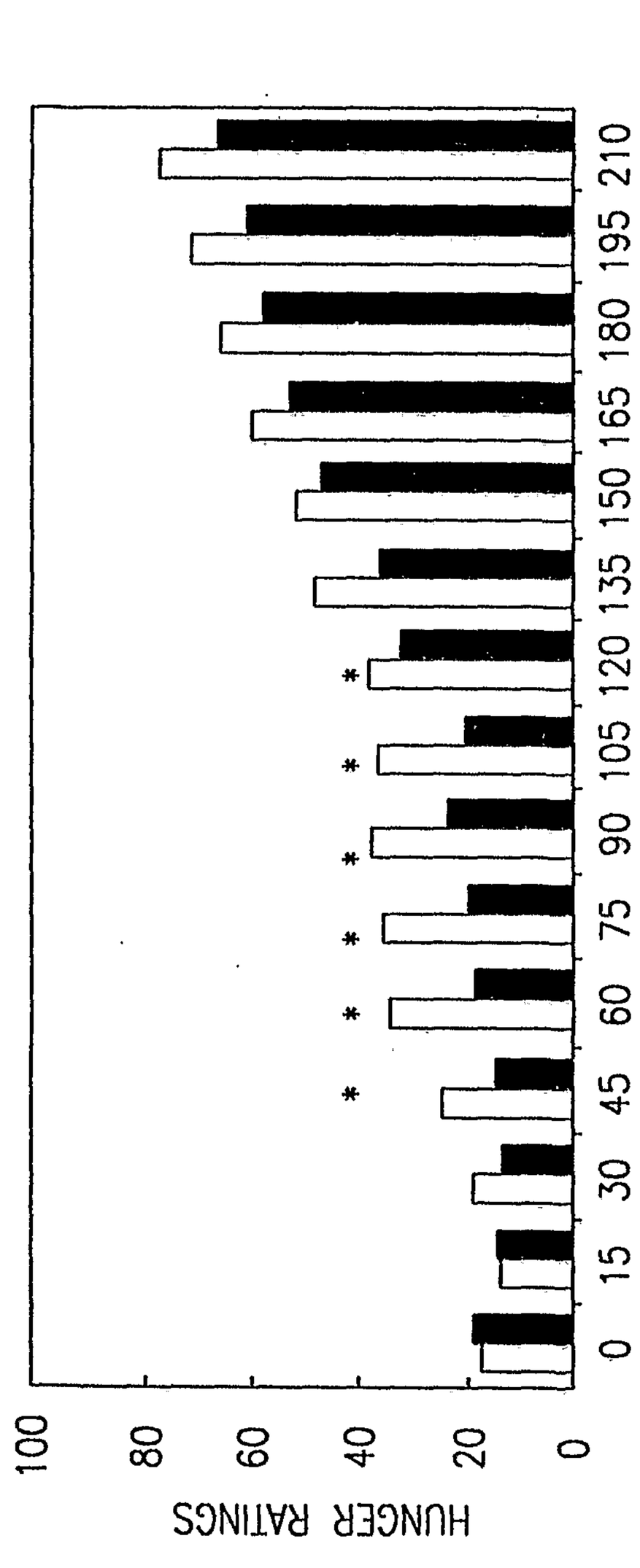

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION OR PLACEBO ADDED TO YOGURT
ON HUNGER RATINGS OVER TIME COMPARED TO PLACEBO
HUNGER RATINGS
100
80
60
40
20
0
0 15 30 45 60 75 90 105 120 135 150 165 180 195 210
TIME (min)
* * * * * *
□ PLACEBO ■ NUTR INT COMP
*= P<.05

