EFFECT OF ISPAGHULA HUSK (FYBOGEL®) ON BODY WEIGHT AND BIOCHEMICAL PROFILES OF THE OBESE NIDDM PATIENTS

ORAPIN CHOOTHAWORNCHAIKUL

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Orapin Choothawornchaikul

Miss Orapin Choothawornchaikul
Candidate

Prof. Surat Komindr, M.D.
Major- Advisor

Assoc.Prof. Winai Dahlan, Ph.D.
Co-advisor

Oravan Puchaiwattananon

Miss Oravan Puchaiwattananon, Ph.D.
Co-advisor

Prof. Liangchai Limlomwongse,Ph.D.
Dean
Faculty of Graduate Studies

Prof. Voranunt Suphipat, Ph.D.
Chairman
Master of Science, Programme in Nutrition
Faculty of Medicine,
Ramathibodi Hospital

Thesis

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on
February 29, 2000

Orapin Choothe.

Miss Orapin Choothawornchaikul
Candidate

Surkomindr, M.D

Prof. Surat Komindr, M.D.
Chairman

Assoc.Prof. Winai Dahlan, Ph.D.
Member

Supujchara Nopchinda

Miss Supujchara Nopchinda, D.Sc.
Member

Oravan Puchaiwattananon

Miss Oravan Puchaiwattananon, Ph.D.
Member

Prof. Liangchai Limlomwongse,Ph.D.
Dean
Faculty of Graduate Studies
Mahidol University

Prakit Vathesatogkit

Prof. Prakit Vathesatogkit, M..D., ABIM., FCCP.
Dean
Faculty of Medicine,
Ramathibodi Hospital
Mahidol University

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ORAPIN CHOOTHAWORNCHAIKUL : EFFECT OF ISPAGHULA HUSK (FYBOGEL®) ON BODY WEIGHT AND BIOCHEMICAL PROFILES OF THE OBESE NIDDM PATIENTS. THESIS ADVISORS : SURAT KOMINDR, M.D., WINAI DAHLAN, Ph.D., ORAVAN PUCHAIWATTANANON, D.Sc, SUPUJCHARA NOPCHINDA, D.Sc. 187 p. ISBN 974-663-692-8

The present study was designed to evaluate the effect of supplementation of Ispaghula husk (Fybogel®) on body weight, fasting plasma glucose(FPG), glycosylated hemoglobin (HbA_{1c}) and serum lipid levels. The study was a 24-week, randomized, double-blind, placebo-controlled, parallel design in 35 obese NIDDM patients with mild to moderate hypercholesterolemia. They were instructed to maintain 1,000 kcal/day diet only for 8 wks followed by 16 wks of treatment with 1 sachet of Fybogel® (3.5 g of Ispaghula) in 150 ml. of water or placebo before 3 mealtimes according to the randomization.

The result showed no statistically differences in all parameters during diet-only phase in both groups. No significant reduction on BW, FPG, HbA_{1c}, and serum lipid levels was observed with placebo treatment. During treatment with Fybogel®, reduction of BW was observed and significant differences from wk8 ($p<.05$) were seen at wk20 (-0.88±1.55 kg) and wk24 (-1.28±1.96 kg). Reductions of FPG and HbA_{1c} by 16.1% and 10.12% respectively ($p<.05$ and .01) were found at wk24. Cholesterol lowering was seen in the moderate to high hypercholesterolemic subjects by 14.2%. In comparison to placebo, Fybogel® treatment reduced significantly in the BW at wk20 and wk24 ($p<.05$), FPG at wk16 ($P<.05$)and wk24 ($P<.01$), TC at wk16 ($P<.05$), HbA_{1c} and LDL-C levels at wk24. Fybogel® did not affect serum levels of HDL-C and triglycerides. Vitamin and mineral status were maintained throughout Fybogel® treatment period.

The results demonstrate that Ispaghula husk (Fybogel®) 3.5 g before 3 meal-times helps to control the body weight, improve the long-term glycemic control and lower total cholesterol levels without adverse effect on vitamin and mineral status.

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อรพินท์ ชูถาวรชัยกุล : ผลของอิสปากุห์ลาฮัสค์ (ฟัยโบเจล) ต่อการเปลี่ยนแปลงของน้ำหนักตัวและค่าทางชีวเคมีของผู้ป่วยอ้วนที่เป็นเบาหวานชนิดไม่พึ่งอินสุลิน (EFFECT OF ISPAGHULA HUSK (FYBOGEL®) ON BODY WEIGHT AND BIOCHEMICAL PROFILES OF THE OBESE NIDDM PATIENTS.) คณะกรรมการควบคุมวิทยานิพนธ์ : สุรัตน์ โคมินทร์, พ.บ., วินัย ดะห์ลัน , Ph.D., อรวรรณ ภู่ชัยวัฒนานนท์, วท.ด., สุภัจฉรา นพจินดา, วท.ด. 187 หน้า. ISBN 974-663-692-8

การศึกษานี้มีจุดประสงค์เพื่อศึกษาผลของการเสริมอิสปากุห์ลาฮัสค์ (ฟัยโบเจล) ต่อน้ำหนักตัว ระดับน้ำตาลและระดับไขมันในเลือด ในผู้ป่วยอ้วนที่เป็นเบาหวานชนิดไม่พึ่งอินสุลินและมีระดับโคเลสเตอรอลสูงเป็นเวลา 24 สัปดาห์ ผู้ป่วยทุกคนได้รับคำแนะนำให้รับประทานอาหารมีปริมาณพลังงาน 1000 แคลอรี่ต่อวัน ตลอดระยะเวลาการศึกษา โดย 8 สัปดาห์แรกผู้ป่วยได้รับคำแนะนำในการควบคุมอาหารเพียงอย่างเดียว หลังจากนั้นแบ่งผู้ป่วยออกเป็น 2 กลุ่มโดยการสุ่ม เพื่อได้รับการเสริมด้วยฟัยโบเจลหรือยาหลอกเป็นระยะเวลา 16 สัปดาห์ โดยผสมฟัยโบเจลหรือยาหลอก 1 ซอง (ฟัยโบเจล 1 ซอง มีปริมาณอิสปากุห์ลา ฮัสค์ 3.5 กรัม) ในน้ำ 150 มิลลิลิตร รับประทานก่อนอาหาร 3 มื้อ ผลการศึกษาพบว่าน้ำหนักตัว ระดับน้ำตาลและไขมันในกระแสเลือด ของทั้ง 2 กลุ่มไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติในช่วงที่ได้รับคำแนะนำเพื่อควบคุมอาหารเพียงอย่างเดียว กลุ่มที่ได้รับการเสริมด้วยยาหลอกพบว่าน้ำหนักตัว ระดับน้ำตาลและไขมันไม่ลดลงอย่างมีนัยสำคัญทางสถิติ กลุ่มที่ได้รับการเสริมด้วยฟัยโบเจล พบว่าน้ำหนักตัวลดลงในสัปดาห์ที่20 0.88 ± 1.55 กิโลกรัม และสัปดาห์ที่24 1.28 ± 1.96 กิโลกรัม จากสัปดาห์ที่8 อย่างมีนัยสำคัญทางสถิติ นอกจากนั้นในสัปดาห์ที่24 พบว่าระดับน้ำตาลในเลือดลดลง 16.1% ค่าของฮีโมโกลบินเอวันซีลดลง 10.1% จากสัปดาห์ที่8 อย่างมีนัยสำคัญทางสถิติ ระดับโคเลสเตอรอลลดลงอย่างมีนัยสำคัญเฉพาะในกลุ่มผู้ป่วยที่มีระดับโคเลสเตอรอลสูงปานกลางถึงสูงมาก โดยลดลง 14.2% เมื่อเปรียบเทียบความแตกต่างระหว่างกลุ่มพบว่ามีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างกลุ่มที่ได้รับฟัยโบเจลและกลุ่มยาหลอกของน้ำหนักตัวในสัปดาห์ที่20 และ 24 ความแตกต่างของระดับน้ำตาลในเลือดที่สัปดาห์ที่16 และ 24 ค่าฮีโมโกลบินเอวันซี โคเลสเตอรอล และแอลดีแอลโคเลสเตอรอลในสัปดาห์ที่24 ฟัยโบเจลไม่มีผลต่อการเปลี่ยนแปลงของระดับเอชดีแอลโคเลสเตอรอล ไตรกลีเซอไรด์ และระดับวิตามินและเกลือแร่ จากผลการศึกษาสรุปได้ว่า การเสริมด้วยอิสปากุห์ลาฮัสค์ (ฟัยโบเจล) 3.5 กรัม ก่อนอาหาร 3 มื้อ ช่วยควบคุมน้ำหนักตัว ระดับน้ำตาล และลดระดับโคเลสเตอรอลโดยไม่มีผลต่อการเปลี่ยนแปลงของระดับวิตามินและเกลือแร่

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LIST OF ABBREVIATIONS

ALT	Alanine aminotransferase
AP	Alkaline phosphatase
AST	Aspartate aminotransferase
BFM	Body fat mass
BMI	Body mass index
BSF	Biceps skinfold thickness
BW	Body weight
CHD	Coronary heart disease
CVD	Cardiovascular disease
cm	Centimeter
d	day
dL	deciliter
DM	Diabetes milletus
FPG	Fasting plasma glucose
FFM	Fat free mass
g	gram
GGT	Gamma glutamyl transferase
Hb	Hemoglobin
Hct	Hematocrit
HDL-C	High density lipoprotein-cholesterol

hr	hour
kcal	kilo calorie
kg	kilogram
L	Liter
LDL-C	Low density lipoprotein-cholesterol
m	meter
mmol	millimole
µg	microgram
µL	microliter
mg	milligram
mL	milliliter
mm	millimeter
MUAC	Mid upper arm circumference
n	number
NCEP	National Cholesterol Education Program
NHANES	National health and Nutrition Examination Survey
NIDDM	Non-insulin-dependent diabetes mellitus
pg	picogram
RBC	Red blood cell
SCFA	Short chain fatty acid
SD	Standard deviation
SISF	Suprailiac skinfold thickness
SSF	Subscapular skinfold thickness
T_3	Triiodothyroxine

T_4	Total thyroxine
TC	Total cholesterol
TSH	Thyroid stimulating hormone
TSF	Triceps skinfold thickness
U	Unit
UAMC	Upper arm muscle circumference
WBC	White blood cell
WHO	World Health Organization
wk	week
y	year

CHAPTER I

INTRODUCTION

Problem, Statement and the Importance of Dietary Fiber

The prevalence of nutritional disorders such as coronary heart disease, diabetes, hyperlipidemia and obesity are commonly occured in industrial part of the world (1). As new technologies that segregated the rapidly digestible fractions of the food supply from the nondigestible fractions of the foods arise, the populations having such technologies available rapidly change their eating habits and consume only the digestible fractions (2). The lifestyle of Thai people nowadays inclines to accept of food consumptive western culture. This converting consumption pattern results in the commencement of various nutritional problems.

One of the most pronounced changes in dietary habit is the reduced intake of dietary fiber (3). Over the past 20 years dietary fiber has emerged as a leading dietary factor in the prevention and treatment of chronic diseases. High fiber intakes are associated with lower serum cholesterol concentrations (4), lower risk of coronary heart disease (5), reduced blood pressure (6), improved gastrointestinal function (7), reduced risks of certain forms of cancer (8), enhanced weight control (9), better glycemic control and lower risks of diabetes mellitus (10).

An epidemiological study of National Health and Nutrition Examination Survey (NHANES) in mortality of U.S. adults population with and without diabetes between 1971-1993 confirmed substantially higher risk of death, lower survival and lower life

expectancy of diabetes adults compared with nondiabetes adults (11). In the past, management of diabetes focused primarily on control of blood glucose. Today, it has been accepted that control of lipids levels is also vitally important (12). Death caused by heart disease occurs 2-3 times more often among persons with diabetes than among those without diabetes (11). Hypercholesterolemia is the major risk factor for atherosclerosis, and average serum lipid levels are higher in diabetes than nondiabetes persons (13). In the data from NHANES II, the relative risk of developing diabetes was 2.9 times greater for obese persons 20-75 y. of age than for normal weight persons (14). Obesity enhances insulin resistance (15,16), it has been shown repeatedly that weight reduction improves blood glucose control in diabetes subjects.

Dietary fiber has been defined as the skeletal remains of plant material resistant to hydrolysis by the digestive enzymes of man (17). This definition was later extended to include all polysaccharides and lignin in the diet that are not digested by endogenous secretions of the human gastrointestinal tract. These substances are classified in many ways. However, from a metabolic standpoint, it is most useful to classify them as either water soluble or not water soluble. As indicated later, the ability to form viscous gels also may be important. Only the water soluble fibers have been reported to have a significant effect on the serum glucose and cholesterol concentration (18,19).

Mechanisms to explain the hypocholesterol effects of dietary fiber remain unclear. Investigators previously attributed these effects to increase fecal excretion of bile acids(20). Recent work indicates soluble fiber may influence cholesterol and lipid metabolism at hepatic or peripheral sites (21). Soluble fibers are almost completely

fermented in the colon to short chain fatty acids, primarily acetate, propionate, and butyrate (22). These fatty acids are absorbed into the portal vein and may inhibit hepatic and peripheral cholesterol synthesis and increase LDL cholesterol clearance (23). Propionate stimulates glycolysis, facilitates glucose use. Changes in the rate of glucose absorption and serum insulin levels may also affect cholesterol and triglycerides levels (23).

High fiber diets promote weight loss for several reasons. Studies using high fiber foods and fiber supplement show high fiber intake increased satiety (24,25), delayed gastric emptying (26) and release of certain gut hormones (27) may contribute to greater satiety. Nutrients such as starch, fatty acids, and nitrogen may be less well absorbed from high fiber foods, providing slightly fewer calorie than from comparable low fiber foods (28).

Along with the potential ability of dietary fiber to reduce the risk of certain diseases, there may be the possibilities of having deleterious effects associated with the intake of high levels of dietary fiber. The major side effect is increase intestinal gas production, resulting in more flatulence. To avoid these side effects, dietary fiber intakes should be increased gradually and fluid intake should be adequate (13). Safety issues surrounding high fiber intake have focused on vitamin and mineral balance. Additional long-term studies are needed to determine whether high-fiber diets using commonly available foods adversely affect vitamin and mineral status.

Ispaghula or psyllium husk, a rich source of dietary fiber is obtained from the outer epidermis of seeds of *Plantago ovata*. It is a rich source of true fiber containing

80-85% dietary fiber with a soluble fiber content of some 80% and it has a variety of beneficial physiological effects (29).

Although nutrition counseling is now routinely used as part of the treatment regimen for those patients with diabetes, hypercholesterolemia and obesity because it is cost-effective, well tolerated, and safe but this is often neglected because of time, education, and behavior modification required. Thus, an increase in soluble fiber intake, by supplementation of ispaghula husk (Fybogel®) could have a significant impact on reducing serum cholesterol level, serum plasma glucose and promote weight loss in obese NIDDM patients.

Objectives

The objectives of the present study were as follow:

1. To investigate whether Fybogel®:can be used to control and reduce body weight in obese subjects.
2. To investigate the effects of Fybogel® on plasma glucose levels in diabetes subjects.
3. To investigate whether Fybogel® can reduce serum lipids levels .
4. To investigate the effects of Fybogel® on vitamin (A, B_1, B_2, B_{12}, C, E, K, folate) and mineral (Mg, P, Ca, Fe, Zn, Cu) status.

CHAPTER II

LITERATURE REVIEW

DIETARY FIBER

A few trips to the library revealed that dietary fiber was not new. Hippocrates (30) wrote in 430 BC that "wholemeal bread clear out the gut and passes through as excrement" suggesting that fiber role in maintaining bowel regularity had long been recognized. Graham, of Graham cracker fame, and Dr.J.H. Kellogg, of cereal fame, also promote dietary fiber in the early 1900s (mentioned in 31).

In the United States, from 1920s to 1943s although several reports on the laxative properties of fibers were published by William and Olmstead. The importance of dietary fiber in human nutrition was not accepted, and few scientific papers on dietary fiber were published during 1950s and 1960s (mentioned in 31).

In South Africa in the late 1940s, Walter found the association of dietary fiber with a decrease incidence of certain diseases in rural blacks (32). Trowell also published articles on the diseases of civilization that were inversely related to intake of dietary fiber (33). In 1956s Surgeon Captain TL Cleave proposed the idea that the diseases of civilization were caused by overconsumption of sugar and a deficiency in dietary fiber intake (34). These epidemiological associations, popularized by Burkitt in the early 1970s (35), stimulated interest and research in dietary fiber that have gained momentum throughout the last two decades.

The essence of the fiber hypothesis can be summarized as follows:

1) Diets high in dietary fiber are protective against a wide variety of westernized diseases.
2) Diets low in dietary fiber may be causative factors in the etiology of westernized diseases.

1. Definition

Fiber is all the constituents derived from the plant cell walls in the diet which are not digested by the endogenous secretion of the human digestive tract. Prior to this the term fiber is bandied about in both the medical and popular literature, and considerable confusion exists as to its precise definition. Terms such as "crude fiber," "unavailable carbohydrate," "indigestible residue," "bulk," and "roughage" have been used. Trowell's definition of fiber is now the most widely accepted. Fiber is a mixture of fibrous and/or viscous undigested plant cell wall polysaccharides (36).

Many analytic methods have been used to measure the fiber content of food. Initially, crude fiber had been developed to describe the residue of food remaining after treatment with strong acid and alkali. This method underestimates the cell wall polysaccharides such as hemicellulose. It consists mostly of cellulose and lignins. All other types of dietary fiber are destroyed by the chemicals. Many food composition tables still report dietary fiber value in terms of crude fiber. These values often bear little resemblance to dietary fiber values because crude fiber does not contain many fiber components (37).

The American organization of Analytical Chemists (AOAC) defined total dietary fiber as the residue remaining after enzyme digestion (38). However, this laboratory

measurement has been criticized because it includes fiber as any "resistant starch" formed during the processing and cooking of foods.

The most logical method is Cummings and Englyst's who defined fiber as the nonstarch polymers remaining after enzyme digestion followed by chromatography measurement of residue sugar (2). A determination of fiber content by this method measures both soluble and insoluble fractions but excludes lignin, which is a very minor dietary constituent.

For the present, dietary fiber defined as "the nonstarch polysaccharide and lignin portions of plant products not digestible or very poorly digestible by the enzymes presented in the upper gastrointestinal tract" is the appropriate definition.

2. Classification

The major fiber components are polysaccharides differ from starch in that the chemical links that join individual sugar units cannot be digested by human enzymes in the small intestine. Dietary fiber is not a single substance but actually a group of substances with similar characteristics. The group consists of cellulose, hemicellulose, pectins, gums and mucilages in addition to the nonpolysaccharide component, lignin. As shown in Table A, these polysaccharides are defined by their sugar residues and the linkage between them (37).

Table A Types of dietary fiber

Name	Chemical structure	Water solubility
Cellulose	Glucose polymers, β(1-4)units	Insoluble
Hemicellulose	Pentose, hexose, uronic acid polymers	Soluble
Pectins	Galactouronic acid polymers, α(1-4) linkage; methylated side groups	Soluble
Gums	Polysaccharides, often methoxylated and acetylated	Soluble
Mucilages	Highly branched polysaccharides (i.e.,Arabinoxylans)	Soluble
Lignins	Aromatic alcohol polymers (phenols)	Insoluble

From Selvendran, 1984 (37).

2.1 Cellulose

Cellulose provides the structural framework for all plant materials. It is the most abundant organic chemical on earth, being found in fruits and vegetable pulps, skin, leaves and outer covering of grain, nuts, seeds, and legumes. Cellulose is a polymer of glucose links by β (1-4) bonds. Cellulose molecules are arranged within the microfibrils in a highly ordered crystalline state in chain 4000-6000 nm long and possibly 4 nm in diameter, each consists of several thousand glucose units. It also has the property of taking up water (0.4 gram water per gram of cellulose) and this explains its ability to increase fecal weight when added to the diet.

2.2 Hemicellulose

Hemicellulose differ structurally from cellulose in that they have fewer glucose units. They are branched polymers of pentose and hexose sugar, xylose, arabinose, mannose, galactose, and their uronic acid derivatives. The proportions depend on the plant source; for instance, xyloglucans are the predominant hemicellulose in parenchymal fruit and vegetable tissues. Various hemicellulose have important physiological action in the gut where they can bind water and cations.

2.3 Pectins

Pectins, a noncellulose polysaccharide, are a complex mixture of colloidal polysacchrides. They are partly esterified rhamnogalacturonans with an α (1-4) linked D-galacturonan chain interspersed with L-rhamnopyranosyl residues with side chain which include D-glucuronic and galacturonic acid. Some acidic groups are methylated. Pectins are found in the primary cell wall and intracellular layer. Their ability to form gels and their ion binding capacity may be important in human nutrition. They are found in apples, citrus fruits, strawberries, and other fruits to a lesser degree.

2.4 Gums

Gums are water soluble viscous polysaccharides of 10,000-30,000 units, mainly glucose, galactose, mannose, arabinose, rhamnose and their uronic acids which may be methoxylated and acetylated. The true plant gums, gum acacia and gum tragacanth are the dried exudates from various plants obtained when the bark is cut or the plant is otherwise injured. These are not part of the cell wall structure but are generally

indigestible and are thus considered a part of dietary fiber. Guar and locust bean gums are examples of gums derived from seeds.

2.5 Mucilages

Mucilages are polysacchrides from seeds and seaweeds used in small amount in the food industry as thickening and stabilising agents by virtue of their water holding and viscous properties. The mucilages of some seeds such as ispaghula husks are bulk laxatives made up of highly branched arabinoxylans. Alginic acid from seaweed is a polymer of (1-4) linked β-D-mannuronic acid or of (1-4) linked α-L-gucluronic acid or a mixture. They are found mixed with the endosperm storage polysaccharide or in special cells in the seedcoat. They retain water and so protect the seed against desiccation.

2.6 Lignins

Lignins, a noncarbohydrate material which are sometimes included in dietary fiber determinations, are a major component of trees and provides structure to the woody portions of plants. They are polymers of aromatic alcohol which encrust the cellulose and hemicellulose during secondary thickening. Lignins constitute a very small part of the diet (1 g/d) and occur mostly in fruits with edible skins and seeds.

The component of dietary fiber described above can be categorized on the basis of physical properties and physiological roles as soluble dietary fiber and insoluble dietary fiber (Table B).

Table B Classification of dietary fibers

Type	Component	Physiology	Major food sources
Insoluble			
Noncarbohydrate	Lignins	Uncertain	All plants
Carbohydrate	Cellulose	Increase fecal bulk	All plants
	Hemicellulose	Decrease transit time	Wheat, rye, vegetables
Soluble			
Carbohydrate	Pectins, gums, Mucilages	Delay gastric emptying; Slow glucose absorption; Lower serum cholesterol	Apple, citrus fruit,oat, Beans

From Anderson, 1986 (39).

1) Soluble dietary fibers

Soluble dietary fibers are dietary fibers which either dissolve or swell when in water or are metabolized by bacteria in the large intestine. Rich sources of soluble dietary fibers include fruits, vegetables, legumes, soy bean fiber, psyllium seeds, dried beans, and oat bran. The influence of soluble dietary fibers on events in the alimentary tract is related to their ability to hold water and form gels and also to their role as substrate for fermentation by colonic bacteria (40,41).

2) Insoluble dietary fibers

Insoluble dietary fibers are dietary fibers that mostly do not dissolve in water and are not digested by bacteria in the large intestine. These dietary fibers

consist primarily of cellulose and some hemicelloses. They lend structure to plant cell and are found in all kinds of plant materials. However, their major source is in the bran layers of cereal grains(41).

3. Effect of fibers on gastrointestinal tract and metabolism

Dietary fiber have a wide range of effects in the gastrointestinal tract as summarized by Heaton (Table C)

Table C Effects of dietary fibers in the gastrointestinal tract

Site	Activity
Mouth	Stimulates saliva
Stomach	Dilutes contents, prolongs storage
Small intestine	Dilutes contents, delays absorption
Large intestine	Dilutes contents, bacterial substrate, traps water, bind cations
Stóol	Softens, enlarges, prevents straining

From Heaton ,1984 (76)

3.1 Mouth and stomach

In the mouth, fiber stimulates the flow of saliva primarily by increasing the volume of food in the mouth. When dietary fiber reaches the stomach, it will dilute the contents and perhaps prolong storage. Pectin and guar gum generally increase

gastric emptying time, while other fibers have no effect. Viscosity of the fiber source may be important variable in gastric emptying, although these data are confusing.

Marlett et al. (42) have postulated that dietary fiber could be altered chemically in the stomach. The pH of the stomach can get as low as 2.0, and acid treatment of dietary fiber can increase the soluble fiber fraction of the fiber.

3.2 Small Intestine

The soluble fibers increase intestinal transit time, whereas the insoluble fibers decrease the intestinal transit time and increase intestinal bulk. The possible effects of fiber within the small intestine include change in mixing, motility, and convection; intraluminal digestion rates; thickness of the unstirred layer; inhibition of maximum transport capacity; altered pH profile; and with long term treatment, altered intestinal morphology (43). There is also speculation that fiber may package carbohydrate molecules and insulate them from the digestive enzymes in the intestine and decrease access to the intestinal wall (44). Certain high fibers may have antienzyme activity. Fiber has been shown to reduce pancreatic enzyme activity and decrease pancreatic enzyme secretion (45).

3.3 Large intestine

Dietary fiber, as well as unabsorbed dietary carbohydrate, undergoes fermentation predominantly in the colon by anaerobic bacteria (46). Soluble fibers such as the pectins, gums, and psyllium or ispaghula are 90% to 99% digested (47), whereas an insoluble fibers such as cellulose is only 10% to 15% digested. Solubility and digestibility are dependent on the chemical composition as well as the particle

size of fiber preparations. The smaller the particle size, the greater the solubility and digestibility. The content and composition of bacteria cell wall amylases with specificity for hydrolysis of α 1-4 and β 1-4 linkages are variable among the bowel flora. These enzymes are inducible after exposure to different types of dietary fibers. The bacterial population of the human intestine is unique to each individual and tends to be stable over time. The relative size of these population can be influenced by fasting, a change in diet, and most importantly, the administration of antibiotics in critically ill patients.

The major end products of dietary fiber metabolism are the short-chain fatty acids (SCFA) acetate, propionate, and butyrate as well as the gases hydrogen, carbondioxide, and methane (44,48). It has been estimated that normally 30 to 80 g of unabsorbed carbohydrate and dietary fiber substrates enter the colon each day and results in the production of 300 to 800 mmol of SCFA (47). SCFA are the predominant anions in the colon and are absorbed by both active and passive diffusive transport systems (49). The ability to convert carbohydrates into SCFA in the colon is a major driving force for colonic salvage of electrolytes and water. In addition, SCFA absorption represents the retention of an additional 100 to 250 kcal daily (50). SCFA are the preferential metabolic fuel for colonic epithelial cells and provide energy by β-oxidation. This phenomenon may account for the profound tropic effects of SCFA on the large intestine. (Figure A)

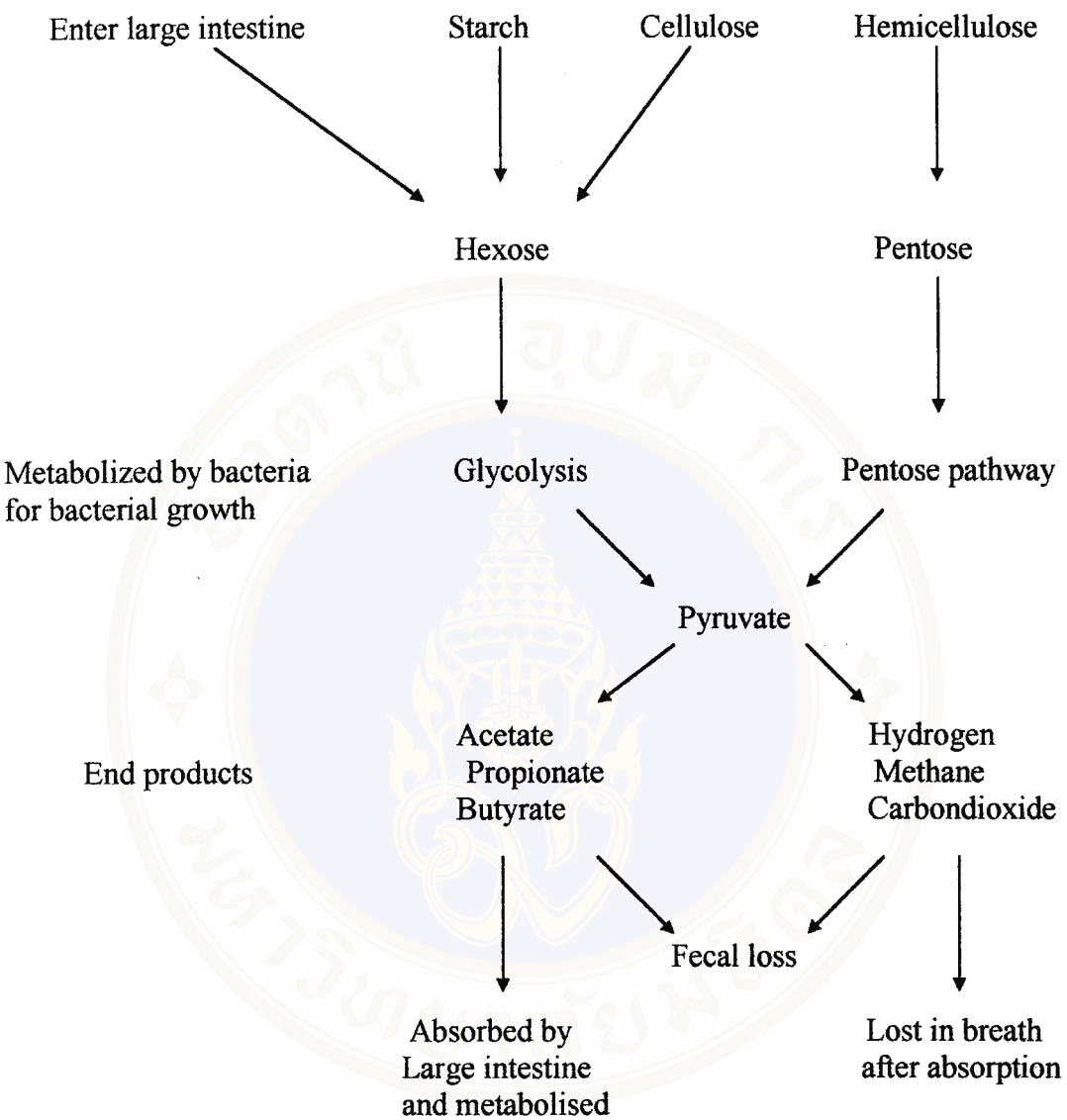

Figure A Mechanisms in the breakdown and assimilation of carbohydrate in the human large intestine

From Mc.Neil,1984 (51).

4. Health benefits of dietary fibers

Although high dietary fiber intake is associated with lower risk or improvements in several chronic diseases, a recent report of the National Academy of Sciences states "there is no evidence that it is dietary fiber rather than the other components of vegetables, fruits, and cereal products that reduces the risk of those diseases" (52).

Vegetarians have higher dietary fiber intakes than nonvegetarians (53). Vegetarians also have lower rates of coronary heart disease and cancer, lower serum total and low-density lipoprotein(LDL) cholesterol concentrations, lower blood pressure, lower body weights, and healthier lifestyle than nonvegetarians (54). In addition, when the dietary fiber content of the diet changes, concentrations of other dietary components such as saturated and unsaturated fats, minerals, and antioxidants also change (55). Thus, although some studies document specific effects of dietary fiber, effects of the entire high-fiber diet must also be considered.

4.1 Serum lipids

Elevated serum cholesterol concentrations, particularly LDL cholesterol, are major risk factors for CHD (56). The National Cholesterol Education Program recommends a low-fat, low-cholesterol diet as a primary treatment for hypercholesterlemia (57). Although diet low in fat and cholesterol are also usually high in fiber, evidence suggests that high intake of soluble fiber may augment the cholesterol-lowering effects of such diets (12,58).

Careful clinical studies in a metabolic research ward indicate that average American diets enriched with soluble fiber from oat bran (59,60) or beans (61,62) can produce net reductions in serum cholesterol concentrations of 15% and LDL-

cholesterol concentrations of 16% over 3 wk. Serum lipid improvements with such diets were sustained over the long-term, with 26% reductions in serum cholesterol concentrations and 24% reductions in LDL-choleserol concentrations over 24 wk (63).

Additional studies indicate that Psyllium mucilloid, a supplement rich in soluble fiber, lowers serum total and LDL-cholesterol concentrations by 15% and 20%, respectively, when consumed with a typical American diet (64). When used to augment a Step I diet, recommended by the American Heart Association, Psyllium mucilloid decreased serum LDL-cholesterol concentrations an additional 9% (65).

4.2 Coronary heart disease

Vegetarians have a lower incidence of CHD than nonvegertarians(66). Although dietary fiber may alter CHD risk factors such as serum lipid concentrations, hypertension, obesity, and diabetes, evidence suggests that diet may also independently affect CHD risk (56).

Morris et al (67) reported that men with a high intake of cereal fiber have a lower rate of CHD than men with a low cereal-fiber intake. The protective effects of cereal fiber in this study could not be related to serum cholesterol concentrations. Khaw and Barret-Conner (68) reported that a 6g increase in dietary fiber intake was associated with a 25% reduction in CHD mortality that was independent of other dietary variables. The protective effect was still statistically significant after multivariate adjustment for other CHD risk factors. Kromhout et al (8) reported that mortality from CHD was fourfold higher in Dutch males whose diets included lower

fiber intakes than in males whose diets included higher fiber intakes. This effect remained significant after multivariate adjustment for other CHD risk factors.

4.3 Obesity

The routine use of high-fiber foods reduces risks for obesity and assists in weight loss and weight maintenance because high-fiber foods tend to be high in carbohydrate and low in fat (54,70). High-fiber foods may promote weight loss and long-term weight maintenance through the interactions of some of the following mechanisms: high-fiber foods take longer to eat, which increases the feeling of satiety: they slow gastric emptying, thereby increasing the feeling of fullness; they decrease serum insulin concentrations; thereby decreasing food intake because insulin stimulates appetite; they decrease the absorption of nutrients, which decreases energy availability; they may increase rates of dietary thermogenesis; their fermentation products, such as SCFA, may decrease food intake; they may stimulate the release of peptides that modify eating behavior; and they may enhance adherence to the diet (54).

Although dietary fiber has considerable theoretical potential as an adjunct to weight loss and long-term weight management, clinical studies have not documented these benefits. Several clinical studies have documented that fiber supplements have a significant impact, thought to be small, as an adjunct to a weight-reducing diet (54,71). High-fiber diets may have particular benefits for obese diabetic individuals (72). Because of encouraging preliminary studies (73-75), further clinical studies are needed to document the effectiveness of high-fiber foods as an adjunct to weight loss.

4.4 Diabetes

The modern era of serious research into dietary fiber commenced in 1976 initiated by Dr. James Anderson in United States and particularly by Dr. David Jenkins in England.

Anderson's initial report suggested that a high carbohydrate diet containing large amounts of dietary fiber caused an improvement in blood glucose control in patients with non-insulin dependent diabetic mellitus (NIDDM) (77). However, his report is difficult to interpret in the absence of a control group and may have been confounded by a reduction in available calorie intake and weight loss. Jenkins' result, however, clearly demonstrated in acute single meal studies, that the addition of soluble fiber to a meal attenuated the postprandial glucose and insulin rise in both insulin dependent and non insulin dependent diabetics (78).

Results of 53 studies that examined the short- or long-term effects of fiber supplements in diabetic individuals were recently reviewed (3). Of these studies, 36 (68%) reported that fiber supplements improved glycemic control, 12 (22%) noted no change, and 6 (11%) did not report the glycemic responses.

High-fiber diets may have special advantages for obese diabetic individuals. Weight-reducing high-fiber diets promptly decrease the need for insulin or oral hypoglycemic agents and quickly decrease serum glucose and lipids (79,80). Because of the benefits that fiber provides for facilitating weight loss and long-term weight maintenance, high-carbohydrate, high-fiber, low-fat diets seem especially suited for obese diabetic individuals.

Of the possible mechanisms of action of viscous gels it would appear that the major effect is the inhibition of convective movement of intestinal content towards

the absorptive brush border of the small intestine. There may also be less effects on digestion, gut motility and GI hormone release.

4.5 Gastrointestinal disorders

Dietary fiber has many health-promoting effects on the gastrointestinal tract (76). Fiber maintains normal function and promotes regularity. Foods rich in soluble fiber, such as oat products, delay gastric emptying and enhance satiety (39). Foods rich in insoluble fiber, such as wheat bran, decrease transit time and increase fecal weight and stool number (39,81).

Madar and Odes (7) recently reviewed the effects of dietary fiber on GI function and diseases. They summarized the literature and indicated the clear benefits of wheat bran, psyllium, and other fibers for individual with constipation. They also presented the rationale for including fiber in the diet to protect against diverticulosis of the colon. The role of dietary fiber in the treatment or prevention of other conditions such as irritable bowel syndrome is still under study.

5. Possible adverse effects of dietary fiber

Some adverse effects may occur with the consumption of 50 to 60 g dietary fiber diets per day, including decreased bioavaiability of certain vitamin and mineral (82). The general public should be encouraged to increase dietary fiber intake gradually, accompanying it with adequate fluid intake, in order to avoid possible side effects such as flatulence, diarrhea and intestinal distention (83). These side effects are caused by bacterial fermentation of dietary fiber with release of volatile fatty acids, carbon dioxide, hydrogen and methane.

A compound not classified as a dietary fiber but often found with it in foods is phytic acid. On a high dietary fiber diet, losses of minerals may occur if they become bound to phytic acid. Most of the phytic acid in our diet comes from seeds such as the cereal grains. Phytic acid is capable of binding minerals such as zinc, iron, calcium, magnesium, and copper in insoluble complexes in the intestine (84). Several studies proposed that calcium balance decreases as consumption of pectin, cellulose, hemicellulose and lignin from fruit and vegetable increases (172). Taper et al. (85) also discovered that high dietary fiber intake (40 g/day) of soy polysaccharide caused a net loss of copper and iron.

However, many studies of vitamin and mineral status in adults on high-fiber diets have not found evidence of deficiency (86). In term of soluble fiber supplements, Mclvor and colleagues (87) gave at least 30 g of guar daily for 16 wk to 8 NIDDM patients, resulting in no significant changes in hematologic or hepato-renal function. Jenkins et al. (88) administered 14-26 g of guar daily for 6 months to 8 diabetic patients and found no evidence of serum zinc, copper, and calcium changes. Tuomilehto et al.(89) gave 15 g of guar daily for 3 months to 12 obese hypercholesterolemic patients and at the end of this time, noted no significant changes in 24-h urinary sodium, potassium, calcium, and magnesium.

Although dietary fiber may combine with bivalent metals resulting in a decreased availability of those minerals, consumption of a complex and balanced diet from a variety of food sources should not lead to overt vitamin and mineral deficiency (83).

6. Dietary fiber recommendations

The consensus recommendations of leading health organizations in the United States (90-92) and other Western countries (93,94) are for a 50- 100% increase in fiber intake. Currently Americans consume 10 to 23 g fiber/d (95). Recommended intake are from 20 to 35 g/d (95). Consistent with the recommendations to increase fiber intake are current dietary guidelines that recommend decreasing fat consumption from the current 37% of energy intake to 30% of energy intake, while increasing consumption of complex carbohydrate foods (96).

7. Health benefits of ispaghula husk (psyllium)

Ispaghula husk or psyllium (the name of ispaghula is better known in Europe than the United States), a rich source of dietary fiber is obtained from the outer epidermis of the seeds of Plantago ovata Forsk. Plantago ovata is native to the Canary Islands and the Mediterranean regions of Southern Europe and North Africa to West Pakistan. It is an annual herb sown in November and December and harvested in March and April. The seed is processed and de-husked through a series of grinding mills and mesh screens to separate the husk and remove the fines. The husk is a rich source of true fiber containing 80-85% dietary fiber with a soluble fiber content of some 80% mucilage. It is composed of a highly branched arabinoxylan that forms a viscous gel when hydrated that allow it to have such an efficient laxative action. (Table D)

Table D Analysis of Ispaghula husk

Analysis method	Englyst	
Total non-starch polysacchride (NSP) %	80.3	
Soluble % of total NSP	81.4	
Soluble/insoluble NSP ratio	4 to 1	
NSP components (% total)		
	Soluble	Insoluble
Rhamnose	1.0	0.1
Arabinose	13.8	5.6
Xylose	44.3	2.9
Mannose	0	1.1
Galactose	1.1	2.0
Glucose	0.1	2.7
Uronic acids	5.1	0.5
Total %NSP	65.4	14.9
Other components (% total)		
Lignin	3	
Protein	2.5	
Fat	0.5	
Ash	3	
Moisture	2	

From Dettmar, 1995 (29)

Fybogel® was developed by Reckitt and Colman and first introduced into the UK market in 1974. The flavored preparation, Fybogel Orange®, was launched in 1982. Fybogel® is now the most prescribed bulk laxative. As Fybogel® contains a naturally occurring source of dietary fiber, which is not absorbed, it carries a very low risk of unwanted effects. It only contains trace levels of phytate. Fybogel Orange® contains 3.5g ispaghula husk per sachet, only low levels of electrolytes, less than 1mmol sodium and potassium per dose, and is both sugar-free and gluten-free.

In clinical studies, the effectiveness of Fybogel®, a pharmaceutical product containing a high level of ispaghula husk, has been demonstrated in those suffering from simple constipation. Fybogel Orange® acts as rapidly as osmotic laxatives and chemical stimulants in relieving the constipation and inducing the first bowel movement.

Several studies have demonstrated that ispaghula husk have the greatest effect on reducing cholesterol levels and the rate of glucose uptake. Studies investigating the glycemic effect have shown reductions in postprandial plasma glucose of between 10% and 20 % compared with placebos (64,97,144,147,148). These studies were both short and long term, on healthy subjects, and diabetic patients. The effect of ispaghula husk on lipemia is very well documented, and reduction in total cholesterol between 4% and 29% have been observed, largely depending on study duration, dosage and baseline plasma cholesterol levels (12,98,162-164). The result is comparable to that of guar gum, Fybogel® is well tolerated without causing any serious side effects (29).

Few studies have demonstrated the effect of ispaghula husk on the maintenance and reduction of the body weight. Alberto et al (99) gave 15 g of psyllium mucilage before each meal for 10 days to 19 obese and 8 NIDDM patients. Body weight decreased a mean of 1,810g in the obese and 1,212g in the diabetic groups. Turnbull et al. (100) determined the effect of Plantago ovata on the appetite and found a significant difference in the fullness at 1 h post-meal between Plantago and placebo. Further studies are needed to investigate the effect of Ispaghula husk on the body weight.

CHAPTER III

MATERIALS AND METHODS

A. Experimental Design

This was a randomized, double-blind, placebo-controlled study, performed on 35 obese NIDDM patients, conducted in Ramathibodi hospital. The study lasted 32 weeks, and was divided into three periods consisted of an 8 weeks dietary advice phase, followed by a 16 weeks treatment period (Fybogel® or placebo) by randomization, and then 8 weeks follow-up period after withdrawal of medication.

Selection of patients

Thirty-five patients were selected to participate in this study according to the inclusion and exclusion criteria listed below.

Inclusion criteria

The following patients were eligible to enter the study:

1) Uncontrolled diabetes with a glycosylated hemoglobin (HbA_{1C}) value above 7.0%.
2) Body mass index (BMI) of more than 25 kg/m^2.
3) Hypercholesterolemia, total cholesterol levels more than 200 mg/dL
4) Aged between 18 and 70 years (male or female).
5) Willing to provide informed consent to participate in the study.
6) Willing to comply with the study procedures, stay on the study for 24 weeks and to be followed up for another 8 weeks.

7) Able to take the study medication, able to understand the study procedure and reliable.

Exclusion criteria

The following patients were excluded from the study:

1) Patients who had impaired hepatic, renal, and thyroid function.
2) Female patients who were pregnant or breast feeding
3) Patients with inflammatory bowel disease, colonic ulceration or partial intestinal obstruction, predisposition to intestinal obstruction, chronic intestinal disease associated with marked disorders of absorption or digestion, condition which might have been exacerbated by increased intestinal gas formation (such as hernias)
4) Patients who had a condition which the investigator believed to interfere with the evaluation or confound the results of the study, or put the patient at undue risk.
5) Patients taking vitamin or mineral supplements containing vitamin A, B_1 (thiamine), B_2 (riboflavin), C, E, B_{12} (cyanocobalamin), folic acid, vitamin K, calcium, phosphorus, magnesium, iron, zinc, and copper.

Dosage schedule

One sachet of Fybogel® (3.5 g of ispaghula husk) or placebo was taken 3 times daily over the treatment period (wks 8 to 24). The study medication was taken up to 30 minutes before each of the morning, mid-day and evening meals.

The contents of a sachet of study medication were emptied into approximately 150 ml of cold water, stirred and drunk immediately.

Concomitant medication

If possible, there was no change of medical treatment during the course of the study. Patients were instructed not to take any vitamin or mineral supplements containing vitamin A, B_1, B_2, C, E, B_{12}, folic acid, vitamin K, calcium, phosphorus, magnesium, iron, zinc, and copper since they may invalidate the safety evaluation. Patients taking prescribed supplements of any of these vitamins or minerals were disqualified. Patients were instructed to consult the investigator before taking any non-prescribed medicine during the study except for paracetamol.

Details of all concomitant medication taken during the study and the daily dosage were recorded by the investigator in the patient's notes. If any medication taken by the subject interfered with the study, the patients were withdrawn.

Study Screening Procedures (week 0)

Potentially suitable patients had the study detail were explained and were asked to sign the informed consent before the beginning of the study.

Demographic details, medical history, coexisting disease and concomitant medication were also recorded. Blood samples for laboratory analysis (fasting cholesterol, and glucose, HbA_{1C}, hematology and routine safety parameters) were taken.

Twenty-four hour dietary recall was taken and knowledge and method of taking dietary record was taught to all subjects.

All subjects were asked to maintain their usual level of physical activity.

Appropriate dietary advice was given to the patient and the following appointments were made.

Follow-up assessments

At each subsequent assessment the following procedures were undertaken:

1) Three-day dietary records were reviewed for accuracy with the patients.
2) Appropriate dietary advice was re-iterated.
3) Blood samples for fasting glucose and lipid profiles were taken at week 4, 8, 16, 24, and 32.
4) Blood samples for HbA_{1C} was taken at week 8, 16, 24, and 32.
5) Blood samples for vitamin and mineral will be taken at week 8 and 24.
6) Weight, height, arm span, upper-arm circumference, 4-skinfold thickness, wrist circumference, and ankle circumference were recorded at week 4, 8, 12, 16, 20, 24 and 32.
7) All adverse events experienced and concomitant medications taken were recorded.

The study medication (a carton labeled week 8 for the appropriate patient number) and proper instructions were given on week 8 of the study. Further medication were dispensed at week 12, 16, and 20. Details of the amount of medication returned at week 12, 16, 20, and 24 were recorded.

Investigator's evaluation

At all visits the details of any adverse events were recorded, including worsening symptoms of a coexisting disease, experienced by the patients since the previous assessment. The investigator also assessed the patient's compliance with the dosing regimen by interviewing and pill counting.

Withdrawal from the study

Any patient could withdraw from the study at any time and for any reason.

The investigator must document a patient's reason for withdrawal, together with the date of withdrawal, and should indicate whether his/her thinks this was related to study medication.

Adverse events

At each visit the investigator asked the patient "Have you had any unwanted symptoms since the last visit?" If the patient answered "yes", full details of all adverse events including duration, severity, relationship to the study medication / change in diet and outcome was made in the patient's study notes.

Study schedule

Each patient was assessed for 8 occasions & according to the study schedule shown in the next page.

Study schedule

ASSESSMENT	WEEK NUMBER							
	0	4	8	12	16	20	24	32
	Dietary advice			Fybogel® or Placebo.				Follow -up
Dietary Advice	X	X	X	X	X	X	X	X
Fybogel® / Placebo				X	X	X	X	
3 day dietary record	X	X	X	X	X	X	X	X
Record of side effect	X	X	X	X	X	X	X	X
Weight and anthropometry	X	X	X	X	X	X	X	X
Blood for - Total T_4, T_3, TSH	X							
Fasting plasma - Glucose, - Lipid profiles (Total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol)	X X		X X		X X		X X	X X
- HbA1c	X		X		X		X	X
- Vitamin (A, B_1, B_2, C, E, B_{12}, folate, K)	X		X				X	
- Mineral (Calcium, Phosphorus, Magnesium, Iron, Zinc, Copper)	X		X				X	
- Haematology assessment (Hb., Hct., Red cell count, White cell count, Platelet count)	X		X				X	
- Biochemistry assessment (Total proteins, Albumin, Urea, Uric acid, Creatinine, Sodium, potassium, Chloride, CO_2, Total and direct bilirubin, Alkaline phosphatase, AST (SGOT), ALT (SGPT), Gamma GT	X		X				X	

Principles of Nutrition Recommendation in this study

Patients can eat food similar to that recommended for the entire family in order to maintain health. Dietary advice principally involved a consideration of energy intake and the proportion of fat, protein and carbohydrate, as well as of other nutrients, to ensure that in every respect optimal nutrition was maintained and to reduced acute and long-term complications.

Nutrition Recommendations for Obese NIDDM

Started from week 0, each patient was received dietary recommendation to promote weight loss and to control serum glucose and lipid levels as shown in Table E.

Table E Dietary prescription (127)

Daily intake	Amount prescribed
Energy	1,000 kcal/day
Carbohydrate	50% of total energy Prefer complex carbohydrate Avoid simple sugars/added sucrose
Fat	30% of total energy
Protein	20% of total energy

This was used as a guideline for planning diet and educating obese NIDDM patients and their families. The principle and the importance of diet recommendation were told to all patients. They were instructed to design and prepare their diets. The booklet about the detail of dietary recommendation (Appendix III) was given to all patients.

B. Assessment of Nutritional Status

1. Anthropometric measurement

1.1 Height (Ht)

The subject was asked to stand straight barefoot on a horizontal platform with his heel together, stretching upward to the fullest extension. The back was as straight as possible against the vertical bar and the horizontal arm of the heightmeter was in contact with the subject's head. The reading was read to the nearest mm.

1.2 Weight (Wt)

By standing barefoot on the accurate weighting scale.

1.3 Body mass index (BMI)

Body mass index was derived from body weight in kilogram divided by the square of height in meters (kg/m^2). A desirable BMI for general population lies between 20-25 kg/m^2 (112).

1.4 Body composition

1.4.1 Mid-arm-circumference (MUAC)

MUAC is used as an indicator of both caloric and protein store. The arm contains subcutaneous fat and muscle. Therefore, a decrease in MUAC may reflect either reduction in muscle mass, a reduction in subcutaneous tissue, or both. Change in MUAC measure can be used to monitor progress during nutritional therapy (113), correlate positively with change in weight. The MUAC was measured in centimeters at the same level as the triceps skinfold thickness. The measurement was taken at the midpoint of the upper left arm between the acromion process of the scapula and tip of

olecranon. After locating the midpoint, the left arm was extended so that it is hanging loosely by the side, with the palm facing inwards. The tape was wrapped gently but firmly around the arm at the midpoint.

1.4.2 Upper arm muscle circumference (UAMC)

The upper arm muscle circumference (UAMC) was calculated from the following formular :

$$\text{UAMC, cm} = (\text{MUAC, cm}) - (0.314 \times \text{TSF, mm}) \quad (114)$$

1.4.3 Four-skinfold thickness

The four subcutaneous skinfolds thicknesses were measured using Harpenden Calipers (115,116) and recorded to the nearest 0.5 millimeter.

Triceps skinfold thickness (TSF)

The pendent right arm triceps skinfold was measured. The site of the measurement was the grasped fat pad at midpoint between acromion process of the scapular and olecranon process of the ulna.

Biceps skinfold thickness (BSF)

The thickness of a vertical fold on the front of the upper right arm, directly above the center of the cubital fossa at the same level as the triceps skinfold was measured.

Subscapular skinfolds thickness (SSF)

The site of the measurement was just below and laterally to the angle of the left shoulder blade, with the shoulder and the right arm relaxed. Skinfolds was grasped at the marked site at the lower tip of the scapular.

Suprailiac skinfolds thickness (SISF)

The site of the measurement was in mid axillary line immediately superior to the iliac creast. The skinfolds was picked up obliquely just posterior to the midaxillary line and parallel to the cleavage lines of the skin.

For all the skinfolds measurement, the subjects stand upright with feet together and arm at the sites.

The skinfolds was gently pulled away from the underlying muscle tissue. The calipers were placed perpendicular to the fold, on the side of marked dial up, at approximately 1 cm. below the forefinger and thump. While maintaining a grasp of the skinfolds, released the calipers so that full tension was placed on the skinfolds. The dial was being read to the nearest 0.5 mm 1-2 seconds after the grip had fully released.

The determination of body fat mass (BFM) and fat-free mass (FFM) was calculated by the method of Durnin and Wormersly's table (117). Skinfolds thickness measurements from multiple anatomical sites were used to estimate body density. The percentage body fat was calculated from the sum (milliliters) of the above four skinfolds measurements of male and female in different ages according to percentage body fat table (117).

2. Dietary assessment

Subjects were instructed about how to record a 3-day (1 weekend day and 2 weekdays) diet history by the dietician. The example of dietary record (Appendix I) was given to all patients. All food items and portions were recorded in the form for 3 day as shown in appendix II. Detailed description of all foods and beverages including brand name and their method of preparation and cooking were recorded. The patients estimated food portion size by using standard household measuring cups and spoons

supplement with a ruler. And the dietitians reviewed the diet records for accuracy with the subjects.

Portion size measures were converted into grams. The food records were analyzed for energy intake and its distribution derived from protein, fat, and carbohydrate. Data were analyzed by using the computerized food composition analysis package "Nutritionist III" modified for Thai food by the Institute of Nutrition, Mahidol University.

C. Biochemical assessment

Forty-two ml of blood was collected at week 0, 8, and 24 while 8 ml of blood was collected in the morning after 12-h overnight fast at week 4, 16, and 32.

The following quantitative assays were performed:

1. Glycemic levels (week 0, 4, 8, 16, 24, 32)

Plasma glucose levels were determined using the enzymatic method described by Barham and Trinder (101) as shown in AppendixIV.

Glycosylated hemoglobin (HbA_{1c}) in whole blood sample were measured by utilized the principle of ion exchange high performance liquid chromatography (HPLC) according to the method of VARIANT^{TM} Hemoglobin Testing System HbA_{1C} Dual Kit as shown in Appendix V

2. Serum lipid levels (week 0, 4, 8, 16, 24, 32)

Serum total cholesterol was measured by means of enzymatic-colorimetric method (119) as shown in Appendix VI.

HDL-cholesterol was determined by method of Bustein and Lopes-Virella (120) as shown in Appendix VII.

Triglycerides was measured by enzymatic hydrolysis of triglycerides with subsequet determination of the liberated glycerol by boeringer Mannheim Triglycerides GPO-PAP Kit (102) as shown in Appendix VIII .

LDL-cholesterol and HDL/LDL ratio were calculated. LDL-C level was calculated from Friedewald's formula (103).

3. Vitamins / Minerals (week 0, 8, 24)

Plasma retinol and α-tocopherol were measured by HPLC according to the method of Bieri et al. (104) as shown in Appendix IX.

Erythrocyte transketorase activity (ETKA) and thiamine pyrophosphate effect (TPPE) was determined by enzymatic method according to the method modified from Dreyfus (105), and Dische (106) as shown in Appendix X.

Erythrocyte glutathione reductase activity (EGRA) and activity coefficient (AC) was determined by enzymatic method according to the method modified from Glatzle et al (107) as shown in Appendix XI.