FIG. 3

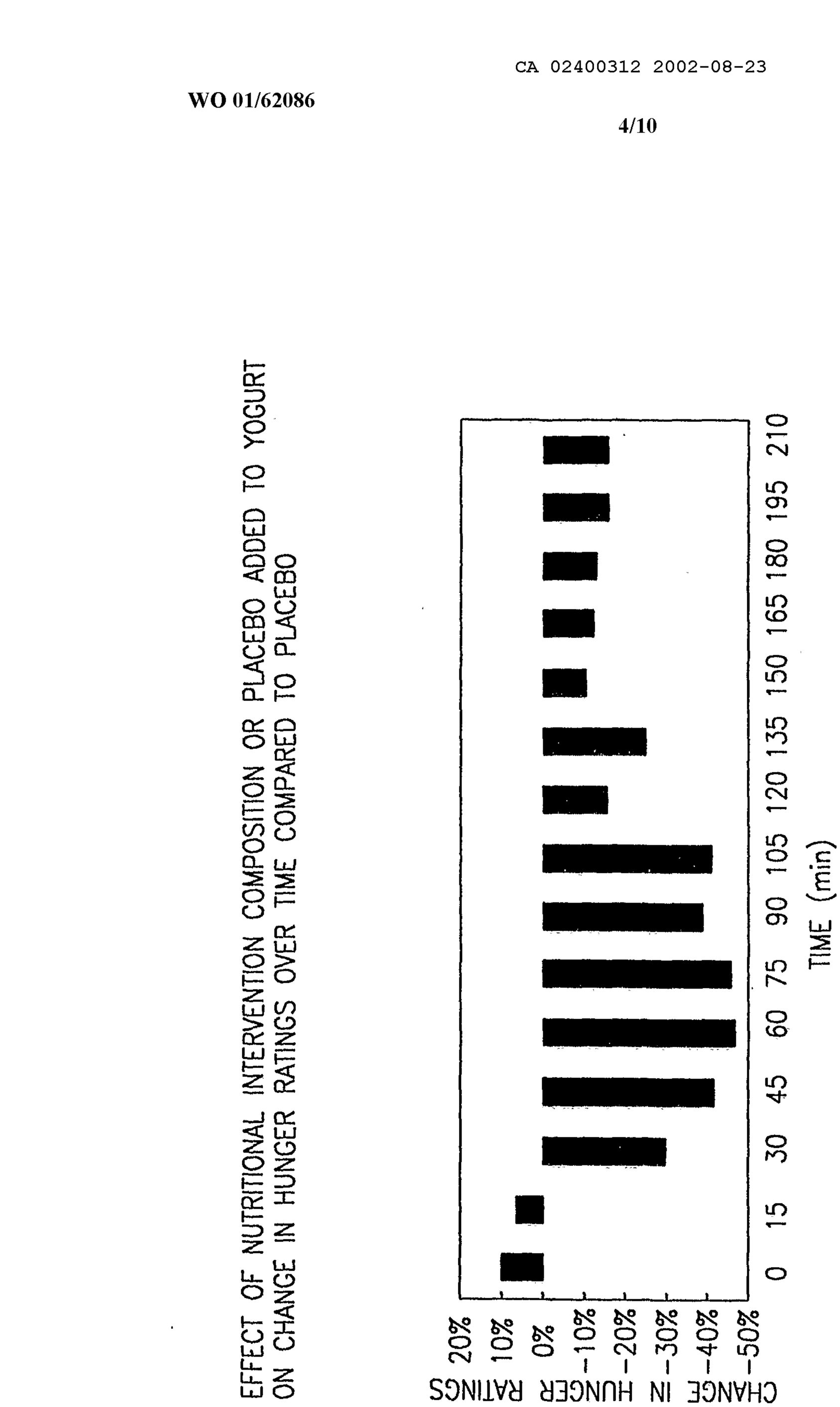

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION OR PLACEBO ADDED TO YOGURT
ON CHANGE IN HUNGER RATINGS OVER TIME COMPARED TO PLACEBO
CHANGE IN HUNGER RATINGS
20%
10%
0%
−10%
−20%
−30%
−40%
−50%
0 15 30 45 60 75 90 105 120 135 150 165 180 195 210
TIME (min)