Ascorbic acid was determined as the derivative of 2, 4-dinitrophenylhydrazine using the method of Stanley et al (108) as shown in Appendix XII.

Serum vitamin B_{12} was measured by γ-counter. Serum folate and red blood cell folate were measured by the microbiological assay using *Lactobacillus casei* and spectrophotometer according to the mehod of Grossowicz et al at the Laboratory of Tropical Disease Hospital.

Prothrombin time (screening test of vitamin K deficiency) was measured at Hematology Laboratory, Ramathibodi Hospital according to the method of Dade® Thromboplastin IS Kit.

Serum calcium and ionized calcium were determined by using a NOVA 7 according to the method of Jack H (109) as shown in Appendix XIII.

Serum phosphorus was determined by method of Golddenberg and Fernandez using a flame atomic absorption spectrophotometer (110) as shown in Appendix XIV.

Serum magnesium was determined by the method of Hausen and Frier using a flame atomic absorption spectrophotometer (111) as shown in Appendix XV.

Iron and total iron-binding capacity (Fe and TIBC) were measureed at General Chemistry Laboratory, Ramathibodi Hospital by means of colorimetric method.

Serum zinc and copper were measured by flame-atomic absorption spectrometry according to the method of model 1100B; perkin-Elmer as shown in Appendix XVI.

4. Hematological Parameters (week 0, 8, 24)

Hemoglobin, hematocrit, red cell count, white cell count and platelet count were measured by H-1 hematology analyzer at Hematological Laboratory, Ramathibodi Hospital.

5. Routine safety Parameters (week 0, 8, 24)

Serum blood urea nitrogen (BUN), creatinine, alkaline phosphatase, SGOT, SGPT, Gamma GT, uric acid, total and direct bilirubin, total proteins, albumin, sodium, potassium, chloride and CO_2 content were measured by SMA-12 at General Clinical Chemistry Laboratory, Ramathibodi Hospital.

E. Statistical Analysis

Results were presented as mean ± SD. The statistical significant difference was considered at the P-value was less than 0.05. Independent-sample T-test was used to determine whether differences between Fybogel® and placebo group at baseline and follow-up period. The changes in variables between time were tested for significance using Repeated-measure of ANOVA models. Student-Newman-Kuels test (SNK) was used to compare multiple comparison for observation. Pair T-test was used to test between time after withdrawal medication.

Statistical analysis were performed by using Statistical Package for the Social Science (SPSS) for Windows Release 7.5.1 (1996), Standard Version.

CHAPTER IV

RESULTS

Part I General characteristics of patients at baseline

Thirty-five obese NIDDM patients receiving treatment at Ramathibodi Hospital participated in this study. They were divided into two groups, 18 patients received Fybogel® and 17 cases received placebo after undergoing 8 week of diet-only phase.

General characteristics of the patients at the beginning of the study are shown in Table 1-9.

Table 1 shows general characteristics of the patients at the beginning of the study. The Fybogel® group consisted of 2 males and 16 females while the placebo group consisted of 2 males and 15 females. The mean age ± SD of Fybogel® and placebo groups were 55.0 ± 8.6 and 52.8 ± 6.5 years, respectively, and there was no significant difference in the age between the two groups. The mean height and weight at baseline were not significantly different. The mean BMI of Fybogel® and placebo groups were 30.3 ± 4.9 and 28.9 ± 3.7 kg/m^2 respectively. They were obese class I according to the criteria of classification of WHO consultation on obesity in adult by BMI(152). Both groups were in poor glycemic control, mean FPG of Fybogel® and placebo group were 214.4 ± 43.3 and 202.6 ± 53.7 mg/dL, and the mean HbA_{1c} levels were 10.4 ± 1.6, and 10.5 ± 1.6 % respectively. Based on the criteria of the National Cholesterol Education Program (NCEP) Expert panel on Detection, Evaluation, and

Treatment of high blood cholesterol in adults (57), both groups had high mean serum TC (> 5.17 mmol/L).

Table 1 General characteristics (mean ± SD) in both groups of patients at the beginning of the study

parameters	Fybogel®	Placebo
Sex : Male/Female	2/16	2/15
Age, year	55.0 ± 8.6	52.8 ± 6.5
Height, cm	157.2 ± 4.2	156.5 ± 5.6
Weight, kg	74.9 ± 13.1	71.0 ± 10.1
BMI, kg/m^2	30.3 ± 4.9	28.9 ± 3.7
FPG, mg/dL	214.4 ± 43.3	202.6 ± 53.7
(mmol/L)	(11.9 ± 2.4)	(11.24 ± 2.9)
HbA_{1c}, %	10.4 ± 1.6	10.5 ± 1.6
TC, mg/dL	254.3 ± 37.1	266.6 ± 42.0
(mmol/L)	(6.6 ± 1.0)	(6.9 ± 1.1)

No significant difference

1. Routine safety parameters at baseline

Table 2 Mean ± SD of baseline Thyroid function tests in both groups of patients

Parameters	Fybogel®	placebo	Reference ranges
T_3	111.74 ± 30.27	117.14 ± 32.13	75-220 ng/dL
Free T_4	1.38 ± 0.31	1.39 ± 0.30	0.8-2.8 ng/dL
Total T_4	7.99 ± 2.32	7.96 ± 1.72	4-11 μg/dL
TSH	2.39 ± 2.14	2.29 ± 1.37	2-11 mU/L

No significant difference

Table 3 Mean ± SD of baseline blood count in both groups of patients

Parameters	Fybogel®	placebo	Reference ranges
Hemoglobin	13.93 ± 0.81	14.13 ± 1.12	12-15 g/dL
Hematocrit	43.21 ± 2.97	43.98 ± 2.71	33-43 %
RBC	4.84 ± 0.50	4.80 ± 0.35	3.5-5.0 × 10^6/mm^3
Platelet	288.67 ± 51.34	280.53 ± 75.56	130-400 × 10^3/mm^3
WBC	8.15 ± 1.92	9.51 ± 1.90	3.2-9.8 × 10^3/mm^3

No significant difference

Table 4 Mean ± SD of baseline Liver function tests in both groups of patients

Parameters	Fybogel®	placebo	Reference ranges
Alkaline phosphatase	82.33 ± 28.75	76.65 ± 27.30	30-120 U/L
Aspartate aminotransferase	24.44 ± 8.13	28.06 ± 18.99	0-35 U/L
Alanine aminotransferase	26.67 ± 14.72	26.24 ± 18.11	0-35 U/L
Gamma-glutamyl transferase	38.44 ± 17.46	41.06 ± 24.58	0-30 U/L
Total bilirubin	11.47 ± 4.68	11.66 ± 5.13	2–18 μmol/L
Direct bilirubin	2.04 ± 0.87	2.23 ± 1.53	0-4 μmol/L

No significant difference

Table 5 Mean ± SD of baseline renal function tests in both groups of patients

Parameters	Fybogel®	placebo	Reference ranges
BUN	14.17 ± 3.71	16.18 ± 4.73	8-18 mg/dL
Creatinine	0.87 ± 0.26	1.01 ± 0.21	0.6-1.2 mg/dL
Uric acid	4.98 ± 1.3	5.21 ± 1.60	2-7 mg/dL

No significant difference

Table 6 Mean±SD of baseline Total protein and albumin in both groups of patients

Parameters	Fybogel®	placebo	Reference ranges
Total protein	72.34 ± 4.54	69.28 ± 7.11	60-80 g/L
Albumin	42.14 ± 2.08	40.62 ± 4.25	40-60 g/L

No significant difference

Table 7 Mean ± SD of baseline Electrolyte in two groups of patients

Parameters	Fybogel®	placebo	Reference ranges
Sodium	139.11 ± 2.87	139.12 ± 2.74	135-147 mmol/L
Potassium	4.62 ± 0.51	4.48 ± 1.02	3.5-5.0 mmol/L
Chloride	103.72 ± 3.54	104.00 ± 3.87	95-105 mmol/L
Carbon dioxide	22.69 ± 2.34	21.94 ± 20.88	22-28 mmol/L

No significant difference

Routine safety parameters at baseline in Fybogel® and placebo groups are presented in Table 2-7. All parameters were within normal ranges except the gamma-glutamyltransferase which was mildly increased.

2. Vitamin and mineral status at baseline

Table 8 Mean ± SD of vitamin status at baseline in both groups of patients

Vitamin	Fybogel®	placebo	Reference ranges
Retinol, S	69.71 ± 18.71	72.87 ± 26.04	20-100 µg/dL
	(2.43 ± 0.65)	(2.54 ± 0.91)	(0.7-3.5µmol/L)
α-tocopherol	1.27 ± 0.31	1.32 ± 0.45	>0.5 mg/dL
,S	(29.49 ± 7.20)	(30.65 ± 10.45)	(>11.6 µmol/L)
Ascorbate, S	0.93 ± 0.28	0.81 ± 0.31	0.4-1.0 mg/dL
	(52.81 ± 15.90)	(45.99 ± 17.60)	(23-57 µmol/L)
Vitamin B_1	%TPPE 0.08 ± 0.38	%TPPE 0.85 ± 3.22	<15
	(ETKA 219.4 ± 46.1)	(ETKA 222.8 ± 52.2)	
Vitamin B_2	AC 1.11 ± 0.15	AC 1.09 ± 0.15	<1.2
	(EGRA 2134.3 ± 615.1)	(EGRA 2080.7 ± 601.6)	
Vitamin B_{12}	293.47 ± 111.12	541.60 ± 231.21	200-900 pg/mL
,S	(216.58 ± 82.01)	(399.70 ± 170.63)	(147-660µmol/L)
Folate, S	12.22 ± 4.16	9.83 ± 5.08	5-16 ng/mL
	(27.68 ± 9.42)	(22.26 ± 11.51)	(11-36mmol/L)
RBC Folate	214.57 ± 102.59	200.04 ± 67.81	150-450 ng/mL
	(486.00 ± 232.37)	(453.09 ± 153.59)	(340-1,020 nmol/L)
Vitamin K	15.06 ± 1.62	14.56 ± 1.01	11-15 seconds
(prothrombin			
time)			

S=serum

No significant difference

Table 9 Mean ± SD of mineral status at baseline in both groups of patient

Mineral	Fybogel®	placebo	Reference ranges
Total calcium, S	2.18 ± 0.08	2.23 ± 0.12	2.20-2.64 mmol/L
Ionized calcium, S	1.21 ± 0.04	1.24 ± 0.07	1.18-1.38 mmol/L
Magnesium, S	0.710 ± 0.096	0.693 ± 0.083	0.8-1.2 mmol/L
Phosphorus, S	1.13 ± 0.16	1.16 ± 0.19	1.0-1.4 mmol/L
IRON, S	85.11 ± 24.97	93.48 ± 14.81	50-150 µg/dL
TIBC, S	277.33 ± 27.90	262.59 ± 34.85	250-370 µg/dL
Zinc, S	101.4 ± 18.5	95.8 ± 16.0	75-120 µg/L
	(15.51 ± 2.83)	(14.66 ± 2.45)	(11.5-18.5 µmol/L)
Copper, S	112.7 ± 19.2	115.4 ± 25.4	70-140 µg/L
	(17.69 ± 3.01)	(18.12 ± 3.99)	(11.0-22.0 µmol/L)

S = serum

No significant difference

Vitamin and mineral statuses in both groups of patients are displayed in Tables 8-9. All parameters were within normal ranges and no significant difference between the two groups was observed.

Part II Effect of dietary counseling, 8-week diet-only and 16-week Fybogel® or placebo supplemenation.

1. Dietary intake

The daily nutrient intake of Fybogel® and placebo groups are presented in Tables10-11. At the beginning of the study, mean ± SD energy intake of Fybogel® and placebo groups were 1,705 ± 157 and 1,780 ± 143 kcal/d, respectively. The percentages of caloric distribution of carbohydrate, protein and fat in Fybogel® group were 46.3%, 20.6%, and 33.1% and in placebo group were 46.3%, 21.6%, and 32.1%, respectively. There was no significant difference in total energy intake and caloric distribution between Fybogel® and placebo groups at the beginning of the study.

After giving dietary advice, mean total energy intake and nutrient distribution of carbohydrate, protein and fat were significantly reduced throughout the study in both groups. Percentage of calories from carbohydrate after dietary advice was significantly higher than before dietary advice in both groups whereas percentage of calories from fat was significantly lower in both groups throughout the study. Throughout the study, there was no significant difference of percentage of calories from protein between the two groups after dietary advice.

Table 10 Daily nutrient intake (mean ± SD) in Fybogel® group at baseline and follow-up periods

Week	Energy	Protein		Fat		Carbohydrate	
	Kcal/day	*g/d*	*%cal*	*g/d*	*%cal*	*g/d*	*%cal*
0	1705 ± 157	87.7 ± 11.0	20.6 ± 2.5	62.5 ± 8.0	33.1 ± 4.0	197.9 ± 35.2	46.3 ± 5.7
4	1247 ± 103[a]	59.4 ± 13.7[a]	19.0 ± 4.0	40.6 ± 4.8[a]	29.3 ± 2.6[a]	161.0 ± 16.2[a]	51.6 ± 2.7[a]
8	1262 ± 124[a]	58.5 ± 8.3[a]	18.6 ± 2.1	41.7 ± 5.4[a]	29.7 ± 1.8[a]	163.1 ± 16.0[a]	51.7 ± 1.5[a]
12	1219 ± 117[a]	61.3 ± 19.8[a]	20.1 ± 6.5	38.4 ± 9.4[a]	29.9 ± 3.1[a]	157.3 ± 14.7[a]	51.6 ± 2.0[a]
16	1300 ± 93[a]	60.2 ± 10.1[a]	18.5 ± 2.9	42.6 ± 4.6[a]	29.5 ± 2.5[a]	169.1 ± 13.5[a]	52.0 ± 1.3[a]
20	1257 ± 122[a]	58.7 ± 12.8[a]	18.6 ± 3.2	40.8 ± 4.3[a]	29.3 ± 2.1[a]	163.8 ± 15.9[a]	52.2 ± 1.6[a]
24	1234 ± 73[a]	56.6 ± 9.8[a]	18.3 ± 2.5	40.1 ± 2.3[a]	29.3 ± 1.6[a]	161.9 ± 9.8[a]	52.5 ± 1.8[a]

[a] significant difference from wk0, P<0.01

Table 11 Daily nutrient intake (mean ± SD) in placebo group at baseline and follow-up periods

Week	Energy	Protein		Fat		Carbohydrate	
	Kcal/day	*g/d*	*%cal*	*g/d*	*%cal*	*g/d*	*%cal*
0	1780 ± 143	96.2 ± 10.5	21.6 ± 1.8	63.3 ± 8.6	32.1 ± 4.2	206.4 ± 28.8	46.3 ± 4.0
4	1197 ± 128[a]	58.0 ± 13.1[a]	19.3 ± 3.5	38.7 ± 5.0[a]	29.1 ± 2.4[a]	154.2 ± 16.5[a]	51.6 ± 1.8[a]
8	1202 ± 108[a]	57.8 ± 7.7[a]	19.3 ± 2.3	39.8 ± 4.3[a]	29.8 ± 1.7[a]	153.2 ± 15.7[a]	50.9 ± 1.5[a]
12	1203 ± 107[a]	53.3 ± 9.4[a]	17.7 ± 2.6	40.4 ± 3.7[a]	30.3 ± 2.4[a]	156.5 ± 17.3[a]	52.0 ± 2.0[a]
16	1291 ± 87[a]	55.3 ± 10.5[a]	17.1 ± 2.7	43.5 ± 2.8[a]	30.4 ± 1.9[a]	169.8 ± 12.6[a]	52.6 ± 1.5[a]
20	1241 ± 107[a]	52.6 ± 11.8[a]	16.8 ± 2.8	41.6 ± 3.3[a]	30.3 ± 2.3[a]	164.1 ± 14.8[a]	52.9 ± 1.4[a]
24	1236 ± 92[a]	52.5 ± 7.0[a]	17.0 ± 2.6	40.8 ± 3.5[a]	29.7 ± 1.6[a]	164.6 ± 12.9[a]	53.3 ± 1.1[a]

[a] significant difference from wk0, P<0.01

2. Effect on body weight and anthropometric measurement

2.1 Body weight (BW)

The mean BW ± SD are displayed in Table 12 and Figure 1(a). Actual weight changes and percentage of weight changes (%changes) from wk0 and wk8 are shown in Table 13 and Figures 1(b),(c). During diet-only phase (wk0-8), there were not significant reduction of BW in both groups. During treatment phase (wk8-24), the BW was significantly reduced in Fybogel® group at wk20 and wk24 ($P<0.05$). the weight reduction was 0.88 kg (1.16%) at wk20 and 1.28 kg (1.61%) at wk24. Whereas the weight change of placebo group increased 0.89 kg (1.23%) at wk24 ($P<0.05$). the difference in BW change from wk8 between two groups was statistically significant at wk20 and wk24 ($P<0.05$).

Table 12 Mean ± SD (kg) of body weight in both groups of patients at baseline and follow-up period

Week	BW (kg)	
	Fybogel®	placebo
0	74.9 ± 13.1	71.0 ± 10.1
4	74.5 ± 12.8	70.3 ± 10.5
8	74.4 ± 12.8	70.3 ± 10.3
12	73.7 ± 12.7	70.2 ± 10.4
16	73.8 12.7	70.5 ± 10.4
20	73.5 ± 12.5[a]	70.6 ± 10.4
24	73.1 ± 12.1[a]	71.2 ± 10.4[a]

[a] Significant difference from week8, $P<0.05$

Table 13 Actual changes of body weight in kilogram and percentage of changes (%) from wk0 and wk8 in both groups of patients

Week	Fybogel®		Placebo	
	kg	(%)	kg	(%)
4 vs 0	-0.42	(-0.50)	-0.69	(-1.05)
8 vs 0	-0.59	(-0.73)	-0.65	(-0.94)
12 vs 8	-0.63	(-0.86)	-0.17	(-0.26)
16 vs8	-0.59	(-0.80)	+0.18	(+0.24)
20 vs 8	-0.88	(-1.16)*	+0.29	(+0.40)
24 vs 8	-1.28	(-1.61)*	+0.89	(+1.23)

*Significant difference from placebo, P<0.05

2.2 Anthropometric measurement

The anthropometric measurement in both groups are presented in Tables 14-16 . The BMI was significantly reduced from wk8 in Fybogel® group at wk24 (P <0.05) whereas it was significantly increased in placebo group at wk24 (P<0.05).There were no significant differences in MUAC, UAMC, and FFM in both groups throughout the study. The mean TSF during the treatment phase of Fybogel® group was significantly lower at the end of the study (P<0.01). The mean BFM in the Fybogel® group was also significantly reduced at the end of the treatment phase (P <0.01), while in the placebo group the mean BFM increased significantly (P<0.01) from wk12.

Table 14 Mean ± SD of BMI (kg/m^2) in both groups of patients at baseline and follow-up periods

Week	BMI (kg/m^2)	
	Fybogel®	Placebo
0	30.35 ± 4.95	28.98 ± 28.71
4	30.16 ± 4.91	28.71 ± 4.13
8	30.08 ± 4.91	28.74 ± 4.14
12	29.82 ± 4.85	28.66 ± 4.13
16	29.84 ± 4.87	28.81 ± 4.16
20	29.72 ± 4.77	28.85 ± 4.11
24	29.57 ± 4.65[a]	29.09 ± 4.15[a]

[a] significant difference from week8 , $P<0.05$

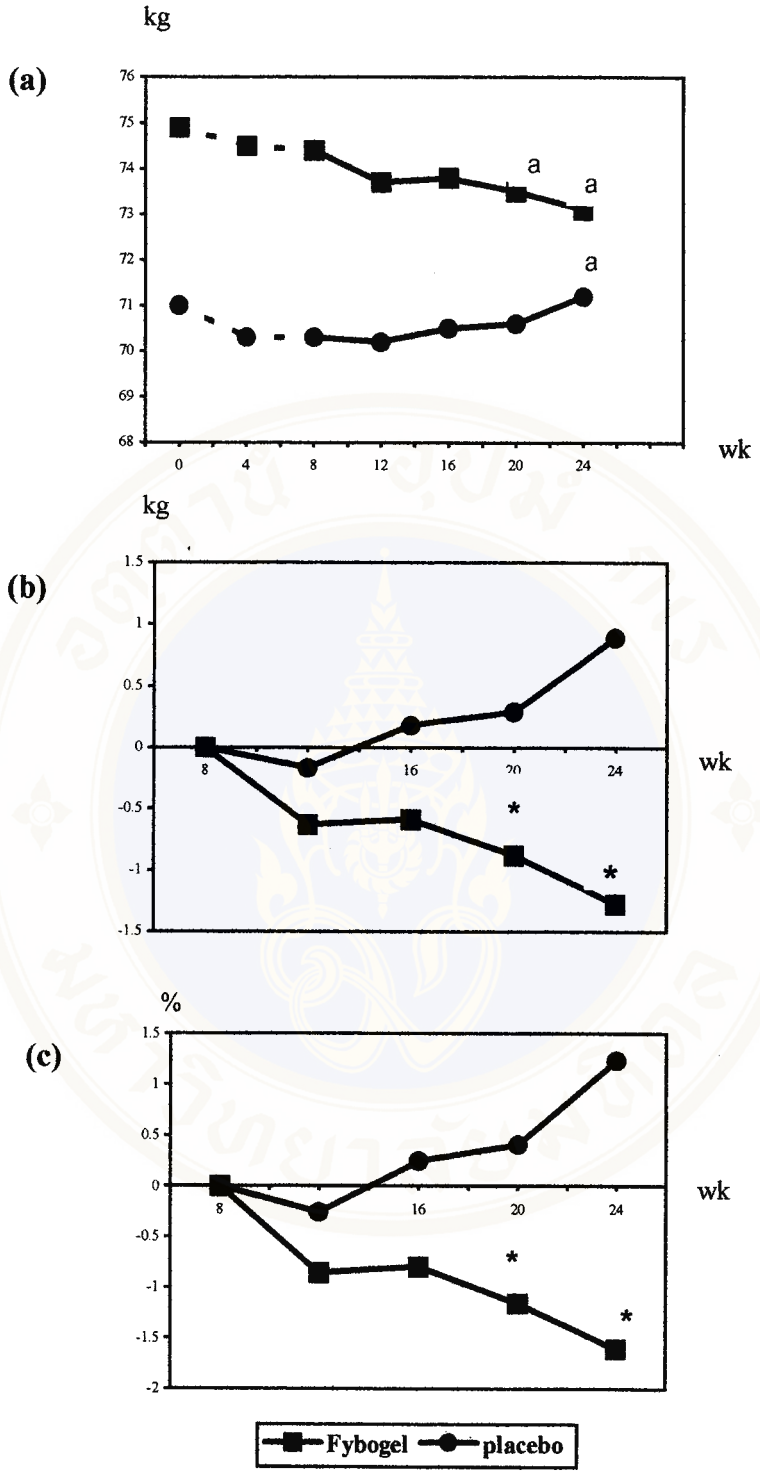

Figure1 Effect of dietary counseling and Fybogel® supplementation on body weight

(a) Mean of BW (----- diet only, ——diet + Fybogel or placebo)

(b) Actual changes of BW from wk8

(c) Percentage of changes of BW from wk8

[a] significant difference from wk 8 (before medication), $p<0.05$

* significant difference from placebo, $P<0.05$

Table 15 Mean ± SD of TSF (mm), MUAC (cm), UAMC (cm) in both groups of patient at baseline and follow-up period

Week	TSF (mm)		MUAC (cm)		UAMC (cm)	
	Fybogel®	Placebo	Fybogel®	placebo	Fybogel®	Placebo
0	23.89 ± 4.65	22.11 ± 5.23	34.21 ± 3.85	33.65 ± 3.45	26.71 ± 3.11	26.70 ± 2.63
4	23.74 ± 4.32	21.51 ± 5.31	34.17 ± 3.27	33.40 ± 3.58	26.71 ± 2.64	26.64 ± 2.79
8	23.66 ± 4.67	21.19 ± 5.45	33.81 ± 3.31	33.15 ± 3.56	26.38 ± 2.52	26.49 ± 2.73
12	23.92 ± 4.05	21.20 ± 5.43	33.86 ± 3.27	33.34 ± 3.65	26.46 ± 2.67	26.68 ± 2.85
16	23.24 ± 3.92	21.08 ± 5.43	33.85 ± 3.34	33.34 ± 3.68	26.55 ± 2.65	26.72 ± 2.84
20	23.22 ± 3.90	21.44 ± 5.37	33.73 ± 3.35	33.39 ± 3.59	26.44 ± 2.90	26.66 ± 2.71
24	22.58 ± 3.75[a]	21.54 ± 5.38	33.47 ± 3.34	33.41 ± 3.60	26.38 ± 2.91	26.64 ± 2.69

[a] significant difference from wk12, $P<0.05$

Table 16 Mean ± SD (kg) of body fat mass and fat-free mass in both groups of patient at baseline and follow-up periods

Week	Body fat mass (kg)		Fat-free mass (kg)	
	Fybogel®	placebo	Fybogel®	Placebo
0	31.30 ± 6.13	27.81 ± 5.72	43.65 ± 7.61	43.16 ± 6.44
4	31.10 ± 5.84	27.43 ± 6.12	43.43 ± 7.49	42.84 ± 6.56
8	30.93 ± 5.97	27.41 ± 6.02	43.42 ± 7.52	42.92 ± 6.35
12	30.53 ± 5.82	26.94 ± 5.66	43.19 ± 7.68	43.21 ± 7.03
16	30.33 ± 5.81	27.35 ± 5.85	43.43 ± 7.61	43.16 ± 6.65
20	30.03 ± 5.77	27.50 ± 5.82	43.44 ± 7.50	43.11 ± 6.56
24	29.64 ± 5.56[a]	27.77 ± 5.96[b]	43.44 ± 7.28	43.44 ± 6.72

[a] significant difference from wk8, P<0.01

[b] significant difference from wk12, P<0.05

3. Effect on glycemic control

3.1 Fasting plasma glucose (FPG)

The mean FPG in both groups are presented in Table 17 and Figure 2 (a). Actual change and percent change of FPG from wk0 and wk8 are shown in Table 18 and Figures 2 (a), (b). During diet-only phase, there was no significant difference of FPG in both groups. During treatment phase, mean FPG of the Fybogel® group was significantly decreased at wk24 ($P<0.01$). Average change of FPG from wk8 was 35.0 mg/dL (16.1%) at wk24 in Fybogel® group whereas there was no significant difference of FPG in the placebo group. The difference change from wk8 of FPG between two groups was statistically significant at wk16 ($P<0.05$) and wk24 ($P<0.01$).

Table 17 Mean ± SD (mg/dL) of fasting plasma glucose in both groups of patients at baseline and follow-up period

Week	FPG (mg/dL)	
	Fybogel®	Placebo
0	214.4 ± 43.3	202.6 ± 53.7
4	189.8 ± 54.8	188.8 ± 78.9
8	215.9 ± 37.8	187.0 ± 71.5
16	194.7 ± 50.3	200.5 ± 51.6
24	180.9 ± 56.1[a]	196.3 ± 57.2

[a] significance difference from week8, $P<0.01$

Table 18 Actual changes of fasting plasma glucose (mg/dL) and percentage of changes (%) from wk0 and wk8 in both groups of patients

Week	Fybogel®		placebo	
	mg/dL	(%)	mg/dL	(%)
4 vs 0	-24.61	(-11.78)	-13.76	(-5.25)
8 vs 0	+1.56	(+2.89)	-15.59	(-6.26)
16 vs 8	-21.28	(-9.06)*	+13.47	(+14.77)
24 vs 8	-35.00	(-16.10)**	+9.29	(+10.40)

*, ** significant difference from placebo, $P<0.05$ and 0.01 respectively

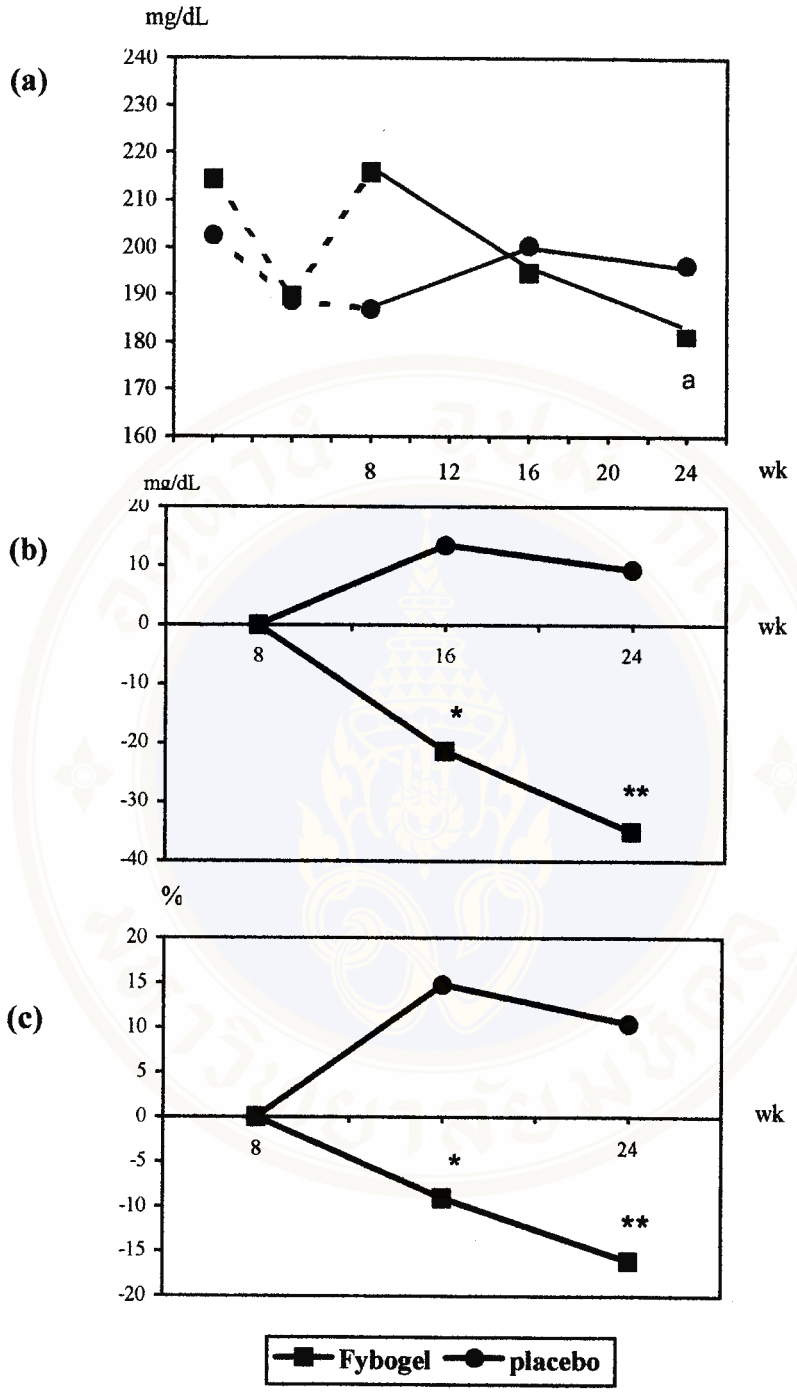

Figure 2 Effect of dietary counseling and Fybogel® supplementation on FPG

(a) Mean of FPG (----- diet only, —— diet + Fybogel® or placebo)

(b) Actual change of FPG from wk8

(c) Percentage of change of FPG from wk8

[a] significant difference from wk8 P<.05,

*,** significant difference from placebo p<.05and .01 respectively

3.2 Glycosylated hemoglobin (HbA_{1c})

The mean HbA_{1c} in both groups are presented in Table 19 and Figure 3 (a). Actual changes and percentage of changes of HbA_{1c} from wk0 and wk8 are shown in Table 20 and Figures 3 (b), (c). During diet-only phase, there was no significant difference of HbA_{1c} between both groups. During treatment phase, mean HbA_{1c} in the Fybogel® group was significantly decreased at wk24 ($P<0.05$). The average levels of HbA_{1c} decreased from 10.1 at wk8 to 9.0 at wk24 (10.12%) in Fybogel® group whereas there was no significant reduction in the placebo group. The changes from wk8 of HbA_{1c} between two groups was statistically significant at wk24 ($P<0.05$).

Table 19 Mean ± SD of HbA_{1c} (%) in both groups of patient at baseline and follow-up period

Week	HbA_{1c} (%)	
	Fybogel®	Placebo
0	10.4 ± 1.6	10.5 ± 1.6
8	10.1 ± 1.4	9.7 ± 1.9
16	9.7 ± 1.5	10.0 ± 1.8
24	9.0 ± 1.4[a]	9.7 ± 1.3

[a] significant difference from wk8, $P<0.05$

Table 20 Actual changes (percentage of changes) from wk0 and wk8 of HbA_{1c} in both groups of patients

Week	Fybogel®		placebo	
	%	%change	%	%change
8 vs 0	-0.34	(-2.62)	-0.78	(-6.29)
16 vs 8	-0.34	(-3.04)	+0.24	(+4.47)
24 vs 8	-1.07	(-10.12)*	-0.05	(+1.53)

* significant difference from placebo,P<0.05

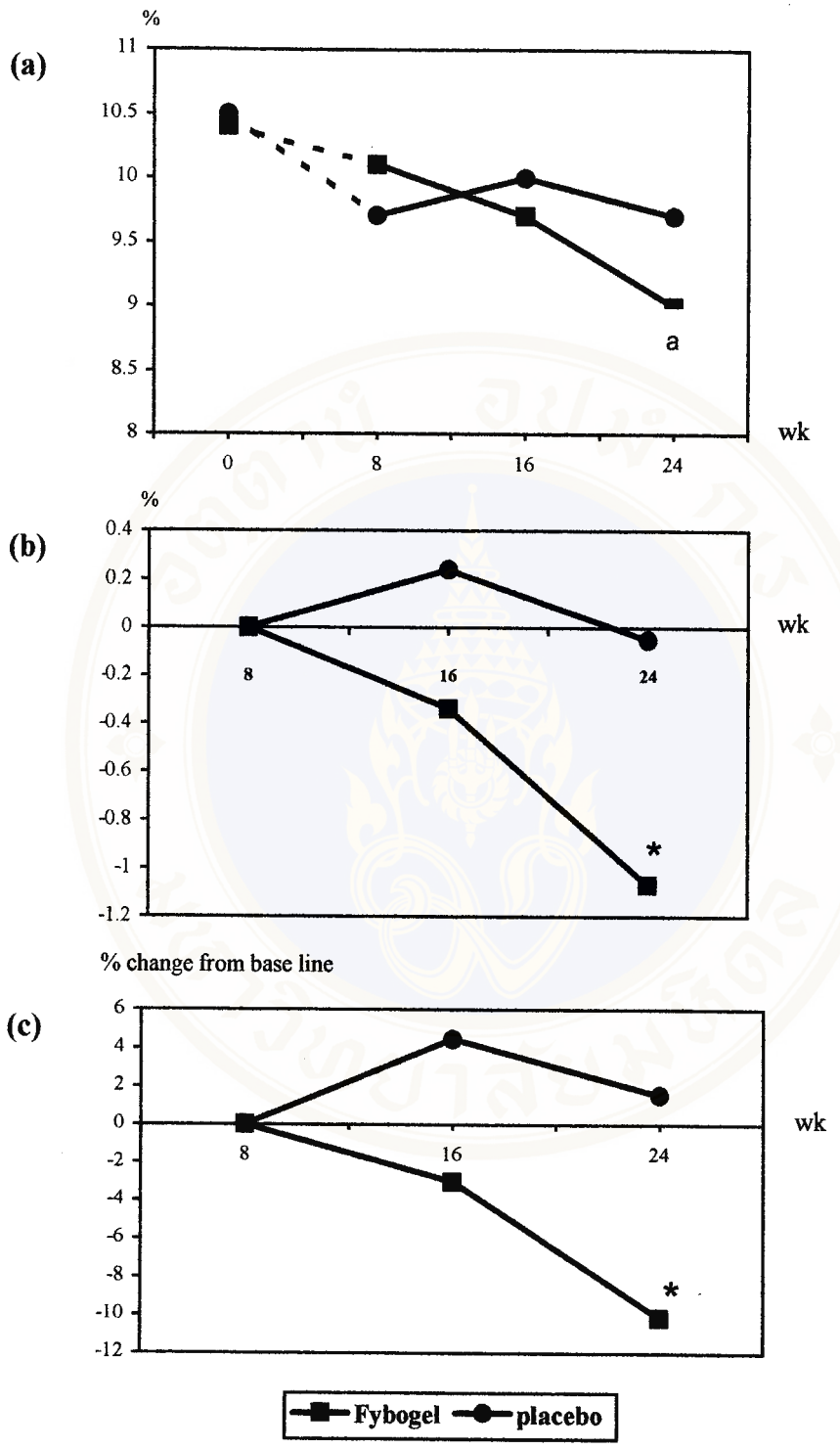

Figure 3 Effect of dietary counseling and Fybogel® supplementation on HbA_{1c}

(a) Mean of HbA_{1c} (----- diet only, —— diet + Fybogel® or placebo)

(b) Actual changes of HbA_{1c} from wk8

(c) Percentage of changes of HbA_{1c} from wk8

[a]significant difference from wk8 P<.05, [*]significant difference from placebo P<.05

4. Effect on serum lipids

4.1 Total cholesterol (TC)

The mean TC levels in both groups are presented in Table 21 and Figure 4. There was no significant difference of mean TC levels between times in both groups. The changes from wk8 of TC between the two groups were also not statistically significant.

Nevertheless, when we focused on the subjects with moderate to high hypercholesterolemia (TC at wk8>240 mg/dL) in Table 22 and Figure 5 (a). The TC reduction was seen significantly at wk24 ($P<0.05$) in Fybogel® group whereas there was no significant difference in the placebo group. Average change of TC at wk24 compare to wk8 was decreased 41 mg/dL (14.2%) as shown in Table 23 and Figures 5 (b),(c). The change of TC level from wk8 between two groups was only statistically significant at wk16 ($P<0.05$).

Table 21 Mean ± SD (mg/dL) of total cholesterol in both groups of patients at baseline and follow-up period

Week	Total cholesterol (mg/dL)	
	Fybogel®	Placebo
0	254.3 ± 37.1	266.6 ± 42.0
4	232.0 ± 49.7	251.1 ± 39.0
8	247.1 ± 42.5	265.8 ± 42.8
16	246.3 ± 34.7	272.4 ± 48.9
24	233.6 ± 40.4	261.6 ± 40.1

No significant difference

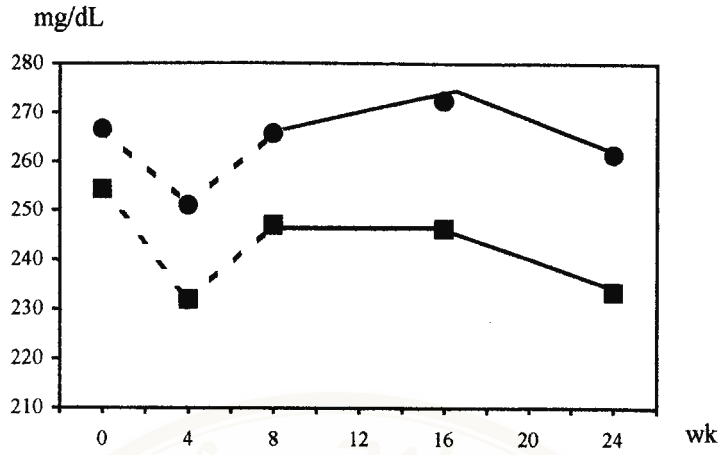

Figure 4 Effect of dietary counseling and Fybogel® or placebo supplementation on TC (mean ± SD)

Table 22 Mean ± SD (mg/dL) of total cholesterol in hypercholesterolemic subjects (greater than 240 mg/dL) at wk8 in both groups of patients

Week	Total cholesterol (mg/dL)	
	Fybogel® (n=8)	Placebo (n=13)
8	285.3 ± 31.0	283.4 ± 30.2
16	255.9 ± 34.0	282.2 ± 45.0
24	244.3 ± 44.4[a]	265.8 ± 39.1

[a] significant difference from wk8, $P<0.05$

Table 23 Actual changes (percentage of changes) of total cholesterol in hypercholesterolemic subjects (greater than 240 mg/dL) from wk8 in both groups of patients

Week	Fybogel®		placebo	
	mg/dL	(%)	mg/dL	(%)
16 vs 8	-29.4	(-10.30)*	-1.2	(-0.40)
24 vs 8	-41.0	(-14.20)	-17.6	(-6.0)

* significant difference from placebo, $P<0.05$

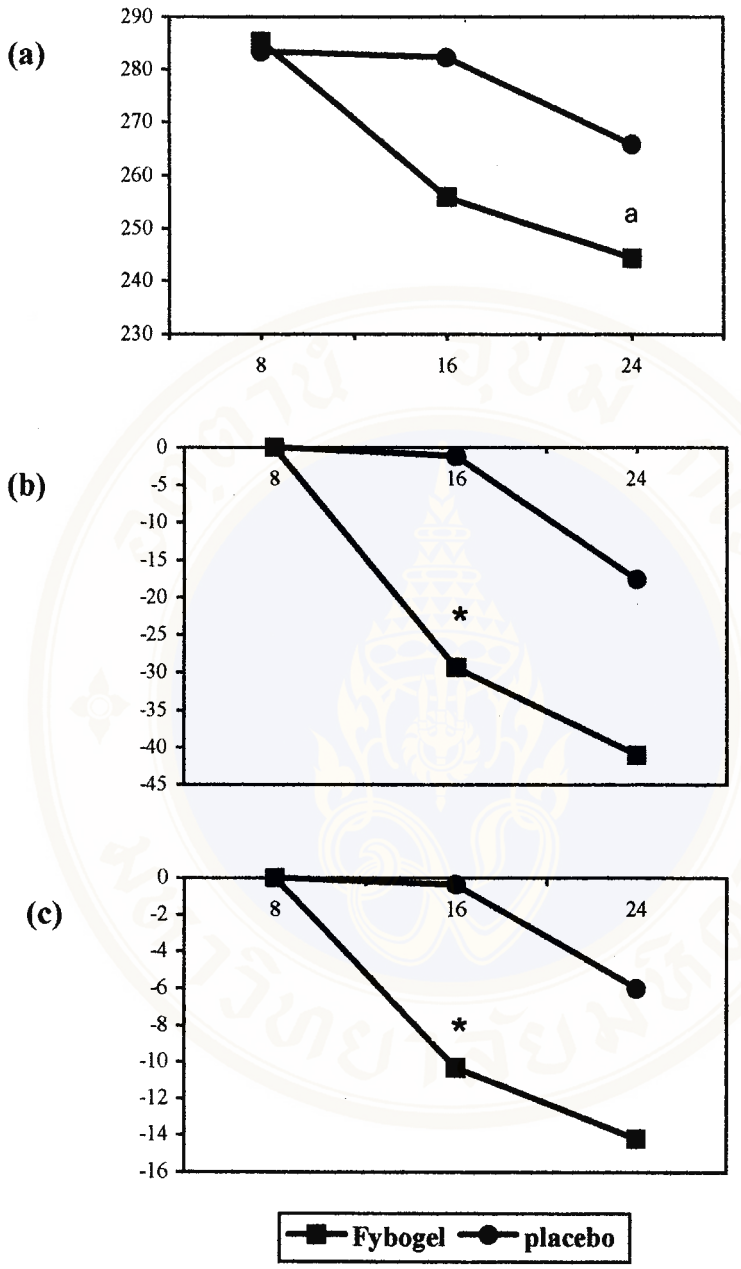

Figure 5 Effect of dietary counseling and Fybogel® supplementation on cholesterol level in hypercholesterolemic subjects (TC>240 mg/dL) at wk8

(a) Mean of TC

(b) Actual change of TC from wk8

(c) Percentages of changes of TC from wk8

[a] significant difference from wk8 P<.05,

* significant difference from placebo p<.05

4.2 Low density lipoprotein cholesterol (LDL-C)

The mean LDL-C levels in both groups are presented in Table 24 and Figure 6 (a) . Actual changes and percentage of changes of LDL-C from wk0 and wk8 are shown in Table 25 and Figures 6 (b),(c). During diet-only phase and treatment phase, mean LDL-C levels were not significantly changes between times in both groups. However, the changes from wk8 of LDL-C levels between the two groups was statistically significant at wk24 ($P<0.05$).

Table 24 Mean ± SD (mg/dL) of LDL-C in both groups of patients at baseline and follow-up period

Week	LDL-C (mg/dL)	
	Fybogel®	Placebo
0	164.2 ± 39.7	168.5 ± 36.3
4	148.2 ± 53.3	157.0 ± 32.4
8	164.5 ± 38.8	166.9 ± 33.8
16	159.8 ± 42.4	162.6 ± 37.7
24	147.8 ± 41.9	171.4 ± 39.2

No significant difference

Table 25 Actual changes (percentage of changes) from wk0 and wk8 of LDL-C in both groups of patients

Week	Fybogel®		placebo	
	mg/dL	(%)	mg/dL	(%)
4 vs 0	-15.94	(-10.90)	-11.47	(-5.49)
8 vs 0	+0.33	(+2.22)	-1.59	(+1.49)
16 vs 8	-4.72	(-2.45)	-4.24	(-1.19)
24 vs 8	-16.72	(-9.51)*	+4.47	(+3.94)

Significant difference from placebo , $P<0.05$

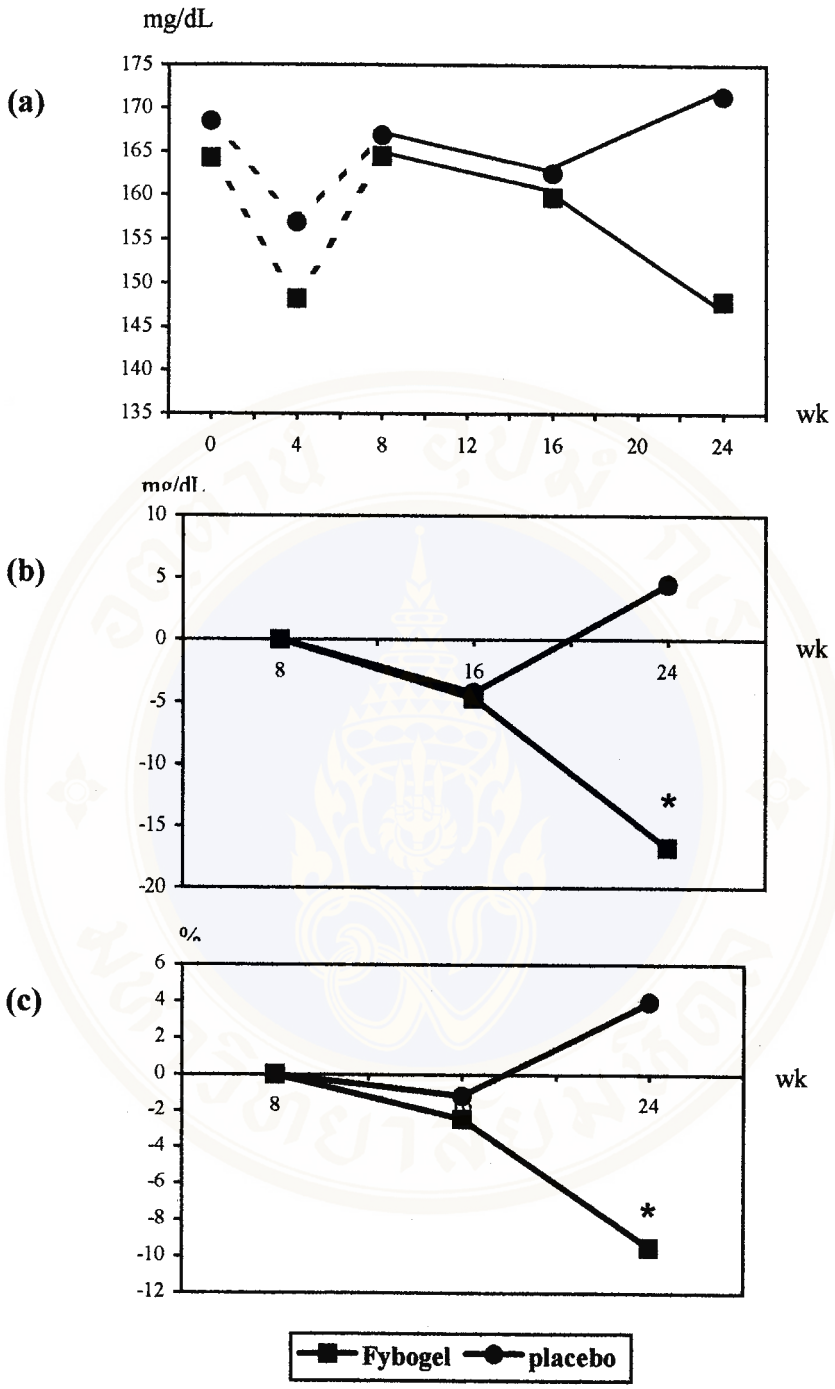

Figure 6 Effect of dietary counseling and Fybogel® supplementation on LDL-C

(a) Mean of LDL-C

(b) Actual changes of LDL-C from wk8

(c) Percentage of changes of LDL-C from wk8

* significant difference from placebo $p<.05$

4.3 High density lipoprotein cholesterol (HDL-C) and Triglyerides

Serum HDL-C and triglycerides concentrations were not significantly changed over time in either within group or between groups as shown in Tables 26-27.

Table 26 Mean ± SD (mg/dL) of HDL-C levels in both groups of patients at baseline and follow-up period

Week	HDL-C (mg/dL)	
	Fybogel®	Placebo
0	55.6 ± 10.7	58.5 ± 13.8
4	54.1 ± 11.7	55.2 ± 15.5
8	52.9 ± 8.8	57.9 ± 13.4
16	53.3 ± 10.8	55.9 ± 15.3
24	51.8 ± 8.0	58.3 ± 14.7

No significant difference

Table 27 Mean ± SD (mg/dL) of triglycerides levels in both groups of patient at baseline and follow-up period

Week	Triglycerides (mg/dL)	
	Fybogel®	Placebo
0	181.2 ± 80.3	200.9 ± 114.0
4	176.4 ± 95.0	195.1 ± 112.2
8	183.2 ± 74.6	205.8 ± 112.5
16	183.3 ± 103.3	228.4 ± 174.3
24	173.4 ± 123.1	227.6 ± 157.3

No significant difference

5. Effect on vitamin and mineral status

Vitamin and mineral status are presented in Tables 28-29. Mean vitamin (serum retinol, ∝-tocopherol, vitaminB_1, vitaminB_2, vitaminC, vitaminB_{12}, folate and RBC folate) and mineral (serum calcium, magnesium, phosphorus, iron, zinc and copper) levels were not significantly changed after treatment in both groups.

6. Effect on routine safety parameters

Routine safety parameters before and after Fybogel® and placebo supplementation are shown in Tables 30-34. Blood count, liver function test, renal function test, protein status and serum electrolyte levels were within normal ranges and were not significantly changed after treatment in both groups.

Table 28 Mean ± SD of vitamin status in both groups of patients before and after supplementation

Vitamin	Fybogel®		Placebo		Reference range
	wk8	wk24	wk8	Wk24	
retinol, S, µg/dL	63.17 ± 20.71	62.15 ± 21.25	76.15 ± 37.07	75.51 ± 33.30	20-100
(µmol/L)	(2.21 0.72)	(2.17 0.74)	(2.66 1.29)	(2.64 1.16)	(0.7-3.5)
α-tocopherol, S,	1.39 ± 0.43	1.52 ± 0.51	1.65 ± 0.58	1.68 ± 0.32	>0.5
mg/dL (µmol/L)	(32.28 9.98)	(35.29 11.84)	(38.31 13.47)	(39.01 7.43)	(>11.6)
ascorbate, S, mg/dL	0.99 ± 0.38	1.03 ± 0.36	0.86 ± 0.29	0.82 ± 0.41	0.4-1.0
(µmol/L)	(56.21 21.58)	(58.48 20.44)	(48.83 16.47)	(46.56 23.28)	(23-57)
Vitamin B_1 , %TPPE	0.80 ± 1.90	0.25 ± 1.07	1.90 ± 4.59	1.85 ± 4.15	<15
ETKA	218.1 ± 53.1	216.8 ± 45.5	205.9 ± 55.7	195.6 ± 67.3	
VitaminB_2 , AC	1.07± 0.14	1.13 ± 0.08	1.06 ± 0.10	1.14 ± 0.14	<1.2
EGRA	2046.8 ± 713.2	1889.8 ± 663.3	2029.5 ± 527.0	1711.0 ± 525.9	
VitaminB_{12},S,pg/mL	393.4 ± 212.55	542.13 ± 239.64	638.07 ± 432.85	723.73 ± 346.26	200-900
(µmol/L)	(290.33 ± 156.86)	(400.09 ± 176.85)	(470.90 ± 319.44)	(534.11 ± 252.59)	(147-660)
folate, S, ng/mL,	11.23 ± 5.00	14.43 ± 5.34	9.92 ± 4.95	11.67 ± 6.88	5-16
(mmol/L)	(25.44 ± 11.33)	(32.68 ± 12.10)	(22.47 ± 11.21)	(26.43 ± 15.58)	(11-36)
RBC folate, ng/mL	244.07 ± 185.58	222.13 ± 67.33	209.77 ± 71.94	237.93 ± 72.53	150-450
(nmol/L)	(552.82 ± 420.34)	(503.12 ± 152.50)	(475.13 ± 162.94)	(538.91 ± 164.28)	(340-1,020)

No significant difference

Table 29 Mean ± SD of mineral status in both groups of patients before and after supplementation

Mineral	Fybogel®		placebo		Reference range
	Wk8	Wk24	Wk8	Wk24	
Total calcium, S, mmol/L	2.22 ± 0.16	2.26 ± 0.08	2.29 ± 0.18	2.29 ± 0.17	2.20-2.64
Ionized calcium, S, mmol/L	1.23 ± 0.07	1.22 ± 0.04	1.24 ± 0.10	1.24 ± 0.09	1.18-1.38
Magnesium, S,mmol/L	0.763 ± 0.104	0.803 ± 0.096	0.775 ± 0.120	1.152 ± 0.138	0.8-1.2
Phosphorus, S,mmol/L	1.18 ± 0.20	1.22 ± 0.14	1.19 ± 0.15	1.11 ± 0.21	1.0-1.4
IRON, S, µg/dL	93.48 ± 14.81	99.49 ± 28.06	83.59 ± 35.60	87.02 ± 32.03	50-150
TIBC, S, µg/dL	274.21 ± 40.27	277.19 ± 29.10	262.59 ± 34.85	268.63 ± 47.27	250-370
Zinc, S, µg/L	103.8 ± 22.2	98.4 ± 13.0	91.7 ± 17.8	90.9 ± 14.1	75-120
(µmol/L)	(15.88 ± 3.40)	(15.06 ± 1.99)	(14.03 ± 2.72)	(13.91 ± 2.16)	(11.5-18.5)
Copper, S, µg/L	125.4 ± 19.4	123.1 ± 27.2	116.4 ± 31.7	121.2 ± 29.0	70-140
(µmol/L)	(19.69 ± 3.05)	(19.33 ± 4.27)	(18.27 ± 4.98)	(19.03 ± 4.55)	(11.0-22.0)

No significant difference

Table 30 Mean ± SD of complete blood count in both groups of patients before and after supplementation

Parameters	Fybogel®		Placebo	
	Wk8	Wk24	Wk8	Wk24
Hemoglobin, g/dL	14.11 ± 1.01	13.77 ± 0.77	13.94 ± 1.00	13.78 ± 1.02
Hematocrit, %	42.94 ± 2.91	42.30 ± 2.26	42.38 ± 3.35	42.34 ± 2.76
RBC, $10^6/mm^3$	5.02 ± 0.43	5.08 ± 0.62	4.89 ± 0.39	4.83 ± 0.45
Platelet, $10^3/mm^3$	279.17 ± 62.78	295.89 ± 62.80	282.59 ± 77.17	276.94 ± 74.15
WBC, $10^3/mm^3$	8.22 ± 2.06	7.80 ± 1.52	8.82 ± 2.01	8.12 ± 1.22