FIG. 4

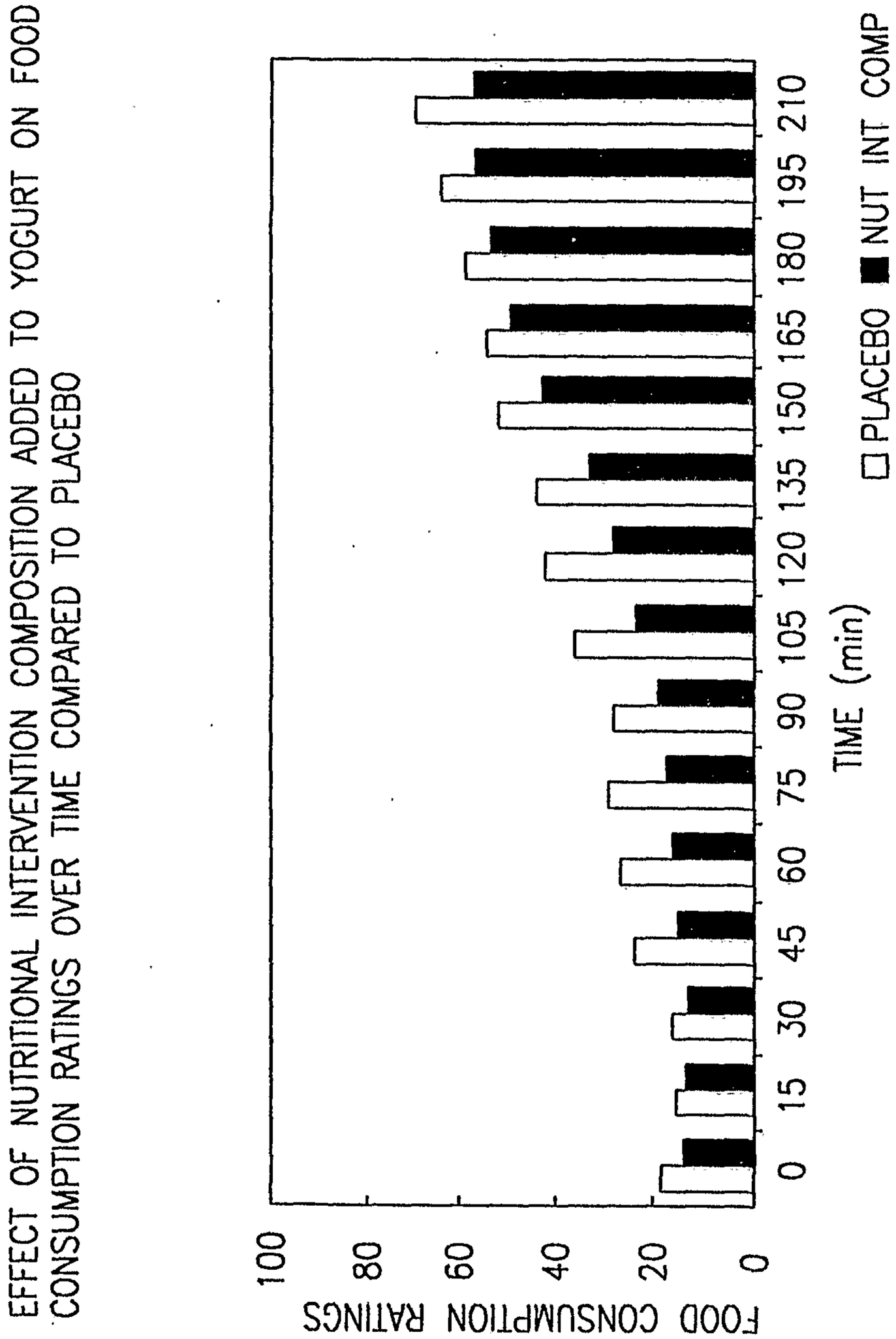

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ADDED TO YOGURT ON FOOD CONSUMPTION RATINGS OVER TIME COMPARED TO PLACEBO
FOOD CONSUMPTION RATINGS
100
80
60
40
20
0
0 15 30 45 60 75 90 105 120 135 150 165 180 195 210
TIME (min)
□ PLACEBO ■ NUT INT COMP