No significant difference

Table 31 Mean ± SD of liver function test in both groups of patients before and after supplementation

parameters	Fybogel®		placebo	
	Wk8	Wk24	Wk8	Wk24
Alkaline phosphatase, U/L	85.83 ± 32.89	77.94 ± 21.33	77.65 ± 29.40	75.12 ± 28.16
Aspartate aminotransferase,U/L	25.56 ± 8.93	22.50 ± 7.88	26.65 ± 18.17	27.47 ± 18.14
Alanine aminotransferase, U/L	28.94 ± 13.55	25.56 ± 12.23	26.65 ± 15.57	26.82 ± 19.90
Gamma-glutamyl transferase, U/L	43.89 ± 21.92	35.56 ± 17.88	41.29 ± 20.58	40.18 ± 23.38
Total bilirubin, µmol/L	12.21 ± 2.38	11.93 ± 3.3	13.05 ± 5.50	11.50 ± 2.85
Direct bilirubin, µmol/L	2.01 ± 0.58	2.48 ± 0.68	2.32 ± 1.35	2.37 ± 1.41

No significant difference

Table 32 Mean ± SD of renal function test in both groups of patients before and after supplementation

Parameters	Fybogel®		placebo	
	Wk8	Wk24	Wk8	Wk24
BUN, mg/dL	15.28 ± 4.47	14.78 ± 3.69	17.00 ± 6.06	16.35 ± 5.66
Creatinine, mg/dL	0.87 ± 0.29	0.85 ± 0.23	1.01 ± 0.29	0.89 ± 0.25
Uric acid, mg/dL	5.06 ± 1.00	5.21 ± 1.04	5.38 ± 1.48	4.98 ± 1.83

No significant difference

Table 33 Mean ± SD of serum total protein and albumin in both groups of patient before and after supplementation

Parameters	Fybogel®		placebo	
	Wk8	Wk24	Wk8	Wk24
Total protein, g/L	74.21 ± 7.65	74.83 ± 5.54	70.49 ± 6.96	72.10 ± 6.13
Albumin, g/L	44.06 ± 4.27	44.38 ± 4.93	41.70 ± 3.45	42.29 ± 4.15

No significant difference

Table 34 Mean ± SD of serum electrolyte in both groups of patients before and after supplementation

Parameters	Fybogel®		Placebo	
	Wk8	Wk24	Wk8	Wk24
Sodium, mmol/L	138.78 ± 3.59	139.11± 3.07	139.65 ± 2.67	140.00 ± 3.00
Potassium, mmol/L	4.50 ± 0.49	4.53 ± 0.41	4.48 ± 0.45	4.46 ± 0.49
Chloride, mmol/L	104.61 ± 3.60	106.28 ± 3.97	105.88 ± 4.57	106.82 ± 3.96
Carbon dioxide, mmol/L	21.82 ± 3.34	21.48 ± 2.85	20.88 ± 3.14	21.16 ± 3.04

No significant difference

Part III Effect of withdrawal of Fybogel® on body weight , glycemic control and serum lipids

Table 35 Mean ± SD of BW, glycemic control and serum lipid after withdrawal of Fybogel® and placebo

parameters	Fybogel® (n=16)		Placebo (n=16)	
	Wk24	Wk32	Wk24	Wk32
BW, kg	72.6 ± 11.1	73.4 ± 11.5 [b]	72.0 ± 10.5	72.3 ± 10.4
FPG, mg/dL	188.4 ± 54.0	230.5 ± 72.0 [a]	195.9 ± 59.1	209.3 ± 65.9
HbA_{1c}, %	9.2 ± 1.4	10.3 ± 1.7 [b]	9.7 ± 1.4	10.2 ± 1.3 [a]
TC, mg/dL	247.1 ± 32.7	253.5 ± 44.1	260.6 ± 41.2	270.6 ± 42.6
LDL-C, mg/dL	149.0 ± 43.6	156.4 ± 43.9	171.6 ± 42.3	180.9 ± 35.2

[a,b]significant difference from wk24 $P<0.05$ and 0.01 respectively

Table 36 Actual change of BW, glycemic control and serum lipid levels after withdrawal of Fybogel® and placebo

Parameters	Fybogel® (n=16)	Placebo (n=16)
	wk32 vs wk24	Wk32 vs wk24
BW, kg	+0.74	+0.30
FPG, mg/dL	+42.13	+13.38
HbA_{1c}, %	+1.10 *	+0.48
TC, mg/dL	+6.38	+10.00
LDL-C, mg/dL	+7.40	+9.28

*significant difference from placebo $P<0.05$

After withdrawal of Fybogel® and placebo at wk24, 16 cases of Fybogel® and 16 cases of placebo group were followed for two months. The mean BW was significantly increased 0.74 kg. in Fybogel® group, while there was no significant change of BW in the placebo group. Means FPG and HbA_{1c} were also significantly increased 42.1 mg/dL ($P<0.05$) and 1.1% ($P<0.01$), respectively in Fybogel® group whereas in the placebo group mean HbA_{1c} was significantly increased 0.48% ($P<0.05$). The changes in HbA_{1c} from wk24 between groups was statistically significant ($P<0.05$). There were no significant changes of TC and LDL-C levels in both groups after withdrawal of supplementation.

CHAPTER V

DISCUSSION

Obesity is characterized by a number of metabolic perturbations such as elevated blood lipid level, hyperinsulinaemia, insulin resistance and propensity for diabetes (121). Very few studies have been carried out which address the question of whether dietary fiber may play an important direct role in alleviating the metabolic aberrations associated with obesity. An effect can obviously be expected since certain fiber facilitate weight reduction. On a theoretical basis fiber treatment may improve the insulin resistance occurring in both obesity and diabetes by reducing the body weight. It remains to be established whether increased fiber intake by obese subjects will reduce their propensity for diabetes. Overweight is another factor responsible for the rise of serum cholesterol levels to above the desirable range. It has been estimated that the weight gain that typically occurs with aging account for a rise in serum cholesterol of approximately 25 mg/dL (122) Although fiber has been increasingly recognized as an important dietary constituent, controversy and confusion still exist about the physiologic effect of fiber. The results of this study are regarding the effects of soluble fibers on body weight, glycemic control, and serum lipid profiles.

Part I General characteristics of patients at baseline

The present study included 35 obese NIDDM patients who had obese class I, poor glycemic control and high serum cholesterol levels. Overweight carries a penalty in that it leads to a worsening of all the elements of the cardiovascular risk profiles, including dyslipidemia and type2 diabetes. On the basis of data from the Framingham Heart Study and from other studies (123), it can be concluded that the degree of overweight is related to the rate of development of cardiovascular disease.

Routine safety parameters and vitamins and minerals status of all patients prior to the study were within normal ranges which imply that the study did not affect the health status of the subjects. (Tables 1-9)

Part II Effect of dietary counseling (8-week diet-only)

Proper nutrition, including not only food selection but also eating behavior and eating cues, represents a critically important component of the effective treatment of obesity. Reducing the amount of energy in the diet from fat is often required, however, moderating overall levels of energy consumption is also important. Current recommended dietary distribution for healthy adults consists of 15-20% of protein, no more than 30% of fat and 50-60% of carbohydrate. In the present study, we found both groups of patients consumed high amount of fat and low carbohydrate at the baseline (Table 10-11). Recent data from doubly labeled water energy intake studies have provided compelling evidence that excessive food intake does contribute to the development of obesity (124,125). It has also been postulated that high in fat contributes to excessive energy intake because of the energy density of fat and because it is poorly regulated from 1 meal to the next, unlike protein and carbohydrate

(126). Many persons find it difficult to reduce the amount of fat in the diet because it contributes to the moistness and flavor of foods.

After giving dietary advice, the patients in both groups improved their eating habits, the mean total energy intake was significantly reduced by 405-583 kcal and the percentage of nutrient distribution from carbohydrate was significantly increased, while the percentage from fat was significantly decreased. However, there was no significant reduction of BW during the diet-only phase (wk0-8) but a tendency to decrease was seen in both groups. It is interesting that both groups seemed to show better weight reduction and metabolic control during wk4 than wk8. (Table13) At wk8 of dietary control the mean FPG and TC seemed to increase in both groups but HbA_{1c} tended to decrease. These findings show that the patients comply to the dietary advice to a certain extent.(69) It implies that tightly regulated food choices and severe energy limitations create difficulties in patient adherence. It also points out that giving dietary advice may be effective only during the first few weeks(127). Inevitably, when there is a change in body weight, the single greatest contributor to successful body weight regulation is the strength of the dietary support patients receive and their adherence to that diet. Some medication may be used to support diet instruction and behavior modification for some people.

Part III Effect of treatments (16-week Fybogel® or placebo supplementation)

3.1 Effect on dietary intake

Studies in the effects of psyllium on energy intake have shown conflicting results. Some reports showed no effect (25,100,128) whereas some demonstrated decreased energy intake leading to weight loss (129). During the treatment phase in the present study, daily energy intake and nutrient distribution were no significantly changed over time either Fybogel® or placebo groups (Tables 10-11). These results may be due to the dietary advice given to the patients before treatment. Food intake decreased in some studies because of ad libitum energy intake (129).

3.2 Effect on body weight and anthropometric measurements.

The results in the present study indicate that the Fybogel® group still had a weight reduction effect even at the end of the treatment period as compared to an increase in the placebo group. (Tables 12-13, Figure1) The sustained significant decrease in the body weight in the fiber group is in agreement with other studies (130,131).

The result in this study, BW reduction was only 1.28 kg (1.61%) in 16 wks Fybogel® supplementation. However, a significant BW loss was reported in only 14 of 58 studies in the literature reviewed by Glore (98) and most of the weight loss were 1 to 2 kg. In addition, the BW of Fybogel® group was significantly different from placebo. This was due to the significant increase of BW in the placebo group (Tables

12-13). BW reduction in the Fybogel® group at the end of the study was confirmed by the significant reduction in BMI, TSF, and BFM at wk24 while FFM was not significantly changed (Table 14-16). Thus , it may indicate the predominate affect of fat on weight reduction.

Eleven out of the 17 soluble fibers materials evaluated in the study reported during the Fourth Vahouny Fiber Symposium in USA produced a statistically significant or appreciable (≥0.5 pounds per week) weight loss when compared to the control group or compared to baseline (132). Only 1 of 4 psyllium treatment caused significant weight loss (132). Some of the factors involved are subject compliance, time of fiber supplementation, fiber type, responders or nonresponders of fiber treatment and fiber's effect.

Subject compliance to protocol requirement may be a problem. High fiber diet, fiber enriched food and supplements are often not pleasingly palatable (132) and may not be consumed as required, especially in non-institutionalized conditions. However, in the present study, all subjects can took the fiber without difficulties because of its orange flavor. The compliance in our study was very well, 91% in placebo and 88% in Fybogel® groups. As a rule, energy deficits of approximately 500 to 1,000 kcal per day should result in average weight loss of 1 to 2 lb per week (133). The dietary compliance was monitored weekly with 3-day dietary records. The result showed only 1.28 kg reduction was seen in 16 wks. It implies that the subjects may underreport their actual energy intake. This has been true especially in obese subjects, in whom the energy intake has been reported 20-35% below actual intake(130,163).

Very few studies applying a dietary fiber supplement over a longer period of time have been published (131,134). In long-term psyllium supplementation there were

no significant weight loss reported and those studies were focused on the hypocholesterolemic effect of the fiber in non obese hypercholesterolemic patients (135,136). In the present study, subjects were obese NIDDM patients with hypercholesterolemia, hence, the effect of Fybogel® was seen. Furthermore, when Fybogel® or placebo was withdrawn at wk24 the mean BW was significantly increased 0.74 kg in Fybogel® group at wk32 (Tables 35-36). This outcome confirmed the effect of Fybogel® in the reduction of BW.

The mechanisms underlying a possible effect of dietary fiber supplement on weight reduction remain unsolved. Increased satiety is believed to be attributed to increased ingestion time. Rigaud D et al.(131) investigated the effect of mixed fiber tablet in mild to moderate overweight patients for 6 months, found that not only the weight loss was higher, but the reduction of hunger feeling was also greater in the fiber-treated group. The increase in volume which fiber mixed with digestive juices and water products induces satiety signals by distention of the stomach. Turnbull WH (100) investigated the effect of plantago ovata seed on appetite found that there was a significant difference in fullness at 1 hour post-meal between plantago and placebo. There was very little evidence in the literature to support this hypothesis (132).

Delayed gastric emptying time and stimulation of the release of several gut hormones may also add to the reduced hunger feelings(137,138).A review of clinical studies evaluating stomach emptying properties of 25 fiber materials shows that 12 delayed stomach emptying, 4 accelerated stomach emptying and 9 had no effect (132). Jarjis HA et al (145) reported no significant effect of ispaghula (Fybogel® and Metamucil®) on gastric emptying due to liquid test meal. On the contrary, a recent

study found that psyllium significantly delay gastric emptying of solid meal in obese patients by echographic evaluation (139).

There is some evidence, however, that certain fiber materials have either a direct or indirect effect on several hormones in the small intestine. Selected fiber materials carry lipids into the ileum and the cecum. Spiller found that perfusion of lipids into the ileum resulted in an increase in plasma concentration of enteroglucagon, neurotensin and peptide YY and perhaps other neurotransmitters have been found to delay stomach emptying and slowing of small bowel transit (132). This phenomenon has been called the ileal brake. These potential mechanisms may play an important role in dietary fiber's possible benefit in weight loss and weight maintenance programs.

The interference with absorption of nutrients is also believed to be one area in which fiber is beneficial for weight reduction (132). Increased fecal energy losses have been reported by Southgate and Durnin (140). A possibility exists that decreased intestinal transit time may somehow influence absorptive capacity. Read, Jenkins and Spiller have confirmed that guar gum given with a meal increase the caloric load in ileostomy reservoir of ileostomy patients (132). A number of investigators have proposed that some fibers carry nutrients into the large intestine where they will be fermented and used as energy by the colonic microflora or be excreted in the feces. In either case this will result in loss of available caloric material to the host and thereby possibly contribute to long term weight management. Heaton reviewed studies of fecal energy loss after administration of dietary fiber materials and found an average energy loss of 100 to 200 kcal/day (132). This is a small but perhaps important mechanism of action in the benefit of fiber over the long run.

3.3 Effect on glycemic control

Although preliminary studies in diabetic patients demonstrated reductions in fasting glucose concentrations (141-143) but interpretation of these studies is complicated by lack of a placebo control (141), the presence of other disease (142), and small sample sizes (143). Pastor JG et al (144) found that psyllium reduced rise in postprandial glucose and insulin concentrations in NIDDM patients. Some researchers failed to detect significant postprandial glucose blunting when psyllium (145) or soy fiber (146) was administered to NIDDM patients. This discrepancy may be due to the type of test meal given with the fiber. In two trials (145,146) in which no effect was observed, the fiber was administered with a liquid test meal. However, when the fiber was given as a supplement to, or a component of, a conventional solid food meal, beneficial effects were found (147-149,151).

Abraham and Metha (150) reported no significant reduction of meal tolerance test with intakes of 21 g/d of psyllium for 3 wks. They explained the cause of lack of glucose response from the relative nutrient composition of their test meal, which contained 46% of the energy as carbohydrate while other studies which showed significant reduction of postprandial glucose used more than 55% of energy as carbohydrate in the test meal. The nutrient distribution in the present study was 51-53% as carbohydrate and the long-term hypoglycemic effects of Fybogel® over placebo in the present study is displayed by the significant reduction of FPG and HbA_{1c} (Tables 17-20). Furthermore, after withdrawal of Fybogel® and placebo for two months the mean FPG and HbA_{1c} were significantly increased in Fybogel® group, whereas only the mean FPG was significantly increased in placebo group (Tables 35-

36) and the mean changes of HbA_{1c} in the placebo group was also significantly increased over Fybogel® group after withdrawal. Findings in the present study confirm the ability of Fybogel® on the glycemic control.

The possible effects of fiber within the gastrointestinal tract include changes in mixing, motility, and convection; intraluminal digestion rate; thickness of the unstirred layer; inhibition of maximum transport capacity; alter pH profile; and, with long-term treatment, altered intestinal morphology (52). Blackburn et al (43) studied in normal and diabetic individuals, suggested that fibers inhibit intestinal motility and thus decreased convection. However, studies in humans showed that only with pectin was there evidence of an increase in the thickness of the unstirred water layer. In addition, certain high fibers may have antienzyme activity (153). Fiber has also been shown to reduce pancreatic enzyme activity and decrease pancreatic enzyme secretion (45,154) and influence the release of gut hormones. The response of gastric inhibitory polypeptide (GIP), a stimulus for insulin secretion, was more attenuated in healthy diabetic subjects and in patients with postgastrectomy dumping syndrome after ingesting fiber-supplemented meals than after control meals (155,156). An interesting observation has been the demonstration of an enhanced release of plasma somatostatin with fiber (157). Somatostatin delayed the absorption of carbohydrate and glucose from the small intestine and could be partly mediating the effects of fiber. Further studies are clearly needed.

Bacterial fermentation of fiber in the colon generates short-chain fatty acids that may inhibit fatty acid mobilization and intestinal synthesis and decrease gluconeogenesis (52). Indeed, this has been the basis of the development of a number of putative oral hypoglycemic agents. The role of the short-chain fatty acids in

enhanced glucose utilization, insulin secretion, and hepatic glucose utilization need further elaboration.

Numerous studies have demonstrated that lowered blood glucose levels after fiber consumption are associated with either unchanged or lower insulin levels (78,144,155). These acute effects cannot be ascribed to increased insulin sensitivity but may be due to the slowed rate of intestinal transit and an attenuated stimulus. However, the observation in chronic ingestion of fiber was associated with lower basal glucose levels and decreased urinary excretion of C-peptide (158) suggest an increased in insulin sensitivity or a decreased demand for insulin. Indeed, in the studies which has been examined, an increase in insulin binding to monocyte receptors for insulin has been found (159,160). This effect may clearly have some importance in the obese patients. The changes in binding, however, must be separated from those of weight reduction and improvement in diabetes control. The present study demonstrates the ability of Fybogel®, a water soluble fiber, in long-term management of weight problem and hyperglycemia in the obese diabetics.

The mechanisms of action of psyllium for glucose reduction in diabetic patients are probably similar to that of other soluble fibers. Several possibilities have been considered.

3.4 Effects on lipids profiles

Most of the diabetic individuals have lipoprotein abnormalities. Cholesterol-lowering efficacy of Fybogel® in this study is seen in the patients with moderate to high hypercholesterolemia (TC>240 mg/dL or 6.2 mmol/L) (Table 22-23). TC was significantly decreased by 14.2% in 16 wks of Fybogel® supplementation. Also, the

trials of oat products suggested that hypercholesterolemic patients were more responsive than normolipidemic persons (161). Brown et al (162) reported the results of a meta-analysis of 67 controlled trials confirmed that viscous polysaccharides significantly reduce total cholesterol concentrations, specifically LDL-C, but did not alter concentrations of HDL- cholesterol or triglycerides. Davidson MH et al. compared difference doses of psyllium seed husk for 24 wks showed that the efficacy of 10.2 g psyllium seed husk/d caused LDL-C 5.3% lower than in the control group (163). The results from the present study were almost identical to theirs. Fybogel® tended to decrease LDL-C by 9.5% at wk24 while LDL-C fluctuated in placebo group and increase by 3.9% at wk24 (Table24-25). And the difference in LDL-C between Fybogel® and placebo groups at wk24 was statistically significant. These result are strengthen by the results from a meta-analysis of 12 studies showing that subjects who consumed a psyllium-enriched cereal had significant reduction in TC and LDL-C concentrations by 5% and 9% respectively, with no change in HDL-C and triglycerides among adults with mild to moderate hypercholesterolemia (164).

Evidences suggest that the soluble fiber which forms viscous gel in the gastrointestinal tract such as ispaghula, appears to be more effective at lowering cholesterol than the soluble fiber without this property (98). Increased viscosity of the intestinal contents entrap bile acids and interfere with micelle formation (12). Fibers bind bile acids and cholesterol which decrease their intestinal absorption and results in more bile acids being delivered to the terminal ileum and colon. Consequently, in the colon more primary bile acids (cholic acid and chenodeoxycholic acid) are converted to secondary bile acids (deoxycholic acids and lithocholic acid) which are less well absorbed and consequently are excreted with the feces (165,177); less bile acids

(especially the primary ones) enter the enterohepatic circulation and return to the liver. More bile acids are synthesized in the liver to replenish the primary pool. Everson showed that 15 g psyllium per day increased total bile acid synthesis by 43% in the hypercholesterolemic men (165). Since negative feedback on hepatic bile acid synthesis exerted by bile acids is diminished, more cholesterol is synthesized in the liver to meet the need for more bile acid synthesis(12). Presumably, less cholesterol is available for incorporation into lipoproteins because of the demands for bile acid synthesis (more fecal excretion of secondary bile acids and more hepatic synthesis of primary bile acids). It has been suggested that soluble fibers may alter sterol metabolism by increasing ileal and fecal losses of bile acids by their sequestration (166).

An alternative mechanism for the cholesterol-lowering action of psyllium husk was suggested recently by MaCall et al (167) who measured the metabolism of apolipoprotein B in African green monkeys after long-term addition of psyllium husk to the diet. They suggested that the cholesterol-lowering effect was due to a reduction in LDL-synthesis. Moreover, the resulting reduction in the cholesterol content of liver cells lead to an up-regulation of the LDL receptors and thus increased clearance of LDL-C.

However, increased bile acid excretion may not be sufficient to account for the observed cholesterol reduction (168). Other suggested mechanisms are in colon. Dietary fiber differs from most nutrients in that it is not digested or absorbed in small intestine and provides nutrients only after being fermented by bacteria in the colon (169). Fermentation of fiber in the colon yields carbondioxide, hydrogen, methane, water and short-chain fatty acid (SCFA). Acetate, propionate, and butyrate were the

principle SCFA produced and are largely absorbed from the colon entering the portal vein. Chen et al (170) demonstrated that propionate inhibited hepatic and peripheral cholesterol synthesis and accelerated LDL-C clearance in cholesterol-fed rats.

Psyllium is a preferential substrate for *Bacteroids ovatus* , a normal bacterial component of human fecal flora (171). It is possible that consumption of psyllium resulted in relative increase in these bacteria and induces other species of bacteria or alters enzyme activity. Such changes could have altered the rate of bacterial degradation of cholesterol.

In the present study, HDL-C levels were not significantly different over the time and between the treatments (Table26-27). Also, the results of the meta-analysis (164) and most study (162) HDL-C levels were not affected by incorporating psyllium-enriched cereal into a low fat diet. Levels of HDL-C are inversely related to the development of coronary heart disease. Because low HDL-C levels (<0.9 mmol/L) are now recognized as a major risk factor for CHD, interventions that protect or elevate HDL-C are desirable (56). So Fybogel® is quite effective in reducing TC, LDL-C without changing HDL-C.

Agree with those previously reported, Fybogel® did not significantly reduce triglycerides in this study. Nevertheless, we observed mean triglycerides tended to decrease in Fybogel® group whereas in placebo group it tended to increase. Because of the large individual variations of triglycerides, there was not seen significant change between two groups.

3.5 Acceptability and safety of Fybogel®

The major disadvantages of increased fiber intake relate to gastrointestinal symptoms. Theoretical concerns about detrimental effects on vitamin or mineral availability have not been documented.

3.5.1 Acceptability of Fybogel®

Increased fiber intake increases fecal bulk and usually increases frequency of bowel movement. Individuals with autonomic neuropathy of the gastrointestinal tract need special consideration. Increased soluble fiber intake may benefit diabetic diarrhea and also promote laxation for individuals with constipation. In our study, Fybogel® may have a beneficial effect in some diabetic individuals with autonomic neuropathy. Three subjects who were constipated could easily defecate after receiving Fybogel®. Increasing the intake of soluble fiber is an accepted method of treating constipation. Psyllium passes through the intestine undigested, to hold water on their hydrophillic sites and thereby stools become bulkier and softer. On the contrary, two subjects who had diarrheal problem complained of more difficult to defecate softer taking Fybogel®. The problem was resolved after more water adding during the mixing process. Eherer AJ et al. (173) reported 18 g/d of psyllium improved fecal consistency, double fecal viscosity, and increased the fecal output of water, cations, and solids in subjects with experimentally-induced secretory diarrhea. The mechanism of this psyllium effect is not known. However, psyllium may have sequestered fecal water and thereby decreased the relative amount of "free" water available to interact with other stool solids. On the other hand, psyllium forms a

viscous gel when it is added to pure water, so the psyllium effect on stool viscosity and consistency may be related to its gel forming property per se.

Although fiber supplementation was associated with a few gastrointestinal symptoms, no major adverse effects were noted. No cases were serious enough to cause a subject discontinuing the study. Adverse effects reported were generally related to minor and transient gastrointestinal discomfort such as gas, bloating at the beginning of the study.

3.5.2 Effect of Fybogel® on vitamin and mineral availability and safety parameters

The effect of dietary fiber on vitamin and mineral balances continues to be a controversial issue. The mechanism by which dietary fiber influences the vitamins and mineral absorption is related to its physiochemical properties. These properties involve the ability of dietary fiber to act as a weak cation exchanger, decrease transit time, dilute mineral concentration by increase fecal bulk, and resist digestion in the large bowel (172).

Nevertheless, it is possible, especially with diets rich in phytate and insoluble fiber, that absorption of calcium, iron, and zinc could be impaired and result in deficiencies if used for a long time in susceptible individual (52). However, there is good evidence suggesting that adaptation can occur in response to eating diets high in dietary fiber. No changes in blood levels of macromineral or micromineral were observed in long-term studies of mixed high fiber diets (86) or soluble fiber-supplemented diets (88). The clearest evidence, however, has come from monitoring vegetarians (172) , who are able to adjust to a high dietary fiber diet and maintain

mineral status comparable to that of nonvegetarians. This adaptation may depend partly on the degree of dietary fiber degradation by large bowel bacteria followed by the absorption of liberated mineral (172). There were very few studies focus on long-term vitamin or mineral status of psyllium supplementation. Enzi G et al. (174) found that plasma iron and calcium levels were significantly reduced after 1-month hydrophillic mucilage treatment but after 4-month treatment, the values of plasma iron, and calcium did not show any further decrease and kept constant throughout the trial. They discussed that the decrease of plasma iron and calcium in the early phase of treatment may be due to the effect of limiting the energy intake 800 kcal/d. The recent studies reported no significant changes on serum iron or zinc levels of psyllium supplementation (64,175). In term of vitamin status, Dennisson et al (176) reported blood vitamin A, D, E, and folic acid were not affected after 5-wks psyllium supplementation in children with hypercholesterlemia. However, the patients in the present study consumed more energy and nutrient intake. Hence, vitamin(serum retinol, ∝-tocopherol, vitaminB_1, vitaminB_2, vitaminC, vitamin B_{12}, folate and RBC folate) and mineral (serum calcium, magnesium, phosphorus, iron, zinc and copper) levels showed no significant changes after 16 wk of Fybogel® supplementation. (Tables 28-29). Furthermore, since Fybogel® contains only trace amount of phytate, therefore, did not interfere with the absorption of vitamin and mineral.

Fybogel® did not cause any adverse effects as confirmed by the normal hematological parameters, liver and renal function tests, protein status, and electrolytes.(Tables 30-34)

Soluble fiber intake can be increased by eating more fruit, vegetable or oat bran. Certain bulk forming laxatives are also high in fiber, convenient, and relatively inexpensive to use. Of these, Fybogel® containing ispaghula husk appears to have the good hypoglycemic, hypocholesterolemic effects and reduce or maintain body weight in the long term. Fybogel® is well accepted and associated with no major side effects.