*FIG. 5*

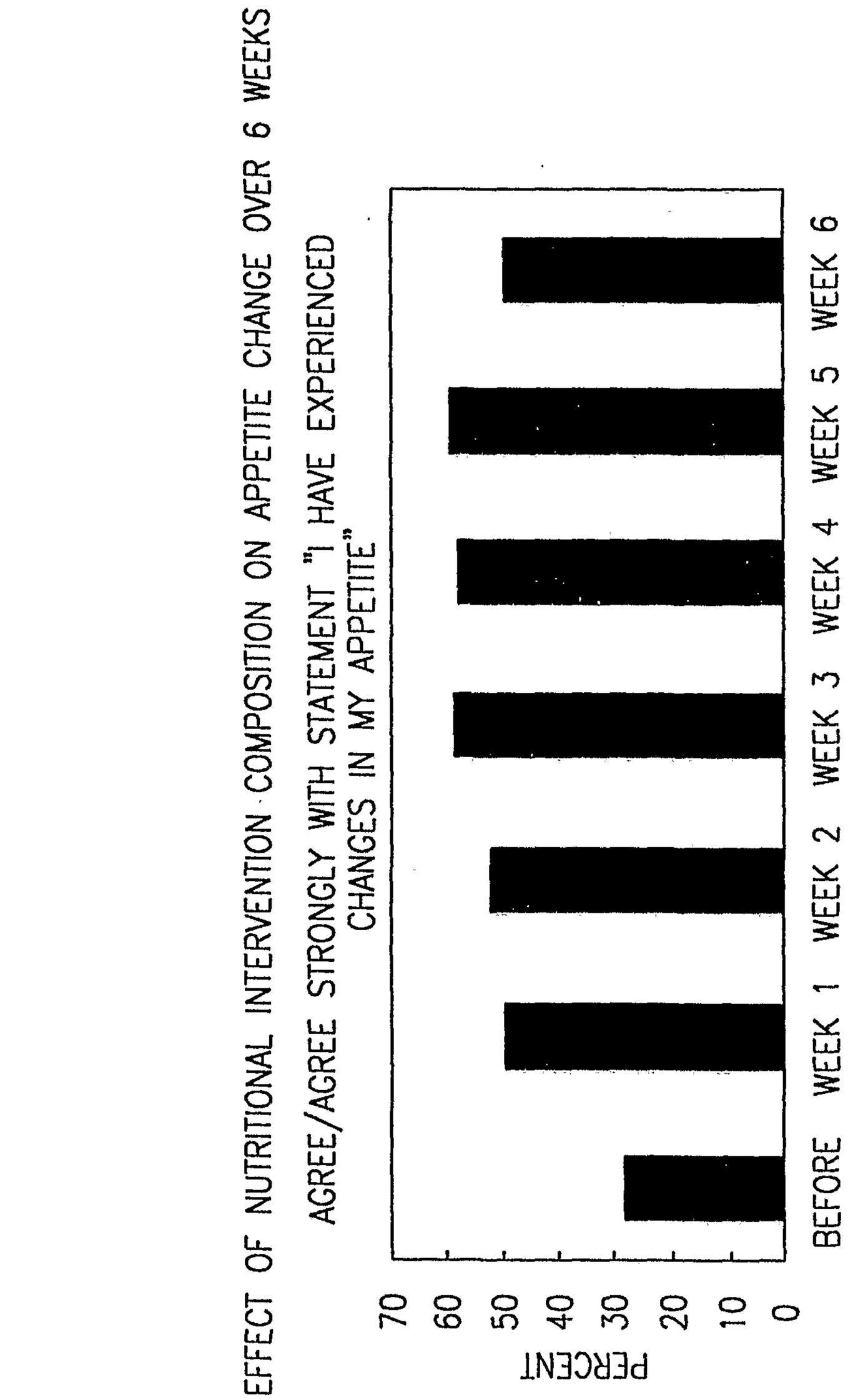

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON APPETITE CHANGE OVER 6 WEEKS
AGREE/AGREE STRONGLY WITH STATEMENT "I HAVE EXPERIENCED CHANGES IN MY APPETITE"
PERCENT
70
60
50
40
30
20
10
0
BEFORE
WEEK 1
WEEK 2
WEEK 3
WEEK 4
WEEK 5
WEEK 6

FIG. 6

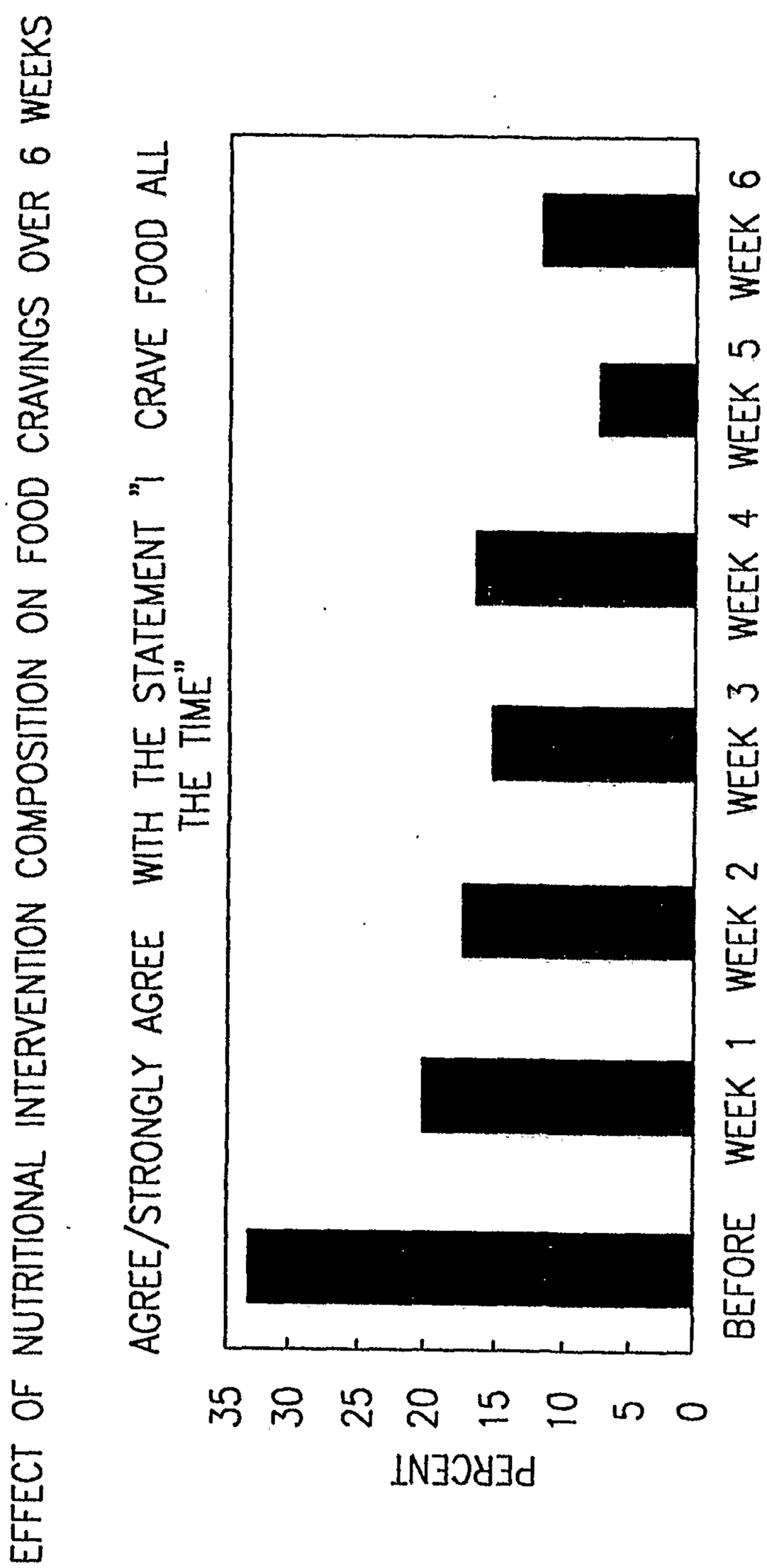

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON FOOD CRAVINGS OVER 6 WEEKS
PERCENT AGREE/STRONGLY AGREE WITH THE STATEMENT "I CRAVE FOOD ALL THE TIME"
35
30
25
20
15
10
5
0
BEFORE WEEK 1
WEEK 2
WEEK 3
WEEK 4
WEEK 5
WEEK 6