CHAPTER VI

SUMMARY AND CONCLUSION

Summary

1. The baseline daily energy intake of Fybogel® and placebo groups were 1,705 ± 157 and 1,780 ± 143 kcal. Both groups had low carbohydrate intake and high fat intake.

2. After dietary counseling, mean daily energy intake was significantly reduced 405-583 kcal in both groups throughout the study. Percentage of energy from carbohydrate was significantly higher and percentage of energy from fat was significantly lower than the baseline period in both groups throughout the study.

3. There was no significant reduction of BW in both groups during diet-only phase (wk0-8). During treatment phase (wk8-24), the BW was significantly reduced in Fybogel® group at wk20 (0.88 kg) and wk24 (1.28 kg) whereas the BW was significantly increased at wk24 (0.89 kg) in placebo group.

4. The BMI and BFM were significantly reduced at wk24 from wk8 in Fybogel® group but increased in placebo group. The TSF was significantly lower from wk12 in Fybogel® group at wk24 but it was not significantly changed in placebo group. The MUAC, UAMC and FFM were not significantly different in both groups throughout the study.

5. FPG was not significantly different during the diet-only phase in both groups. During treatment phase, FPG of Fybogel® group was significantly decreased by 35.0

mg/dL (16.1%) at wk24 whereas there was no significant reduction in the placebo group. The change of FPG from wk8 between the two groups was statistically significant at wk16 and wk24.

6. HbA_{1c} was not significantly different during the diet-only phase in both group. During treatment phase, HbA_{1c} in Fybogel® group was significantly decreased from 10.1 at wk8 to 9.0 at wk24 (10.12% reduction) whereas there was no significant reduction in the placebo group. Changes of HbA_{1c} from wk8 between the two groups was statistically significant at wk24.

7. TC levels were not significantly changed in both groups either during diet-only or treatment phase. Hypocholesterolemic effect of Fybogel® was seen in the moderate to high hypercholesterolemic subjects (TC>240 mg/dL at wk8).TC level in Fybogel® group was significantly decreased from wk8 by 41 mg/dL (14.2%) at wk24 whereas there was no significant difference in the placebo group. The change of TC levels from wk8 between the two groups was statistically significant at wk16.

8. LDL-C levels were not significantly changed between times in both groups either during diet-only or treatment phase. The changes from wk8 of LDL-C levels between the two groups were statistically significant at wk24.

9. HDL-C and triglyceride concentrations were not significantly changed over time in either within group or between groups.

10. There were no significant changes of vitamin and mineral status after treatment with Fybogel® and placebo.

11. There were no significant changes of routine safety parameters after treatment with Fybogel® and placebo.

12. After withdrawal of the treatment for 2 months, BW was significantly increased for 0.74 kg in Fybogel® group while it was not significantly changed in the placebo group. FPG and HbA_{1c} were also significantly increased for 42.1 mg/dL and 1.1%, respectively in Fybogel® group, whereas in the placebo group, FPG was no significantly changed and HbA_{1c} was significantly increased 0.48%. These confirmed the effects of Fybogel® on weight reduction and improve glycemic control.

Conclusion

In the present study, all subjects were obese class I NIDDM with hypercholesterolemia which were high risks of having cardiovascular disease. Their high fat and low carbohydrate intake were improper nutrition. Although after dietary advice, the subjects improved their eating habits but it seemed work for the first few weeks only. BW, FPG and TC levels tended to decrease in wk4 more than wk8. During treatment phase, the result showed significant weight loss, improved glycemic control in Fybogel® group whereas there was no significant reduction of BW, FPG and HbA_{1c} in the placebo group. Hypocholesterolemic effect of Fybogel® was seen in the subjects with moderate to high hypercholesterolemia (TC>240 mg/dL) only. LDL-C levels tended to decrease after Fybogel® treatment and a significant difference was present when compared to the placebo. Fybogel® treatment did not affect on serum levels of HDL-C and triglycerides. In addition, the vitamin and mineral status as well as the safety parameters were not significantly changed after Fybogel® treatment.

Nutrition counseling is important as part of the treatment for those patients suffering from obesity, diabetes and hypercholesterolemia but certain medication may be needed to support the diet instruction and behavior modification in some patients. Fybogel® containing ispaghula husk appears to affect weight reduction or maintenance, improve glycemic control and reduce hypercholesterolemia in the long term.

REFERENCES

1. Trowell HC, Burkitt DP. Refined Carbohydrate foods and Disease. London: Acadamic Press, 1975.
2. Prosky L, Devries JW. Controlling Dietary Fiber in Food Products. New York: Van Nostrand Reinhold, 1992.
3. Anderson JW, Smith BM, Gustafson NJ. Health benefits and practical aspects of high-fiber diets. Am J Clin Nutr 1994;59(suppl):1242s-7s.
4. Anderson JW, Gustafson NJ. Hypocholesterolemic effects of oat and bean products. Am J Clin Nutr 1988;48:749-53.
5. Anderson JW, Deakin DA, Floore TL, Smith BM, Whitis SE. Dietary fiber and coronary heart disease. Crit Rev Food sci Nutr 1990;29:95-147.
6. Anderson JW, Plant fiber and blood pressure, Ann Intern Med 1983;98:843-6.
7. Madar Z, Odes HS. Dietary research. Basel, Switzerland:Karger,1990.
8. Kromhout D, Bosschieter EB, De Lezenne CC. Dietary fiber and 10-year mortality from coronary heart disease, cancer, and all causes: The Zutphen study. Lancet 1982;2:518-22.
9. Anderson JW, Bryant CA. Dietary fiber: diabetes and obesity. Am J Gastroenterol 1986;81:898-906.
10. Anderson JW, Akanji AO. Dietary fiber- an overview. Diabetes care 1991;14: 1126-31.
11. Ken GU, Cowie C, Maureen I. Mortality in adults with and without diabetes in National cohort of the US population, 1971-1993. Diabetes care 1998;21:13-18.

12. Anderson JW, Tietyen-Clark J. Dietary fiber: Hyperlipidemia, Hypertension, and Coronary heart disease. Am J Gastroenterol 1986;81:907-18.

13. Grundy SM. Small LDL, atherogenic dyslipidemia, and the metabolic syndrome. Circulation 1997;95:1-4.

14. Van Itallie T. Health implications of overweight and obesity in the United States. Ann Intern Med 1985;103:983-8.

15. Naquleparan M, Savage PJ, Unger RH, Bennet PH. A simplified method using somatostatin to assess in vivo insulin resistance over a range of obesity. Diabetes 1979;28:980-3.

16. Olefsky JM, Kolterman OG. Mechanisms of insulin resistance in obesity and non-insulin dependent (type2) diabetes. Diabetes 1986;17:684-92.

17. Trowell HC, Godding E, Spiller G. Fiber bibliographies and terminology. Am J Clin Nutr.1978;31:1489-90.

18. Nuttal FQ. Dietary fiber in the management of diabetes. Diabetes 1993;42:503-8.

19. Hunninghake DB, Miller VT, Lakosa JC,et al. Hypocholesterolemic effects of dietary fiber supplement. Am J Clin Nutr 1994;59:1050-4.

20. Miettinen TA, Tarpila S. Effect of pectin on serum cholesterol, fecal bile acids and biliary lipids in normolipidemic and hyperlipidemic individuals. Clin Chim Acta 1977;79:471-7.

21. Anderson JW, Story L, Sieling B, et al. Hypocholesterolemic effects of oat bran or bean intake for hypercholesterolemic men. Am J Clin Nutr 1984;40:1146-52.

22. Chen WL, Anderson JW, Jennings D. Propionate may mediate the hypocholesterolemic effects of certain soluble plant fibers in cholesterol fed rats. Proc Soc Exp Biol Med 1984;175:215-20.

23. Anderson JW. Physiology and metabolic effects of dietary fiber. Federation Proc 1985;44:2902-8.

24. Wilmshurst P, Crawley JCW. The measurement of gastric transient time in obese subjects using 24Na and the effects of energy content and guar gum on gastric emptying and satiety. Br J Nutr 1980;44:1-6.

25. Rigaud D, Ryttig KR, Leeds AR, Bard D, Apfelbaum M. effects of a moderate dietary fibre supplement on hunger rating, energy input and faecal energy output in young, healthy volunteers. Int J Obesity 1987;11(suppl1):73-78.

26. Holt S, Heading RC, Carter DC, et al. Effect of gel fiber on gastric emptying time and absorption of glucose and paracetamol. Lancet 1979;1:636-9.

27. Jenkins DJA, Bloom SR, Albuquerque RH, et al. Pectin and complications after gastric surgery normalisation of postprandial glucose and endocrine responses. Gut 1980;21:574-9.

28. Zecharia M, Odes HS. Dietary research. Basel, Switzerland: Karger AG.1990.

29. Dettmar PW. The health benefits of non-starch polysaccharide (Dietary fiber) and the key role of ispaghula husk. Fibre symposium 1995; March:5-9.

30. Adams F. The genuine works of Hippocrates. Baltimore: Wiliams and Wilkins, 1939.

31. Slavin JL. Dietary fiber: Mechanisms or magic on disease prevention?. Nutrition Today. 1990; Nov/Dec:6-10.

32. Trowell HC. Non-infective disease in Africa. London:Edward Arnold,1960.

33. Trowell HC. Dietary fiber, ischemic heart disease and diabetes mellitus. Proc Nutr Soc 1973;32:151-7.

34. Cleave TL. The neglect of natural principles in current medical practice. J Roy Nav Med Serv 1956;42:55-83.

35. Burkitt DP. Epidemiology of cancer of the colon and rectum. Cancer 1971;28:3-13.

36. Trowell HC. Definition of dietary fiber and hypotheses that it is a protective factor in certain diseases. Am J Clin Nutr. 1976;29:417.

37. Selvendran RR. The plant cell wall as a source of dietary fiber: chemistry and structure. Am J Clin Nutr 1984;39:320-7.

38. AOAC. Method#985.29 Total dietary fiber in food . In official methods of analysis of the association of official analytical chemists, ed. Helrich K. Arington,VA:AOAC,1990.

39. Anderson JW. Fiber and health: an overview. Am J Gastroenterol 1986;81:892-7.

40. Guthrie HA and Piccia no MF. Carbohydrate. St.louis:Mosby,1995:88.

41. Kritchevsky D. Dietary fiber. Ann Rev Nutr 1988;8:301-8.

42. Marlett JA, Chesters JG, Longacre ML, Bogdanske JJ. Recovery of soluble dietary fiber is dependent on the method of analysis Am J Clin Nutr 1989;50:479-85.

43. Blackburn NA, Redfern JS, Jarjis H, Holgate AM, Hanning I, et al. The mechanism of action of guar gum in improving glucose tolerance in man. Clin Sci 1984;66:329-36.

44. Jenkin DJA, Wolever TMS, Taylor RH, Ghafari H, Jenkins AL, et al. Rate of digestion of foods and postprandial glycaemia in normal and diabetic subjects. Br Med J 1980;281:14-7.

45. Sommer H, Kasper H. The effect of dietary fiber on the pancreatic excretory function. Hepato-gastroenterology 1980; 27:477-83.

46. Cummings JA, Englyst HN. Fermentation in the human large intestine and the available substrates. Am J Clin Nutr 1987;45:1243.

47. Levine GM. Fiber. St.Louis: Mosby, 1994.

48. Eastwood MA. Passmore R. Dietary fiber. Lancet 1983;332:202-5.

49. Ruppin H. Bar-Meir S. Soergel KH,, et al. Absorption of short-chain fatty acids by the colon. Gastroenterology 1980;78:1500-7.

50. Roediger WEW. Role of anaerobic bacteria in the metabolic welfare of the colonic mucosa in man. Gut 1980;21:793-8.

51. Mc Neil NI. The contribution of large intestine to energy supplies in man. Am J Clin Nutr 1984;39:338-42.

52. Vinik AI, Jenkins DJA. Dietary fiber in the management of diabetes. Diabetes Care 1988;11:160-73.

53. Kritchevsky D, Tepper SA, Goodman G. Diet, nutrition intake and metabolism in populations at high and low risk for colon cancer: relationship of diet to serum lipids. Am J Clin Nutr 1984;40:921-6.

54. Anderson JW. Dietary fiber and human health. Hort Science 1990;25:1488-95.

55. Margetts BM, Beilin LJ, Vandongen R, Armstrong BK. A randomized controlled trial of the effects of dietary fibre on blood pressure. Clin Sci 1987;72:343-50.

56. Expert Panel on Detection, Evaluation, and treatment of high Blood Cholesterol in Adults. Circulation 1994;89:1329-445.

57. National Cholesterol Education Program. Report of the Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults. Arch Intern Med 1988;148:36-69.

58. Anderson JW, Gustafson NJ. Hypocholesterolemic effects of oat and bean products. Am J Clin Nutr 1988;48:749-53.

59. Kirby RW, Anderson JW, Seiling B, et al. Oat-bran intake selectively lowers serum low-density lipoprotein cholesterol concentrations of hypercholesterolemic men. Am J Clin Nutr 1981;34:824-9.

60. Anderson JW, Story L, Sieling B, Chen W-JL, et al. Hypocholesterolemic effects of oat-bran or bean intake for hypercholerolemic men. Am J Clin Nutr 1984;40:1146-55.

61. Anderson JW, Gilinsky NH, Deakins DA, et al. Lipid responses of hypercholesterolemic men to oat bran and wheat bran intake. Am J Clin Nutr 1991;54:678-83.

62. Anderson JW, Gustafson NJ, Spencer DB, Tietyen J. Serum lipid responses of hypercholesterolemic men to single and divided doses of canned beans. Am J Clin Nutr 1990;51:1013-9.

63. Anderson JW, Story L, Seiling B, Chen W-JL. Hypocholesterolemic effects of high-fiber diets rich in water-soluble plant fibers: long-term studies with oat-bran and bean supplemented diets for hypercholesterolemic men. J Can Diet Assoc 1984;45:140-9.

64. Anderson JW, Zettwoch N, Feldman T, Tietyen-Clark J, et al. Cholesterol-lowering effects of psyllium hydrophillic mucilloid for hypercholesterolemic men. Arch Intern Med 1988;148:292-6.

65. Anderson JW, Floore TL, Geil PB, O'Neal DS, Balm TK. Hypocholesterolemic effects of difference bulk-forming hydrophillic fibers as adjuncts to dietary therapy in mild to moderate hypercholesterolemia. Arch Intern Med 1991;151:1597-602.

66. Kahn HA, Phillipes RL, Snowdon DN, Choi W. Association between reported diet and all-cause mortality: twenty-one-year follow-up on 27,530 adults Seventh-day adventist. Am J Epidemiol 1984;119:775-87.

67. Morris JN, Marr JW, Clayton DG. Diet and heart: a postscript. Br Med J 1977;2:1307-14.

68. Khaw KT, Barrett-Connor E. Dietary fiber and reduced ischemic heart disease mortality rates in men and women: a 12-year prospective study. Am J Epidemiol 1987;126:1093-102.

69. Gary WN, Balm TK. Synergistic effects of psylluim in the dietary treatment of Hypercholesterolemia. South Med J;83:1131-7.

70. Anderson JW, Bryant CA. Dietary fiber: diabetes and obesity. Am J Gastroenterol 1986;81:898-906.

71. Rossner S, VonZweigbergk D, Ohlin A, Ryttig K. Weight reduction with dietary fibre supplements: results of two double-blind randomized studies. Acta Med Scand 1987;222:83-8.

72. Anderson JW. High-fiber diets for obese diabetic men on insulin therapy: short-term and long-term effects. In: Vahouny GV, Ed. Dietary fiber and obesity. New York: Alan R Liss, Inc,1985.

73. Blundell JE, Burley VJ. Satiation, satiety and the action of fiber on food intake. Int J Obesity 1987;11(suppl 1):9-25.

74. Duncan KH, Bacon JA, Weinsier RL. The effects of high and low energy density diets on satiety, energy intake, and eating time of obese and nonobese subjects. Am J Clin Nutr 1983;37:763-7.

75. Levine AS, Tallman TR, Grace MK, Parker SA, Billington CJ Levitt MD. Effect of breakfast cereals on short-term food intake. Am J Clin Nutr 1989;50:1303-7.

76. Heaton KW. Dietary fiber in perspective. Human Nutr Clin Nutr 1983;37c:151-70.

77. Anderson JW , Ward K. Long- effects of high-carbohydrate, high-fiber diets on glucose and lipid metabolism: a preliminary report on patients with diabetes. Diabetes care 1978;1:77-82.

78. JenkinsDJA, Leeds AR, Gassull MA, Cochet B, Alberti KG. Decrease in postprandial insulin and glucose concentrations by guar and pectin. Ann Intern Med 1977;86:20-23.

79. Nuttall FQ. Perspectives in Diabetes: Dietary fiber in the management of Diabetes. Diabetes 1993;42:503-8.

80. Anderson JW. High-fiber diets for obese diabetic men on insulin therapy: short-term and long-term effects. In: Vahouny GV, ed. Dietary fiber and obesity. New York: Alan R Liss, Inc,1985. 49-68.

81. Jenkins DJA, Peterson RD, Thorne MJ, Ferguson PW. Wheat fiber and laxation: dose response and equilibration time. Am J Gastroenterol 1987;82:1259-63.

82. Position of the American Dietetic Association. Health implications of dietary fiber-technical support paper. J Am Diet Assoc 1988;88:216-21.

83. Anderson JW, Gustafson NJ, Bryant CA, Tietyen-Clark J. Dietary fiber and diabetes: a comprehensive review and practical application. J Am Diet Assoc 1987;87:1189-97.

84. Whitney EN, Cataldo CB, Roffes SR. The carbohydrates: Sugar, Starch, and Fiber. 3nd ed. New York: West publishing Company, 1991.78-90.

85. Taper LJ, Milam RS, Mc Callister MS, et al. Mineral retention in young men consuming soy-fiber-augmented liquid-formula diets. Am J Clin Nutr 1988;48:305-10.

86. Anderson JW, Ferguson SK, Karounos D, O'Malley L. Seiling B, Chen WL. Mineral and vitamin status on high-fiber diets: Long-term Studies of diabetic patients. Diabetes Care 1980;3:38.

87. Mclvor MW, Cummings CC, Mendeloff AI, Long-term ingestion of guar gum is not toxic in patients with non-insulin- dependent diabetes mellitus. Am J Clin Nutr 1985;41:891-8.

88. Jenkin DJA, Wolever TMS, Bacon S, Nineham R, Lees R, et al. Diabetic diets: high carbohydrate combined with high fiber. Am J Clin Nutr 1980;33:1729-33.

89. Tuomilehto J, Karttunen P, Vinni S, Kostiainen E, Uusitupa M. A double-blind evaluation of guar gum in patients with dyslipidemia. Hum Nutr Appl Nutr 1983;37:109-16.

90. US Department of Health and Human Services, US Government Printing Office, Public Health Service. Healthy people 2000: Washington health promotion and disease prevention objectives. Washington, DC:1990.

91. Council on Scientific Affairs, American Medical Association. Dietary fiber and health. JAMA 1989;262:542-6.

92. American Dietetic Association. Position of the American Dietetic Association: health implications of dietary fiber. J Am Diet Assoc 1993;93:1446-9.

93. National Advisory Committee on Nutrition Education. Proposals for nutritional guidelines for health education in Britain. Lancet 1983;12:835-7.

94. Food Directorate, Health Protection Branch. Guideline concerning the safety and physiological effects of novel fibre sources and food products containing them. Ottawa: Department of National Health and Welfare,1988.

95. Pilch SM. Physiologic effects and health consequences of dietary fiber. Life sciences Research Office, Bethesda, MD: Federation of American Societies for Experimental Biology, 1987.

96. National Academy of Sciences. Diet and Health. Washington, DC: National Academy Press, 1989.

97. Karstorm B, Vessby B, Asp NG, Ytterfors A. Effects of four meals with different kinds of dietary fiber on glucose metabolism in healthy subjects and non-insulin-dependent diabetic patients. Eur J Clin Nutr 1988;42:519-26.

98. Glore SR, Treeck DV, Knehans AW, Guild M. Soluble fiber and serum lipids: A literature review. J Am Diet Assoc. 1994;94:425-36.

99. Alberto CF, Jose AF, Adolfo C, et al. Decrease in serum lipids glycemia and body weight by plantago psyllium in obese and diabetic patients. Arch Invest Med 1983;14:259-67.

100. Turnbull WH, Thomas HG. The effect of a Plantago ovata seed containing preparation on appetite variables, nutrient and energy intake. Int J Obesity 1995;19:338-42.

101. Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. Analyst 1972; 97: 142-5.

102. Peridochrom triglycerides. FRG: Boehringer Mannheim Gmbh Diagnostica, 1982.

103. Friedewald WT, Levy RI, Frederiekson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin chem 1972; 18: 499-502.

104. Bieri JG, Tolliver TJ, Catignani GL. Simultaneous determination of α-tocopherol and retinol in plasma or red cells by high pressure liquid chromatography. Am J Clin nutr 1979; 32: 2143-9.

105. Dreyfus PM. Clinical application of blood transketolase determination. N Engl J Med 1962; 267: 596-8.

106. Dische Z. Qualitative and quantitative colorimetric determination of heptoses. J Biol Chem 1953; 204: 983-7.

107. Glatzzle D, Korner WF, Christeller S, Wiss D. Method for the detection of a biochemical riboflavin deficiency: stimulation of NADPH2 dependent

glutathione reductase from human erythrocyte by FAD in vitro. Intern J Vitamin Res 1971; 40: 161-83.

108. Stanley T, Omaye J, Turnbull JD, Sauberlich HE. Selected methods for the determination of ascorbic acid in animal cells, tissues and fluids. Methods Enzymol 1979; 62: 3-11.

109. Jack H. Evaluation of an Instrument (NOVA7) for direct Potentionmetric Analysis of sodium and potassium in blood and their indirect potentionmetric determination in urine. Clin Chem. 1979; 25: 757-63.

110. Goldenberg H, Fernandez. A simplified method of the estimation of inorganic phosphate in body fluid. Clin Chem. 1966; 12: 871-81.

111. Hausen JL and Frier EF. Determination of magnesium by atomic absorption spectrophotometry. Am J Med 1967; 33: 158-65.

112. Garrow JS, Webster J. Quetelet's index (W/H2) as a measure of fatness. Intern J Obes 1985; 9: 147-53.

113. Harries AD, Jones LA, Heatly RU, Newcombe RG, Rhodes J. Precision of anthropometric measurements: the value of midarm circumference. Clin Nutr 1984; 2: 193-6.

114. Blackburn GL, Thornton PA. Nutritional assessment of the hospitalized patients. Med Clin North Am 1979;63:1103-15.

115. Grant JP, Custer PB, Thurlow J. Symposium on surgical: Current techniques of nutritional assessment nutrition. Surg clin North Am 1981; 61: 437-63.

116. Bjorntorp P. Regional patterns of fat distribution. Ann Intern Med. 1985; 103: 994-5.

117. Durnin JUGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness measurements on 481 men and women age from 16 to 72 years. Br J Nutr. 1974; 32: 77-97.

118. Analytical methods for flame spectroscopy. Varian Techtron Pty. Springvale, Victoria, Australia 1974.

119. Monotest cholesterol. FRG: Boehringer Mannheim Gmbh Diagnostica, 1982.

120. Lopes-Virella MF, Stone P, Ellis S, Colwell JA. Cholesterol determination in high density lipoprotein separated by three different method. Clin chem 1977; 23: 882-4.

121. Pi-sunyer FX. Weight and non-insulin-dependent diabetes mellitus. Am J Clin Nutr 1996;63(suppl):426s-9s.

122. Grundy SM. Nutrition and diet in the management of hyperlipidemia and atherosclerosis. In: Shils ME, Olson JA, Sike M, eds. Modern Nutrition in Health and Disease. Vol. 2. 9th., ed. Philadelphia : Lea & Febiger, 1999, p. 1199-216.

123. Rabkin SW, Mathewson GA, Hsu PH. Relation of body weight to development of ischemic heart disease in a cohort of young North American men after a 26 year observation period: the Manitoba study. Am J Cardiol. 1977;39:452-8.

124. Bandini LI, Schoeller DA, Cy HYN, Dietz WH. Validity of reported energy intake in obese and nonobese adolescents. Am J Clin Nutr. 1990;52:421-5.

125. Litchtman SW, Pisarski K, Berman ER. Discrepancy between self-reported and actual calorie intake and exercise in obese subjects. N Eng J Med. 1992;327:1893-8.

126. Flatt JP, Ravussin E, Acheson KR, JeQuier E. Effects of dietary fat on post-prandial substrate oxidation and on carbohydrate and fat balances. J Clin Invest. 1985;76:1019-24.

127. Nonas CA. A model for chronic care of obesity through dietary treatment. J Am Diet Assoc 1998;98(suppl 2): S16-S22.

128. Gelissen CI, Brodie B, Eastwood M. Effect of plantago ovata (psyllium) husk and seeds on sterol metabolism: studies in normal and ileostomy subjects. Am J Clin Nutr 1994;59:395-400.

129. Steven J, Levitsky DA, VanSoest PJ, et al. Effect of psyllium gum and wheat bran on spontaneous energy intake. Am J Clin Nutr 1987;46::812-7.

130. Rossner S, Zweigbergk DV, Ohlin A, Ryttig K. Weight reduction with dietary fibre supplements. Acta Med Scand 1987;222:83-8.

131. Riguad D, Ryttig KR, Angel LA, Apfelbaum M. Overweight treated with energy restriction and a dietary fibre supplement: A 6-month randomized, double-blind, placebo-controlled trial. Int J Obesity 1990;14:763-9.

132. Bonfield CT. Dietary fiber and body weight management. In: Kritchevsky D, Bonfield CT, ed. Dietary fiber in health and disease. New York: Eagan Press,1995:459-65.

133. Horn LV, Donato K, Kumanyika S,Winston M, Prewitt TE, Snetselaar L. The dietitian's role in developing and implementing the first federal obesity guidelines. J Am Diet Assoc 1998;98:1115-7.

134. Ryttig KR, Tellnes G, Fagerthun H. A dietary fibre supplement and weight maintenance after weight reduction: a randomized, double blind, placebo-controlled long-term trial. Int J Obesity 1989;13:165-71.

135. Jensen CD, Haskell W, Whittam JH. Long-term effects of water-soluble dietary fiber in the management of hypercholesterolemia in healthy men and women. Am J Cardiology 1997;79:34-7.

136. Levin EG, Miller VT, Muesing RA, et al. Comparison of psyllium hydrophillic mucilloid and cellulose as adjunct to prudent diet in the treatment of mild to moderate hypercholesterolemia. Arch Intern Med 1990;150:1822-7.

137. Jenkin DJA, Bloom sr, Albuquerque RH, et al. Pectin and complications after gastric surgery: normalisation of postprandial glucose and endocrine responses. Gut 1980;21:574-9.

138. Smith GP, Gibbs MD. The satiating effect of cholycystokinin. Ann NY Acad Sci 1985;48:417-23.

139. Bergmann JF, Chassany O, Petit A, Triki R, Caulin C, Segrestaa JM. Correlation between echographic gastric emptying and appetite: influence of psyllium. Gut 1992;33:1042-3.

140. Southgate DAT, Durnin JVGA. Calorie conversion factors; an experimental reassessment of the factors used in the calculation of the energy value of human diets. Br J Nutr;24:517-35.

141. Fagerberg SE. The effects of a bulk laxative (Metamucil) on fasting blood glucose, serum lipids and other variables in constipated patients with non-insulin dependent adult diabetes. Curr Ther Res 1982; 31:166-72.

142. Uribe M, Dilbildox M, Malpica S, et al. Beneficial effects of vegetable protein diet supplemented with psyllium plantago in patients with hepatic encephalopathy and diabetes mellitus. Gastroenterology 1985; 88: 901-7.

143. Frati-Munari AC, Fernandez-Harp JA, Becerril M, Chavez-Negrete A, Banales-Ham M. Decrease in serum lipids, glycemia and body weight by plantago psyllium in obese and diabetic patients. Arch Invest Med (Mex) 1983;14:259-68

144. Pastor JG, Blaisdell PW, Balm TK, Asplin CM, Pohl SL. Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in patients with non-insulin dependent diabetes. Am J Clin Nutr 1991; 53: 1431-5.