FIG. 7

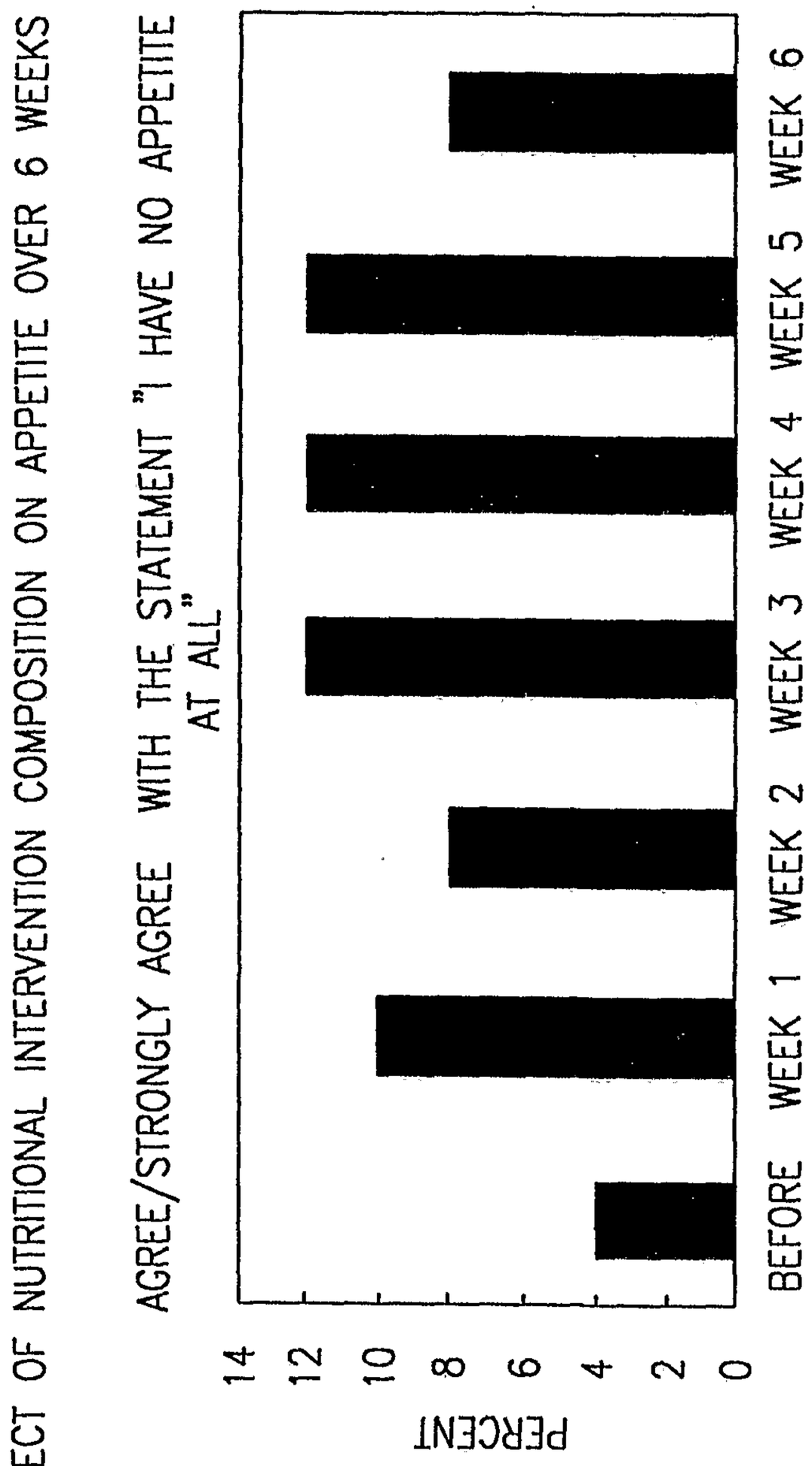

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON APPETITE OVER 6 WEEKS
AGREE/STRONGLY AGREE WITH THE STATEMENT "I HAVE NO APPETITE AT ALL"
PERCENT
0
2
4
6
8
10
12
14
BEFORE WEEK 1
WEEK 2
WEEK 3
WEEK 4
WEEK 5
WEEK 6