145. Jarjis HA, Blackburn NA, Redfern JS, Read NW. The effect of ispaghula Fybogel and Metamucil and guar gum on glucose tolerance in man. Br J Nutr 1984; 51: 371-8.

146. Thomas BL, Laine DC, Goetz F. Glucose and insulin response in diabetic subjects: acute effects of carbohydrate level and the addition of soy polysaccharide in defined-formula diets. Am J Clin Nutr 1988; 48: 1048-52

147. Parsons SR. Effect of high fiber breakfasts on glucose metabolism in noninsulin-dependent diabetics. Am J Clin Nutr 1984; 40: 66-71.

148. Florholmen J, Arvidsson-Lenner R, Jorde R, Burhol PG. The effect of Metamucil on postprandial blood glucose and plasma gastric inhibitory peptide in insulin-dependent diabetics. Acta Med Scand 1982; 212: 237-9.

149. Karlstrom B, Vessby B, Asp NG, Ytterfors A. Effects of four meals with different kinds of dietary fiber on glucose metabolism in healthy subjects and noninsulin dependent diabetic patients. Eur J Clin Nutr 1988; 42: 519-26.

150. Abraham ZD, Metha T. Three-week psyllium-husk supplementation: effect on plasma cholesterol concentrations, fecal steroid excretion, and carbohydrate absorption in men. Am J Clin Nutr 1988;47:67-74.

151. Green- pastors J, Blaisdell PW, Balm TW, Asplin CM, Pohl SL. Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in patients with non-insulin-dependent diabetes. Am J Clin Nutr 1991;53:1431-5.

152. Burton BT,Foster WR. Health implication of obesity: An NIH consensus development conference. J Am Diet Assoc 1985;85:1117.

153. Jenkin DJA, Wolever TMS, Taylor RH, et al. Rate of digestion of foods and postprandial glycaemia in normal and diabetic subjects. Br Med J 1980;281:14-7.

154. Dunaif G, Scheeman BO. The effect of dietary fiber on human pancreatic enzyme activity in vitro. Am J Clin Nutr 1981;34:1034-5.

155. Kay RM, Grobin W, Track NS. Diets rich in natural fiber improve carbohydrate tolerance in maturity-onset, non-insulin dependent diabetics. Diabetologia 1981;20:18-21.

156. Morgan LM, Goulder TJ, Tsiolakis D, Marks V, Alberti KGMM. The effect of unabsorpable carbohydrate on gut hormones: modification of postprandial GIP secretion by guar. Diabetologia 1979;14:85-9.

157. Shimoyama R, Uehara S, Itagaki Y, Izumiyama S, Hirayama A. Effects of guar intake on plasma somatostatin-like immunoreactivity in diabetic patients. Hokkaido Igaku Zasshi 1982;57:727-32.

158. Mann JI. Lines to legumes: changing concepts of diabetic diets. Diabetic Med 1984;19:21-4.

159. Pederson O, Hjollund E, Lindskov HO, et al. Increased insulin receptor binding to the monocytes from insulin-dependent diabetic patients after a low-fat, high-starch, high-fiber diet. Diabetes Care 1982;5:284-91.

160. Ward GM, Simpson RW, Simpson HCR, Naylor BA, Mann JI, Turner RC. Insulin receptor binding increased by high carbohydrate low fat diet in non-insulin-dependent diabetics. Eur J Clin Invest 1982;12:93-6.

161. Ripsin CM, Keenan JM, Jacobs DR Jr, Elmer PJ, Welch RR, Van Horn L, et al. Oat products and lipid lowering: a meta-analysis. JAMA 1992; 267: 3317-3325.

162. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr 1999;69:30-42.

163. Davidson HM, Maki KC, Kong JC, Dugan LD, Torri SA, Hall HA, et al. Long-term effects of consuming foods containing psyllium seed husk on serum lipids in subjects with hypercholesterolemia. Am J Clin Nutr 1998;67:367-76.

164. Olson BH, Anderson SM, Becker MP, Anderson JW, Hunninghake DB, Jenkins DJA, et al. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: results of a meta-analysis. J Nutr 1997; 127: 1973-80.

165. Everson GT, Daggy BP McKinley C, Story JA. Effects of psyllium hydrophillic mucilloid on LDL-cholesterol and bile acid synthesis in hypercholesterolemic men. J Lipid Res 1992;33:1183-92.

166. Rigaud D, Ryttig KR, Leeds AR, Bard D, Apfelbaum M. effects of a moderate dietary fibre supplement on hunger rating, energy input and faecal energy output in young, healthy volunteers. Int J Obesity 1987;11(suppl1):73-78.

167. McCall MR, Metha T, Leathers CW, Foster DM. Psyllium husk: effect on the metabolism of apolipoprotein B in African green monkeys. Am J Clin Nutr 1992;56:385-93.

168. Federation of American Societies for Experimental Biology. Physiological effects and health consequences of dietary fiber. Washington, DC: US Department of Health and Human Services. 1987.

169. Nishin PM, Freedland RA. The effects of dietary fiber feeding on cholesterol metabolism in rats. J Nutr 1990;120:800-5.

170. Chen WL, Anderson JW, Jennings D, Propionate may mediate the hypocholesterolemic effects of certain soluble plant fibers in cholesterol-fed rats. Proc Soc Exp Biol Med. 1984;175:215-8.

171. Salyers AA, Harris CJ, Wilkins TD. Breakdown of psyllium hydrocolloid by strains of Bacteroides ovatus from the human intestinal tract. Can J Microbiol 1978;24:336-8.

172. Dreher ML. Handbook of dietary fiber : potential adverse effects of dietary fiber. New York: Marcel Dekker;1987.

173. Eherer AJ, Santa CA, Porter J, Fordtran JS. Effect of psyllium, Calcium polycarbophil, and wheat bran on secretory diarrhea induced by phenolphthalein. Gastroenterology 1993;104:1007-12.

174. Enzi G, Inelmen EM, Crepaldi G. Effect of a hydrophillic mucilage in the treatment of obese patients. Pharmatherapeutica 1980;2:421-8.

175. Bell LP,Hectrone K, Reynolds H, et al. Cholesterol-lowering effects of psyllium hydrophillic mucilloid: adjunct therapy to prudent diet for patients with mild to moderate hypercholesterolemia. JAMA 1989;261:3419-23.

176. Dennison BA, Levine DM. Randomized, double-blind, placebo-control, two-period crossover clinical trial of psyllium fiber in children with hypercholesterolemia. J Pediat 1993;123:24-9.

177. Jenkins DJA, Wolever TMS, Vidgen E, et al. Effect of psyllium in hypercholesterolemia at two monounsaturated fatty acid intakes. Am J Clin Nutr 1997;65:1524-33.

APPENDIX I

Example for dietary record

STUDY NO._____

แบบบันทึกรายการอาหารที่รับประทานใน 3 วัน

ชื่อ .....วันที่ ..... ถึง วันที่ .....

ข้อแนะนำในการบันทึก

1. บันทึกอาหารทุกมื้อทุกชนิดรวมทั้งขนม และเครื่องดื่มที่ท่านรับประทานตลอดวันตั้งแต่ท่านตื่นนอนจนเข้านอน (เฉพาะส่วนที่ท่านรับประทานเท่านั้น)
2. บันทึกอาหารที่รับประทานทั้งที่บ้านและนอกบ้านถ้าเป็นมื้อพิเศษให้ระบุด้วยเช่น งานเลี้ยงแต่งงาน เป็นต้น
3. ข้อความต่อไปนี้เป็นสิ่งจำเป็นในการบันทึก
   ก. ระบุเครื่องประกอบของอาหารแต่ละชนิดพร้อมทั้งปริมาตร โดยของแข็งให้ระบุเป็นช้อนตวงหรือทัพพีส่วนของเหลวระบุเป็นซี.ซี. หรือระบุตามที่ตวง-วัดที่ใช้อยู่ในบ้าน ถ้าไม่สามารถประมาณปริมาณได้ ให้พยายามบันทึกในรูปขนาดเช่น ขนาดเล็ก กลาง ใหญ่ หรือขนาดกว้างยาวของอาหารที่ใช้ เช่นผัดเปรี้ยวหวานต้องระบุว่ารับประทานแตงกวาประมาณ 4 ช้อนโต๊ะ มะเขือเทศ 2 ช้อนโต๊ะ เนื้อหมู 2 ช้อนโต๊ะ หรือระบุว่ารับประทานแตงกวาประมาณครึ่งลูกใหญ่ มะเขือเทศ 1 ลูกเล็ก เนื้อหมู 5 ชิ้น ขนาดชิ้นละ 1x2 ซม.ปริมาตร เครื่องดื่มควรระบุเป็นปริมาตรหรือขนาด เช่น โคล่า 1 ขวดกลาง หรือ 290 ซีซี. เป็นต้น
   ข. อาหารที่รับประทานปรุงอย่างไร เช่นปลาทูทอด ไก่ย่าง เป็นต้น
   ค. การเติมน้ำตาล น้ำเชื่อม เกลือ หรือน้ำปลา ลงในเครื่องดื่ม อาหาร ของหวานชนิดต่างๆ ให้ระบุปริมาณด้วยเช่น น้ำตาล 2 ช้อนชา ในกาแฟ 1 แก้ว
   ง. ระบุปริมาณน้ำดื่ม และปริมาณน้ำจากอาหารที่รับประทานทุกมื้อ

ตัวอย่างการบันทึกอาหาร

วันที่.....

มื้ออาหาร และสถานที่	เวลา	ประเภท	อาหาร	ปริมาณ
เช้า	7.00 น.	ข้าวต้มกุ้ง	ข้าวต้ม (เฉพาะเนื้อข้าว)	2 ทัพพี
ที่บ้าน			กุ้งน้ำจืด	2 ช้อนโต๊ะ (5 ตัว)
			น้ำข้าว	1/2 ถ้วยตวง (120 ซีซี.)
			น้ำตาล	1 ช้อนชา
		ปลาทูทอด	ปลาทู	1 ตัว
			น้ำมันพืช (กุ๊ก)	1 ช้อนโต๊ะ
		กุนเชียงทอด	กุนเชียง	2 ช้อนโต๊ะ
			น้ำมันพืช (กุ๊ก)	1 ช้อนโต๊ะ
		กาแฟ	กาแฟ	1 ช้อนชา
			น้ำตาล	2 ช้อนชา
			นมสด (ตราหมี)	2 ช้อนโต๊ะ
			น้ำ	150 ซีซี.
อาหารว่าง	10.00 น.	สาคูเปียกเผือก	สาคู	1/2 ถ้วยตวง
ที่ทำงาน			เผือก	1ช้อนโต๊ะ
			น้ำตาล	1ช้อนโต๊ะ
กลางวัน	12.00 น.	ก๋วยเตี๋ยวเนื้อ	เส้นก๋วยเตี๋ยว	1 ทัพพี
ที่ทำงาน			ถั่วงอก	2 ช้อนโต๊ะ
			เนื้อสด	2 ช้อนโต๊ะ
			ลูกชิ้น	5 ลูก
			น้ำมันกระเทียมเจียว	2 ช้อนชา
			น้ำก๋วยเตี๋ยว	1/2 ถ้วยตวง (120 ซีซี.)
			น้ำตาลทราย (ปรุงรส)	2 ช้อนชา
		ปอเปี๊ยะสด	แป้งปอเปี๊ยะ	3 แผ่น
			กุนเชียง	2 ช้อนชา
			เต้าหู้	2 ช้อนโต๊ะ

มื้ออาหาร และสถานที่	เวลา	ประเภท	อาหาร	ปริมาณ
			ถั่วงอก	2 ช้อนโต๊ะ
			เนื้อปู	1 ช้อนโต๊ะ
			น้ำราด (รสออกค่อนข้างหวาน)	1 ช้อนโต๊ะ
		สับปะรด	สับปะรดขนาด 2x3 นิ้ว	1 ชิ้น
			น้ำตาล	1 ช้อนชา
		COKE	COKE ขวดกลาง	290 ซีซี.
อาหารว่าง	15.00 น.	กล้วยบวดชี	กล้วยน้ำว้า (1 ลูก ผ่า 4 ชิ้น)	4 ชิ้น
ที่ทำงาน			น้ำกะทิ	4 ช้อนโต๊ะ
			น้ำตาล	2 ช้อนโต๊ะ
		น้ำเปล่า	น้ำ	1/2 แก้ว (120 ซีซี.)
อาหารเย็น	18.00 น.	ข้าวสวย	ข้าว	2 ทัพพี
ที่บ้าน		ต้มยำไก่ใส่เห็ด	เนื้อไก่	2 ช้อนโต๊ะ
			เห็ดฟาง	2 ช้อนโต๊ะ
			น้ำต้มยำ	1/4 ถ้วยตวง (60 ซีซี.)
			มะนาว	1 ช้อนโต๊ะ
			น้ำตาล	2 ช้อนชา
		ผัดคะน้าหมูกรอบ	ผักคะน้า	1 ถ้วยตวง
			หมูกรอบ	2 ช้อนโต๊ะ
			น้ำมันพืช (กุ๊ก)	1 ช้อนโต๊ะ
		ไข่เจียวหมูสับ	ไข่	1 ฟอง
			หมูสับ	1 ช้อนโต๊ะ
			น้ำปลา	1/2 ช้อนชา
			น้ำมันพืช (กุ๊ก)	2 ช้อนโต๊ะ
อาหารว่าง	23.00 น.	ส้ม	ส้มเขียวหวาน ขนาดเส้นผ่า	2 ลูก
		เขียวหวาน	ศูนย์กลาง 2 1/2 นิ้ว	
ก่อนนอน		นมสด	นมสด หนองโพธนิดหวาน	1 กล่อง

APPENDIX II

Food record form

STUDY NO._____

แบบบันทึกรายการอาหารที่รับประทานใน 3 วัน

ชื่อ .....วันที่ ..... ถึง วันที่ .....

ข้อแนะนำในการบันทึก

1. บันทึกอาหารทุกมื้อทุกชนิดรวมทั้งขนม และเครื่องดื่มที่ท่านรับประทานตลอดวันตั้งแต่ท่านตื่นนอนจนเข้านอน (เฉพาะส่วนที่ท่านรับประทานเท่านั้น)
2. บันทึกอาหารที่รับประทานทั้งที่บ้านและนอกบ้านถ้าเป็นมื้อพิเศษให้ระบุด้วยเช่น งานเลี้ยงแต่งงาน เป็นต้น
3. ข้อความต่อไปนี้เป็นสิ่งจำเป็นในการบันทึก
   ก. ระบุเครื่องประกอบของอาหารแต่ละชนิดพร้อมทั้งปริมาตร โดยของแข็งให้ระบุเป็นช้อนตวงหรือทัพพีส่วนของเหลวระบุเป็นซี.ซี. หรือระบุตามที่ตวง-วัดที่ใช้อยู่ในบ้าน ถ้าไม่สามารถประมาณปริมาณได้ ให้พยายามบันทึกในรูปขนาดเช่น ขนาดเล็ก กลาง ใหญ่ หรือขนาดกว้างยาวของอาหารที่ใช้ เช่นผัดเปรี้ยวหวานต้องระบุว่ารับประทานแตงกวาประมาณ 4 ช้อนโต๊ะ มะเขือเทศ 2 ช้อนโต๊ะ เนื้อหมู 2 ช้อนโต๊ะ หรือระบุว่ารับประทานแตงกวาประมาณครึ่งลูกใหญ่ มะเขือเทศ 1 ลูกเล็ก เนื้อหมู 5 ชิ้น ขนาดชิ้นละ 1x2 ซม.ปริมาตร เครื่องดื่มควรระบุเป็นปริมาตรหรือขนาด เช่น โคล่า 1 ขวดกลาง หรือ 290 ซีซี. เป็นต้น
   ข. อาหารที่รับประทานปรุงอย่างไร เช่นปลาทูทอด ไก่ย่าง เป็นต้น
   ค. การเติมน้ำตาล น้ำเชื่อม เกลือ หรือน้ำปลา ลงในเครื่องดื่ม อาหาร ของหวานชนิดต่างๆ ให้ระบุปริมาณด้วยเช่น น้ำตาล 2 ช้อนชา ในกาแฟ 1 แก้ว
   ง. ระบุปริมาณน้ำดื่ม และปริมาณน้ำจากอาหารที่รับประทานทุกมื้อ

วันที่.....

มื้ออาหาร และสถานที่	เวลา	ประเภท	อาหาร	ปริมาณ

APPENDIX III

ความสำคัญของการควบคุมอาหารต่อการรักษาโรคเบาหวาน

การควบคุมอาหารมีความสำคัญมาก สำหรับผู้เป็นโรคเบาหวาน เพราะสาเหตุหนึ่งของโรคเบาหวาน คือ อาหาร โดยเฉพาะอาหารจำพวกแป้ง ข้าว และน้ำตาล ซึ่งร่างกายไม่สามารถใช้ให้เป็นประโยชน์ได้เต็มที่ จึงจำเป็นต้องมีการควบคุมให้อยู่ในปริมาณที่ร่างกายจะใช้ได้ การควบคุมอาหารนี้จะเป็นการช่วยลดการทำงานของตับอ่อน ในการผลิตฮอร์โมนอินซูลินให้น้อยลงด้วย

ปัจจุบันการควบคุมอาหารจะเน้นหนักในแง่ของการควบคุมปริมาณกำลังงานที่ได้รับจากอาหารมากกว่าการควบคุมปริมาณของอาหารจำพวก ข้าว แป้ง เพียงอย่างเดียว การควบคุมอาหารจะช่วยให้ผู้เป็นโรคเบาหวานมีน้ำหนักลดลงอยู่ในเกณฑ์มาตรฐาน ซึ่งเมื่อน้ำหนักลดลง ระดับน้ำตาลในเลือดก็จะกลับสู่ปกติได้ นอกจากนั้นการควบคุมอาหารยังช่วยลดภาวะแทรกซ้อนต่องๆของโรคเบาหวานซึ่งโรคแทรกซ้อนนี้จะมีอันตรายมากกว่าโรคของเบาหวานเองเสียอีก ดังนั้นจึงต้องเข้าใจว่าไม่ว่าจะใช้ยารักษาด้วยหรือไม่ก็ตาม การควบคุมอาหารเป็นเรื่องสำคัญที่สุด ผู้เป็นโรคเบาหวานอย่างรุนแรงอาจจะกลับสู่ภาวะปกติได้ ถ้าสามารถทำให้น้ำตาลในเลือดลงลง โดยรู้จักปฏิบัติในการควบคุมอาหาร ตรงกันข้าม ผู้ที่ไม่ได้ควบคุมอาหาร อาการของโรคอาจจะกำเริบรุนแรงได้

จุดมุ่งหมายของการควบคุมอาหาร

1. เพื่อให้สามารถรักษาระดับน้ำตาลในเลือดให้อยู่ในระดับปกติ
2. เพื่อควบคุม หรือจำกัดปริมาณกำลังงานที่ได้รับจากอาหารให้อยู่ในปริมาณพอเหมาะ เป็นการควบคุมน้ำหนักตัวให้อยู่ในระดับมาตรฐาน
3. เพื่อช่วยลดภาวะแทรกซ้อนต่างๆซึ่งอาจเกิดขึ้นในผู้ป่วยโรคเบาหวาน โดยเฉพาะโรคแทรกทางเส้นเลือด เช่น โรคหลอดเลือดตีบแข็ง โรคหัวใจขาดเลือด เป็นต้น
4. เพื่อช่วยป้องกันอาหารหมดสติ เนื่องจากภาวะความเป็นกรดในเลือดสูง หรือภาวะน้ำตาลในเลือดต่ำเกินไป
5. เพื่อช่วยให้ร่างกายได้รับสารอาหารครบตามความต้องการของร่ายกาย
6. เพื่อช่วยให้ผู้เป็นโรคเบาหวาน มีสุขภาพแข็งแรง สามารถใช้ชีวิตและทำงานต่างๆได้เหมือนคนปกติธรรมดาทั่วไป

การเลือกอาหารสำหรับผู้เป็นโรคเบาหวาน

การควบคุมอาหารให้ได้ผลนั้น ผู้เป็นโรคเบาหวานควรจะต้องเลือกรับประทานอาหารให้ถูกต้อง ทั้งปริมาณและประเภทของอาหาร โดยเลือกรับประทานให้ครบทุกหมวดในปริมาณที่พอเหมาะ

เพื่อช่วยในการเลือกอาหารให้เป็นไปได้ง่าย สะดวกและถูกต้อง ได้มีการจำแนกอาหารออกเป็น 6 หมวด ตามรายการอาหารแลกเปลี่ยน ผู้เป็นโรคเบาหวานควรทำความเข้าใจกับรายการอาหารแลกเปลี่ยนให้ดีเสียก่อน เพื่อให้รู้จักใช้อาหารแลกเปลี่ยนในหมวดเดียวกันได้ถูกต้อง และเป็นการช่วยให้ผู้ป่วยสามารถเลือกรับประทานอาหารได้หลายชนิด นอกจากนั้นผู้เป็นโรคเบาหวานควรจะทราบด้วยว่าตนควรรับประทานอาหารในแต่ละหมวดเท่าไรในวันหนึ่ง

1. <u>หมวดนม</u>

นมเป็นอาหารที่มีประโยชน์ต่อร่างกาย ประกอบด้วยโปรตีน ไขมัน คาร์โบไฮเดรต เกลือแร่และวิตามิน นมสดที่ขายตามท้องตลาดมี 2 ชนิด คือ นมชนิดจืด และชนิดหวาน ผู้เป็นโรคเบาหวานควรรับประทานนมชนิดจืดเท่านั้น และหลีกเลี่ยง นมช็อคโกแล็ต สตรอเบอรี่ โกโก้ โอวัลติน และนมข้นหวาน นอกจากนั้นนมที่ไม่มีไขมันยังเหมาะสำหรับผู้ที่อ้วนและมีไขมันในเลือดสูง นมชนิดนี้มีคุณค่าเท่ากับนมชนิดอื่น แต่ไม่มีไขมัน จึงไม่ทำให้อ้วนและไม่เพิ่มไขมันในเลือด

2. <u>หมวดผัก</u>

ผักมีวิตามิน และเกลือแร่สูง มีกากมาก จึงควรรับประทานผักมาก ๆ ทั้งผักสดและผักสุก โดยเฉพาะผักประเภทใบ สามารถรับประทานได้มากตามความต้องการ การรับประทานผักจะช่วยได้มากในระยะแรกของการเริ่มควบคุมอาหาร เพราะจะช่วยเพิ่มปริมาณอาหารทำให้อิ่มได้นาน ไม่หิวเร็ว นอกจากนั้นกากในผักจะช่วยให้น้ำตาลถูกดูดซึมได้น้อยลง จึงทำให้ระดับน้ำตาลในเลือดไม่สูง ทั้งยังช่วยให้ท้องไม่ผูก

3. <u>หมวดผลไม้</u>

ผลไม้จะให้วิตามินและเกลือแร่ต่างๆ ผลไม้มีน้ำตาลอยู่โดยธรรมชาติ จึงควรระมัดระวังในการเลือกรับประทาน ผลไม้บางชนิดมีรสหวานจัด ผู้เป็นโรคเบาหวานจึงควรหลีกเลี่ยง เพราะจะทำให้ระดับน้ำตาลในเลือดสูง แม้จะรับประทานเพียงเล็กน้อย ผลไม้บางชนิดที่มีน้ำตาลไม่มากก็ควรรับประทานตามจำนวนที่กำหนดให้ เพราะถ้ารับประทานมากเกินไป ก็อาจจะทำให้น้ำตาลในเลือดสูงได้เช่นกัน นอกจากนั้นผลไม้กระป๋อง ผลไม้ที่ปรุงแต่งด้วยน้ำตาล เช่น เชื่อม กวน แช่อิ่ม ควรหลีกเลี่ยงเช่นเดียวกัน

4. <u>หมวดข้าว แป้ง ธัญพืช</u>

เป็นอาหารที่มีคาร์โบไฮเดรตมาก ซึ่งร่างกายสามารถเปลี่ยนเป็นน้ำตาลได้ทั้งหมด ผู้เป็นโรคเบาหวานสามารถรับประทานอาหารหมวดนี้ได้ทุกมื้อเพราะเป็นอาหารที่ให้พลังงาน แต่ไม่ควรรับประทานมากเกินไป เพราะจะทำให้ระดับน้ำตาลในเลือดสูงได้ ควรจำกัดการรับประทานอาหารหมวดนี้ให้อยู่ในปริมาณที่กำหนดให้เท่านั้น

5. <u>หมวดเนื้อ</u>

เนื้อสัตว์จะให้โปรตีน จึงควรรับประทานเนื้อสัตว์ให้เพียงพอกับความต้องการของร่างกายเพื่อการเจริญเติบโตและซ่อมแซมส่วนที่สึกหรอ เนื้อสัตว์ที่รับประทานควรเลือกชนิดที่ไม่ติดมัน ควรงดหนังสัตว์ทุกชนิด เช่น หนังหมู หนังเป็ด หนังไก่ เป็นต้น ผู้สูงอายุไม่ควรรับประทานไข่แดงมากกว่าวันละ 1 ฟอง เพราะจะทำให้เกิดภาวะแทรกซ้อนเกี่ยวกับหลอดเลือดได้ง่าย

6. <u>หมวดไขมัน</u>

อาหารหมวดนี้จะให้พลังงานและความร้อน การรับประทานให้พอเหมาะจะทำให้ได้พลังงานที่เหมาะสมกับระดับการควบคุมน้ำหนักตัวด้วย ถ้ารับประทานมากเกินไปจะทำให้อ้วน นอกจากนั้นควรเปลี่ยนจากการใช้ไขมันที่ได้จากสัตว์ เช่น น้ำมันหมูมาใช้แทนน้ำมันพืชในการปรุงอาหารแทน เพราะน้ำมันพืชจะช่วยป้องกันไม่ให้ไขมันในเลือดสูง (ยกเว้นน้ำมันมะพร้าว น้ำมันปาล์ม และกะทิ)

ข้อแนะนำการปฏิบัติตนในการใช้อาหารบำบัดโรคเบาหวาน

1. ผู้เป็นโรคเบาหวานจำเป็นจะต้องทราบและเข้าใจถึงจุดมุ่งหมายของการควบคุมอาหาร
2. ผู้เป็นโรคเบาหวานควรรับประทานอาหารให้ถูกต้อง โดยเลือกประเภทและปริมาณอาหารให้เหมาะสมและสามารถใช้รายการอาหารแลกเปลี่ยนที่ทดแทนกันได้ในการเลือกอาหาร
3. ผู้เป็นโรคเบาหวานควรรับประทานอาหารให้เป็นเวลาอย่างสม่ำเสมอ
4. ควรรับประทานผักมากๆ โดยเฉพาะผักประเภทใบ ไม่ว่าจะเป็นผักสดหรือผักสุกก็ตาม
5. ควรหลีกเลี่ยงอาหารที่มีไขมันสูง เช่น เนื้อสัตว์ติดมัน หนังหมู หนังเป็ด หนังไก่ เป็นต้น
6. ควรหลีกเลี่ยงไขมันที่ได้จากสัตว์ เช่น มันหมู มันไก่ และเปลี่ยนมาใช้น้ำมันพืชแทน เช่น น้ำมันข้าวโพด น้ำมันถั่วเหลือง ยกเว้นน้ำมันมะพร้าว น้ำมันปาล์ม และกะทิ
7. ควรหลีกเลี่ยงขนมหวาน โดยการรับประทานผลไม้สดแทน
8. ควรหลีกเลี่ยงการเติมน้ำตาลทุกชนิดลงในอาหาร

9. ควรหลีกเลี่ยงเครื่องดื่มที่ใส่น้ำตาล น้ำอัดลม และแอลกอฮอล์
10. เมื่อมีอาการอ่อนเพลีย มือสั่น ใจสั่น หิว และเหงื่อออกให้รีบรับประทานน้ำตาลทันที เช่น น้ำหวาน ท๊อฟฟี่ เพราะเป็นอาการที่มีน้ำตาลในเลือดต่ำเกินไป ซึ่งเป็นภาวะที่อันตรายมาก