FIG. 8

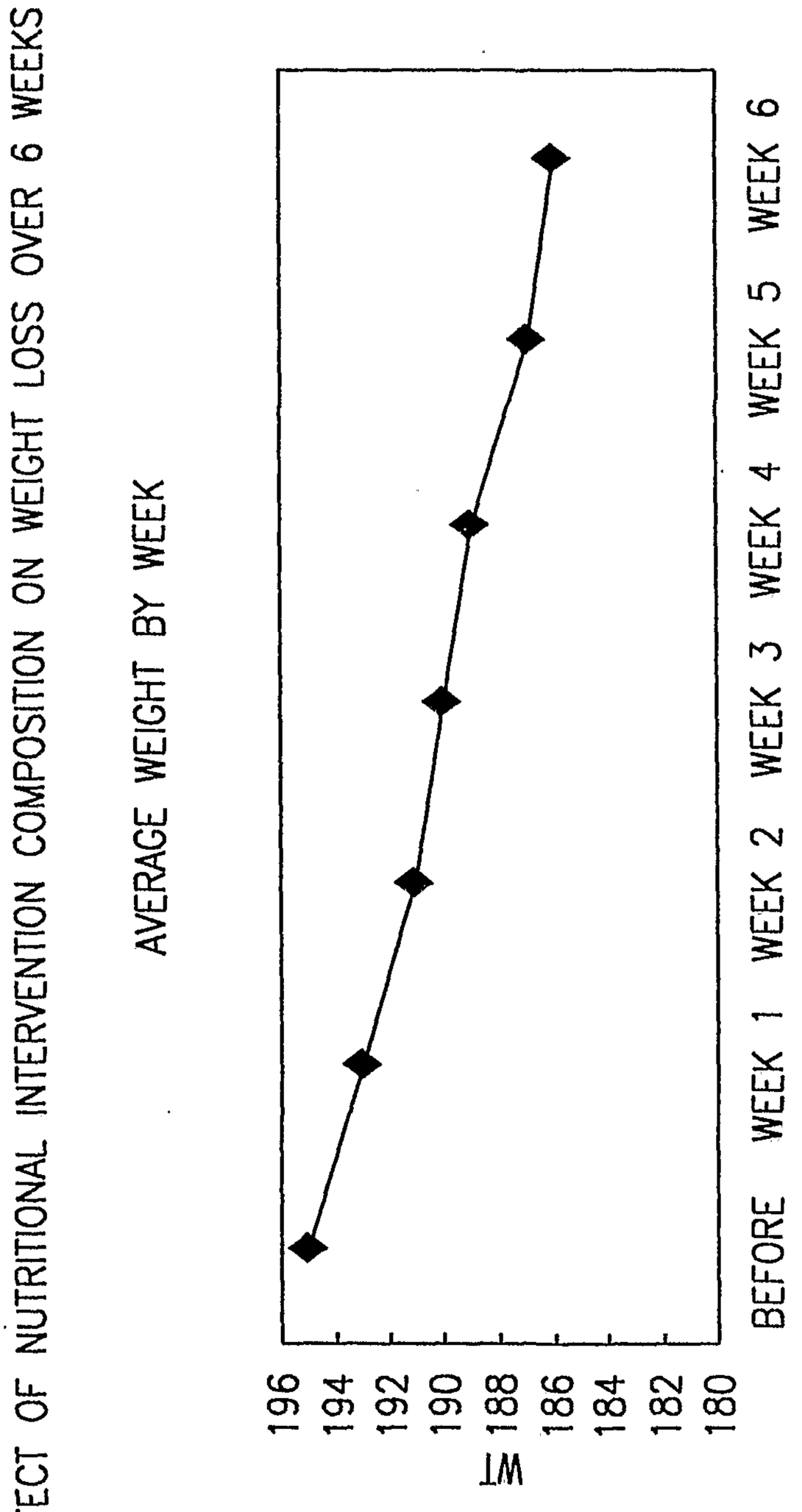

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON WEIGHT LOSS OVER 6 WEEK
AVERAGE WEIGHT BY WEEK
WT
96
94
92
90
88
86
84
82
80
BEFORE
WEEK 1
WEEK 2
WEEK 3
WEEK 4
WEEK 5
WEEK 6

FIG. 9

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EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON SATIETY RATINGS OVER 6 WEEKS

| | TEST GROUP | | | | | | |
|---|---|---|---|---|---|---|---|
| | BEFORE | WEEK 1 | WEEK 2 | WEEK 3 | WEEK 4 | WEEK 5 | WEEK 6 |
| BASE: TOTAL COMPLETERS | (113) | (113) | (113) | (113) | (113) | (113) | (113) |
| | A | | | | | | B |
| I HAVE EXPERIENCED CHANGES IN MY APPETITE | 3.3 | 2.7 | 2.6 | 2.4 | 2.5 | 2.4 | 2.6 |
| I CRAVE FOOD ALL THE TIME | 3.2 | 3.7 | 3.5 | 3.6 | 3.6 | 3.8 | 3.7 |
| I HAVE NO APPETITE AT ALL | 4.4 | 3.9 | 3.9 | 3.8 | 3.8 | 3.7 | 3.8 |

*FIG.10*

EFFECT OF NUTRITIONAL INTERVENTION COMPOSITION ON HUNGER RATINGS OVER TIME COMPARED TO PLACEBO