การเลือกอาหาร

แบ่งออกเป็นหมวดต่างๆตามรายการอาหารแลกเปลี่ยนดังนี้

อาหารแลกเปลี่ยน คืออาหารในหมวดเดียวกัน ในปริมาณที่กำหนดจะให้คุณค่าอาหารโดยเฉลี่ยใกล้เคียงกัน จึงสามารถแลกเปลี่ยนหรือแทนกันได้ การใช้รายการอาหารแลกเปลี่ยนเป็นการให้ผู้ป่วยสามารถเลือกรับประทานอาหารได้หลายชนิด

อาหารในหมู่เดียวกัน 1 ส่วน จะให้พลังงานและสารอาหารเท่ากัน

ตัวอย่าง เช่น ธัญพืช 1 ส่วน อาจได้แก่ ข้าวสวย 1/2 ถ้วยตวง หรือ 1 ทัพพี หรือขนมจีน 2 จับ อาหารทั้ง 2 ชนิดนี้ มีปริมาณแตกต่างกัน แต่ให้สารอาหารและพลังงานเท่ากัน จึงสามารถใช้แทนกันได้ ถ้ากำหนดให้บริโภคธัญพืช 1 ส่วน อาจเลือกรับประทานข้าวสวย 1/2 ถ้วยตวง (1 ทัพพี) หรือรับประทานขนมจีน 2 จับก็ได้

อาหารแลกเปลี่ยนประเภทต่างๆ

1) หมวดข้าว, แป้ง, ธัญพืช

ข้าว 1 ส่วน ให้โปรตีน 2 กรัม, คาร์โบไฮเดรต 15 กรัม, กำลังงาน 68 แคลอรี่

ปริมาณของข้าว, แป้ง, ธัญพืช 1 ส่วน ที่ใช้แลกเปลี่ยนกัน ได้แก่

ข้าวสวย.....1/2 ถ้วยตวง หรือ 65 กรัม หรือ 1 ทัพพี

ก๋วยเตี๋ยวสุก.....1/2 ถ้วยตวง หรือ 65 กรัม

บะหมี่สุก.....1/2 ถ้วยตวง หรือ 65 กรัม

มักกะโรนีสุก.....1/2 ถ้วยตวง หรือ 65 กรัม

ขนมจีน.....1-2 จับ

ขนมปัง.....1 แผ่น หรือ 25 กรัม

ขนมปังกรอบหรือแครกเกอร์.....1 แผ่นใหญ่ หรือ 2 แผ่นเล็ก

ขนมปังแฮมเบอร์เกอร์/ขนมปังฮอทดอกส์.....1/2 ก้อน

มันแกว.....1 หัวเล็ก หรือ 1/2 ถ้วยตวง

มันฝรั่ง.....1 หัวเล็ก

มันเทศสุก.....1/4 ถ้วยตวง

เผือกสุก.....1/3 ถ้วยตวง

ข้าวโพดสุก.....1/2 ฝัก หรือ 1/3 ถ้วยตวง

ถั่วเขียวสุก หรือ ถั่วดำสุก หรือ ถั่วแดงสุก หรือ ถั่วเหลืองสุก.....1/2 ถ้วยตวง

2. หมวดเนื้อสัตว์และไข่

เนื้อ 1 ส่วนให้โปรตีน 7 กรัม, ไขมัน 5 กรัม, กำลังงาน 73 แคลอรี่

ปริมาณของเนื้อสัตว์ 1 ส่วนที่ใช้แลกเปลี่ยนกันได้แก่

เนื้อหมู วัว เป็ด ไก่.....30 กรัม หรือ 2 ช้อนโต๊ะ หรือ 14 ชิ้นเล็ก

ตับ.....30 กรัม หรือ 5 ชิ้น

เนื้อปลา, เนื้อปู, หอย.....30 กรัม หรือ ¼ ถ้วยตวง หรือ 2 ช้อนโต๊ะ

ไข่.....1 ฟองใหญ่

ไส้กรอก.....1-1 1/2 แท่ง

กุ้งขนาดกลาง.....6-9 ตัว

ปลาทูขนาดกลาง.....1 ตัว

เต้าหู้ขาว, อ่อน.....100 กรัม หรือ 3/4 หลอด

เต้าหู้เหลือง, แข็ง.....65 กรัม หรือ 1/2 ชิ้น

เนยแข็ง.....30 กรัม

หมายเหตุ น้ำหนักของเนื้อคือน้ำหนักของเนื้อสุก และไม่รวมน้ำหนักของหนัง เช่น หนังเป็ด หนังไก่ เป็นต้น

3. หมวดผัก

แบ่งเป็น 2 ประเภท

3.1 ผัก ก.

ผักก. 1 ส่วนให้กำลังงานน้อยมาก จึงรับประทานได้ตามต้องการ

ผักคะน้า	ผักตั้งโอ๋	แตงกวา
ผักกวางตุ้ง	หน่อไม้	มะละกอดิบ
ผักกาดชนิดต่างๆ	เห็ดสด	มะเขือต่างๆ
ผักตำลึง	หัวปลี	หัวไชเท้า
ผักบุ้ง	ถั่วพู	ผักกะเฉด
บวบ	ฟักเขียว	ถั่วงอก
ดอกกุ่ยช่าย	น้ำเต้า	ผักชะอม
กะหล่ำปลี		

3.2 ผัก ข.

ผัก ข. 1 ส่วนให้โปรตีน 2 กรัม, คาร์โบไฮเดรต 5 กรัม กำลังงาน 28 แคลอรี่ (ปริมาณผัก ข. 1 ส่วน เท่ากับ 1/2 ถ้วยตวง หรือ 100 กรัม หรือ 2 ทัพพีเล็ก)

ฟักทอง	เมล็ดถั่วลันเตา	มะรุม
สะตอ	ถั่วฝักยาว	สะเดา
ใบขี้เหล็ก	ดอกแค	หัวผักกาดแดง
หอมหัวใหญ่	ถั่วแขก	หัวผักกาดเหลือง

4. หมวดผลไม้

ผลไม้ 1 ส่วน ให้คาร์โบไฮเดรต 10 กรัม, กำลังงาน 40 แคลอรี่

ปริมาณผลไม้ 1 ส่วนที่ใช้แลกเปลี่ยนกัน ได้แก่

กล้วยหอม.....1/2 ผล

กล้วยน้ำว้า.....1 ผล

กล้วยไข่.....2 ผลเล็ก หรือ 1 ผลใหญ่

เงาะ..... 4 ผล

ชมพู่.....2 ผล

มะละกอ.....1/2 ถ้วยตวง หรือ 6 ชิ้นขนาดคำ

มังคุด.....2 ผลใหญ่

มะม่วงดิบ.....1/2 ผล

แตงโม.....1 ถ้วยตวง หรือ 10 ชิ้นขนาดคำ

พุทรา.....2-4 ผล

ฝรั่ง.....1/4 ผลกลาง หรือ 40 กรัม

ลางสาด.....8 ผล

ลิ้นจี่สด.....4 ผล

ส้มเขียวหวาน.....1 ผลกลาง

ส้มเกลี้ยง.....1 ผล

ส้มโอ.....2 กลีบ หรือ 1/4 ผลเล็ก

สับปะรด.....1/2 ถ้วยตวง หรือ 6 ชิ้นขนาดคำ

แอปเปิล.....1 ผลเล็ก หรือ 1/2 ผลใหญ่

น้ำส้มคั้น.....1/2 ถ้วยตวง

น้ำสับปะรด.....1/3 ถ้วยตวง

ผลไม้ที่ควรงด

องุ่น, ทุเรียน, ละมุด, มะม่วงสุก, น้อยหน่า, ขนุน, ลำไย, ลูกเกด, ลูกพรุน, อ้อย, ผลไม้กระป๋อง, ผลไม้สำเร็จรูป, ผลไม้แช่อิ่ม, ผลไม้เชื่อม, ผลไม้กวน

5. หมวดไขมัน

ไขมัน 1 ส่วน ให้ไขมัน 5 กรัม, กำลังงาน 45 แคลอรี่

น้ำมันพืช.....1 ช้อนชา	สลัดน้ำใส.....1 ช้อนชา
เนย, มาการีน.....1 ช้อนชา	สลัดน้ำข้น.....1 ช้อนโต๊ะ
เบคอน.....1 ชิ้น	ครีมใส่กาแฟ.....2 ช้อนโต๊ะ

ไขมันที่ควรงด : น้ำมันหมู, น้ำมันมะพร้าว, น้ำมันปาล์ม, กะทิ, มันหมู, หนังไก่, หนังหมู, หนังเป็ด

6) หมวดนม

นม 1 ส่วน ให้โปรทีน 8 กรัม, ไขมัน10 กรัม, คาร์โบไฮเดรท 12 กรัม, กำลังงาน 170 แคลอรี่

นมสดธรรมดา.....1 ถ้วยตวง หรือ 240 ซีซี

นมสดไม่มีไขมัน* .....1 ถ้วยตวง หรือ 240 ซีซี

นมระเหย.....1/2 ถ้วยตวง หรือ 120 ซีซี

นมผง.....1/4 ถ้วยตวง หรือ 4 ช้อนโต๊ะ

นมผงไม่มีไขมัน* .....1/4 ถ้วยตวง หรือ 4 ช้อนโต๊ะ

* นมไม่มีไขมัน 1 ส่วน จะให้โปรทีน 8 กรัม, คาร์โบไฮเดรท 12 กรัม, กำลังงาน 80 แคลอรี่

นมที่ควรงด : นมที่เติมน้ำตาล, นมข้นหวาน, นมช็อกโกแล็ต, สตรอเบอรี่, โกโก้, โอวัลติน

รายการอาหารแลกเปลี่ยน 6 หมวด

กำลังงาน 1,000 แคลอรี่ (โปรทีน 20 %, ไขมัน 30 %, คาร์โบไฮเดรท 50 %)

ดื่มนมได้			**ไม่ดื่มนม**		
1. แป้ง	5	ส่วน	1. แป้ง	6	ส่วน
2.เนื้อ	4	ส่วน	2. เนื้อ	5	ส่วน
3. ไขมัน	3	ส่วน	3. ไขมัน	3	ส่วน
4. นม (พร่องมันเนย)	1	ส่วน	4. นม (พร่องมันเนย)	-	ส่วน
5. ผัก (ผัก ข.)	2	ส่วน	5. ผัก (ผัก ข.)	2	ส่วน
6. ผลไม้	2	ส่วน	6. ผลไม้	2	ส่วน

หมายเหตุ : - ผัก ก. (ประเภทใบ) = ไม่จำกัดจำนวน

- น้ำตาล เติมได้ = 2 ช้อนชา

APPENDIX IV

Determination of glucose

The levels of glucose in plasma were determined using the enzymatic method described by Barham and Trinder (Barham, 1972). Plasma was obtained from blood, which was preserved by the glycolysis inhibitor, sodium fluoride, mixed with the anti coa.gulant, calcium oxalate. Glucose oxidase (GOD) catalizes the oxidation of glucose in the accordance with the following equation:

1). Glucose + O_2 + H_2O_2 $\xrightleftharpoons{GOD}$ Gluculonic acid + H_2O_2

Hydrogen peroxide formed was reacted with 4-aminoantipyrine and 4-hydroxybenzoic acid which was catalized by enzyme peroxidase (POD) as the following equation:

2). H_2O_2 + 4-Aminoantipyrine + 4-hydroxybenzoic acid $\xrightleftharpoons{POD}$ N-(4-antipyryl)-p-benzoquinone imine.

Since the amount of quinoneimine dye formed is in molar equivalent to the amount of glucose, the concentration of the dye in the test tube would represent the amount of glucose in the specimen. The dye concentration was quantitated by spectrophotometer at wavelength 510 nm. Glucose concentration was calculated according to the following equation:

Glucose concentration = (A*100) / As

Where A is the absorbance of the specimen reaction tube and there was 100 mg per deciliter standard glucose in the standard reaction tube. The amount of glucose concentration was expressed as mg/dL. Appropriate dilution was made if the specimen

contained high level of glucose. When a series of hourly plasma glucose of each individual were analyzed, the area under the curve plotted between the glucose concentrations against the time of blood withdrawals can be calculated using computer integration (Wolever, 1986, Komindr, 1987).

APPENDIX V

Determination of glycosylated hemoglobin (HbA_1)

Glycosylated hemoglobin in whole blood samples were measured at Hematology Laboratory, Ramathibodi Hospital by utilized the principle of ion exchange high performance liquid chromatography (HPLC) according to the method of VARIANT™ Hemoglobin Testing System HbA_{1C} Dual Kit.

principle of the procedure

Hemolyzed samples are maintained at a constant 12°C ± 2°C in the autosampler chamber. The VARIANT's two dual-piston pumps deliver a programmed buffer gradient of increasing ionic strength to the system. Prepared samples are automatically injected into the analytical flow path and applied to the cation exchange column, where the hemoglobin is separated due to the attraction of the hemoglobin to the column material. The separated hemoglobin then passes through the flow cell of the filter photometer, where changes in the absorbance (415 nm) are measured; background variations are corrected by and additional filter at 690 nm. A built-in integrator performs reduction of raw data collected from each analysis. A calibrator is analyzed with each run to adjust the calculation parameters for the determination of HbA_{1C}. A chromatogram of the changes in the absorbance is plotted versus the retention time. Each chromatogram printout is accompanied by a report identifying each peak detected, plus the relative percent and retention times of each peak. To aid

in the interpretation of results, windows (e.g. ranges) have been established for the most frequently occurring hemoglobins based on their characteristic retention times. Prior to analysis, a simple preparation of the patient sample is required to hemolyse the blood and to remove Schiff base by incubation at 15-30°C for 10 minutes.

APPENDIX VI

Determination of serum total cholesterol

An Enzymatic-colorimetric method was employed to measure serum total cholesterol by using Boeringer Mannheim Monotest cholesterol Kit (Cat. No 236691). The test principle are as follow (Monotest, 1982):

$$\text{cholesterol ester} + H_2O \xrightarrow{\text{cholesterol esterase}} \text{cholesterol} + \text{ROOH}$$

$$\text{cholesterol} + O_2 \xrightarrow{\text{cholesterol oxidase}} \Delta^4\text{-cholestenone} - H_2O_2$$

$$2\ H_2O_2 + \text{4-aminophenazone} + \text{phenol} \xrightarrow{\text{peroxidase}} \text{4-(p-benzoquinone-mono-imino)phenazone} + 4\ H_2O$$

Boeringer Mannheim reagents

Tris buffer (pH 7.7)	100	mmol/L
Magnesium aspartate	50	mmol/L
4-aminoantipyrine	1	mmol/L
Sodium cholate	10	mmol/L
Phenol	6	mmol/L
3, 4 dichlorophenol	4	mmol/L
Hydroxypolyethoxy-n-alkanes	0.3	%

Cholesterol esterase	≥ 0.4 U/mL
Cholesterol oxidase	≥ 0.25 U/mL
Peroxidase	≥ 0.2 U/mL

Procedure

Dissolved 31 g of buffer cholesterol (Cat. No. 236691) with 500 mL distilled water. The reagent solution was ready to use after 10 minutes and stable for 4 weeks at 2° to 8°C

1 mL of reagent solution prepared above and 0.01 mL serum were added to test tubes, and incubated at 37°C for 10 min. The absorbance of and sample were by spectrophotometer at wavelength 500 nm against the reagent blank (Δ A) within 60 min.

The standard cholesterol concentration of 100, 200, 300 and 400 mg/dL were prepared and treated the same as sample.

If the cholesterol concentration exceeded 700 mg/dL or 25.9 mmol/L. 0.1 mL of sample was diluted with 0.2 mL of 0.9% NaCl solution and assay was repeated. Multiply the results by 3.

Calculation

$$\text{Cholesterol} = \frac{5.17 \times \Delta A \text{ (sample)}}{\Delta A \text{ (standard)}} \quad \text{(mmol/L)}$$

APPENDIX VII

Determination of high density lipoprotein cholesterol (HDL-C)

The method of Bustein (Bustein, 1970) and Lopes-Virella (Lopes, 1977) were used for the determination of HDL-C. The Chylomicron, very low density lipoprotein (VLDL) and low density lipoprotein (LDL) are precipitated by addition of phosphotungstic acid and magnesium chloride. After centrifugation the supernatant fluid contains the HDL-C fraction, which is assayed for HDL-C cholesterol liquicolor test kit.

Precipitant

Phosphotungstric acid	0.55 mmol/L
Magnesium chloride	25 mmol/L

four parts of precipitant were distilled with one part of distilled water. This precipitant was stable up to the expire date specified when stored at 15° to 25°C.

Procedure

Add 200 μL of serum and 500 μL of precipitant were pipetted into centrifuge tubes. The solution was mixed and allowed to stand for 10 minutes at room temperature and was centrifuged at 4000 rpm for 10 min.

After centrifugation, separate the clear supernatant. from the precipitate within 1 hour. Pipette 100 μL of supernatant and the cholesterol content was determined by the

enzymatic colorimetric method as already described. The standard cholesterol concentration of 10, 25, and 50 mg/dL were prepared and treated as same as the sample.

Calculation

$$\text{HDL-C} = 5.43 \times \Delta A \text{ (sample)} \quad \text{(mmol/L)}$$

Estimation of low density lipoprotein cholesterol (LDL-C)

LDL-C level was calculated from Friedewald's formula (Friedewald, 1972) as follow:

$$\text{LDL-C} = \text{total cholesterol} - (\text{triglycerides}/5) - \text{HDL-C}$$

APPENDIX VIII

Determination of serum triglycerides

Enzymatic hydrolysis of triglycerides with subsequent determination of the liberated glycerol by Boeringer Mannheim Triglycerides GPO-PAP Kit (Cat. No. 701904) was used to measure serum triglycerides (Peridochrom, 1982). The enzymatic reactions are as follow:

$$\text{triglycerides} + 3\ H_2O \xrightarrow{\text{lipase}} \text{glycerol} + 3\ \text{RCOOH}$$

$$\text{glycerol} + \text{ATP} \xrightarrow{\text{glycerol kinase}} \text{glycerol-3-phosphate} + \text{ADP}$$

$$\text{glycerol-3-phosphate} + \text{O2} \xrightarrow{\text{glycerol phosphate oxidase}} \text{Dihydroxyacetone phosphate} + H_2O_2$$

$$H_2O_2 + \text{4-aminophenazone} + \text{4-chlorophenol} \xrightarrow{\text{peroxidase}} \text{4-(p-benzoquinone-monoimino)-phenazone} + 2\ H_2O + \text{HCl}$$

Boeringer Mannheim reagents

Buffer solution

Tris buffer pH 7.6	0.15	mmol/L
Magnesium sulphate	17.5	mmol/L
EDTA, disodium salt	10	mmol/L
4-chlorophenol	3.5	mmol/L

Sodium choleate	0.15	%
Potassium hexacyanoferrate (II)	6	μmmol/L
Hydroxypolyethoxy-n-alkanes	0.12	%
ATP	≥ 0.5	mmol/L
4-aminophenazone	0.35	mmol/L
Lipases	≥ 3	U/mL
Glycerol phosphase oxidase	≥ 2.5	U/L
Glycerol kinase	≥ 0.2	U/L
Peroxidase	≥ 0.15	U/mL

Procedure

Immersed one reagent strip kit (Cat. No. 701904) in one bottle of buffer solution contents of 32 mL and stirred the bottle contents for 10 second. Allow to stand in solution for 5 minutes, stirred once again for 10 second, and then discarded reagent strip.

0.01 mL of serum was added to 1.0 mL of reagent solution prepared above to the test tubes. The test tubes were mixed and incubated at 20-25 °C for 10 minutes, the absorbance of the sample were read against the reagents blank (ΔA) within 60 min. at 500 nm.

If triglycerides concentration exceeded 1000 mg/dL or 11.4 mmol/L, one part of sample was diluted with 5 parts of 0.9% NaCl solution and repeated assay. Multiple the result by 5.

Calculation

$$\text{Triglycerides} = 2.29 \times \frac{\Delta A \text{ (sample)}}{\Delta A \text{ (standard)}} \quad \text{(mmol/L)}$$

APPENDIX IX

Determination of plasma retinol and α-tocopherol

Plasma retinol and α-tocopherol were measured by the method of Bieri et al (Bieri, 1979).

Reagents

1. All-trans retinal; Flukg AG, Cat NO. 8283
2. Internal Standard : Retinyl acetate; sigma No R-3000
3. DL α-tocopherol Art 8283 Merck.
4. d α-tocopheryl acetate No T-3001 Sigma.
5. Methanol (HPLC grade) 9093-03 JT-Baker.
6. Absolute-Ethanol pro analysis Merck.
7. Hexane (HPLC grade) 9304-03 Baker Analyzed.

Preparation of standard solution

Stock standard solution of retinol (0.01 g/dL) was prepared in hexane. Retinyl acetate (0.01 g/dL) was used as internal standard and prepared in ethanol. Alpha tocopherol and tocopheryl acetate was prepared in absolute ethanol and the concentrations checked by spectrophotometry. Dilution of these stock standards, the working standards were made regulargly as indicated below.

Extinction coefficients use were:

$E^{1\%}_{1\,cm}$: retinol, 1850 at 325 nm.,

retinyl acetate, 1565 at 325 nm.,

α-tocopherol, 75.8 at 292 nm. and

α-tocopheryl acetate, 43.6 at 285 nm.

Standard Curves

For quantitaton, internal standard of retinyl acetate and α-tocopheryl acetate were used. To prepared a standard curve for the peak area ratios, a constant amount of retinyl and tocopheryl acetate were combined with variable amounts of the retinol and α-tocopheryl acetate, were injected into the HPLC instrument and the peak area ratios measured.

Sample preparation

Frozen plasma samples were thawed, mixed and centrifuged at 2500g for 5 min to removed fibrous debris. Added 100 μl of a mixture of internal standard (retinylacetate and α-tocopheryl acetate) to 100 μl of plasma and vortex-mixed for 30 seconds. Then we added 200 μl of hexane to this mixture and the contents of the tubes were vortex-mixed for 45 seconds. Precipitated protein was removed by centrifugation (3000g for 5 minutes) at room temperature. 100 μl of aliquots of the organic phase was removed from each sample and the solvent was evaporated under nitrogen. Aliquot from each sample was dissolved in 100 μl of methanol.

Chromatographic system

The HPLC instrumentation was from Shimadzu LC-10AD equipped with SPD-10A UV-VIS detector, SIL-10A auto injector and a reversed phase HRC-ODS column (4.6 mm id * 15 cm) packed with octadesylsilica. The mobile phase was absolute methanol with the flow rate of 1 ml/min. Analyses were identified by retention time and quantitated by peak area ratios between retinol α-tocopherol and internal standard. The reference standard of retinol was supplied by the National Institute of Standard and Technology USA.

APPENDIX X

Determination of erythrocyte transketolase activity (ETKA) and thiamin pyrophosphate effect (TPPE).

principle

Transketolase, a thiamin pyrophosphate (TPP) dependent enzyme, catalyzes the following two reactions in the pentose phosphate pathway (Bamji, 1981):

1. Xylulose-5-phosphate + ribose-5-phosphate $\rightleftharpoons$ Sedoheptulose-7-phosphate + glyceraldehyde-3-phosphate
2. Xylulose-5-phosphate + erythrose-4-phosphate $\rightleftharpoons$ Fructose-6-phosphate + glyceraldehyde-3-phosphate

ETKA was determined by the method modified from Dreyfus (Dreyfus, 1962), and Dische (Dische, 1953). The analysis involved the incubation of hemolyzed red bleed cell in buffer medium with an excess of ribose-5-phosphate, in the presence or absence of excess TPP. ETKA obtained without the addition of TPP represents the absolute enzyme activity and is dependent upon the coenzyme available in the erythrocytes. The addition of TPP permits an estimation of apoenzyme uncomplexed, as well as the maximum potential activity.

Preparation of blood samples

Fresh heparinized blood was centrifuged at 2,000 r.p.m. for 5 minutes. The plasma and buffy coat were removed from the blood cell by suction. The remaining erythrocytes were washed 3 times with 0.9 % sodium chloride solution. The

suspension was centrifuged for 5 minutes at 2,000 r.p.m. The supernatant were discarded. After the third washing, the layers of white blood cells and platelets were completely removed. The remaining 80-95 % red blood cells concentrate were diluted to the proper concentration for determination of ETKA. One part of packed washed erythrocytes was added to one part of distilled water and then hemolysate was mixed. The hemolysate was kept frozen at -20°C and the determination of ETKA was carried out within 2 weeks after hemolysate preparation.

Reagents

1. Substrate, 0.018 M ribose-5-phosphate pH 7.4

1.31 g of ribose-5-phosphate was dissolved in 150 mL of distilled water and adjusted to pH 7.4 with KOH solution, then distilled water was added to make 250 mL solution.

2. Standard sedoheptulose, barium salt

2.1. Stock standard, 40 mmol/Liter

1.70 mg of sedoheptulose was dissolved in 100 mL of saturated benzoic acid.

2.2. Working standard, 1, 2 and 4 mmol/L

Each 1 mL of stock standard was diluted to 10 mL, 20 mL, and 40 mL with saturated benzoic acid to make the working standard, 4, 2, and 1 mmol/L, respectively.

2.3. Saturated benzoic acid

2.9 g of benzoic was dissolved in distilled water and adjusted volume with distilled water to 1,000 mL.

2.4. 0.143 M Krebs-Ringer phosphate buffer, pH 7.4

The following solutions were prepared, then they were mixed and adjusted to pH 7.4 with diluted HCl (1 mol/Liter) :

20 mL of NaCl solution (9 g/Liter)
515 mL of KCl solution (11.5 g/Liter)
100 mL of K_2HPO_4 solution (17.5 g/Liter)
5 mL of $MgSO_4$, $7H_2O$, solution (38 g/Liter)

2.5. 0.002M thiamin pyrophosphate (TPP) in buffer

92.16 mg of TPP was dissolved in buffer solution to make 100 mL solution.

2.6. Trichloroacetic solution, 150 g/Liter

15 g of trichloroacetic acid was dissolved in distilled water to make 100 mL solution.

2.7. 3% cysteine solution

3 g of L-cysteine-HCl was dissolved in 50 mL distilled water, then few drops of 5-6 N HCl was added and the solution was stirred until it dissolved. The volume was adjusted to 100 mL solution.

Procedure

Each determination of ETKA was carried out in a set of three micro test tubes measuring 0.4 by 4 cm. Test tube no. 1 and 2 contained 10 microliters of buffer. Test tube no. 3 contained 10 microliter of the same buffer, and 0.002 M thiamin pyrophosphate (TPP). To each of these three tubes, 10 microliters of erythrocytes

hemolysate was added. When the content had been thoroughly mixed, the tubes were placed in an incubator at 37°C for 30 minutes to ensure saturation of the enzyme with added TPP.

After a period of preincubation, 20 microliters of 15% trichloroacetic acid and 20 microliters of 0.018 M ribose-5-phosphate were added to tubes no.1 which thus served as a control blank. To tube no. 2 and 3, 20 microliters of ribose-5-phosphate were added. All of the tubes were then reincubated for 30 minutes at 37°C. The reaction in tube no. 2 and 3 were stopped promptly by adding 20 microliters of 15% trichloroacetic acid. Then the tubes were thoroughly agitated, and centrifuged at 2,500 r.p.m. for 10 minutes. Aliquots of the clear supernatant were then use for sedoheptulose determination which was carried out by the colorimetric formation of sedoheptulose with cysteine and sulfuric acid described by Dische (Dische, 1953). One mL of a mixture of distilled water and concentrated sulfuric acid (5 part of distilled per 12 parts of concentrated acid) was added to 20 microliters of each clear supernatant from each assay tube. The tubes were then agitated and heated for 4 minutes in 100 °C water bath. The mixtures were allowed to cool to room temperature. Then 20 microliter of a 3% cysteine solution was added to each tube and the tubes were again agitated. The reaction tubes were allowed to stand at room temperature for at least 17 hours, at which time total heptose values were obtained by reading the difference in absorbance against blank between 510 and 540 nm. The assay was done in triplicate.

Calculation

ETKA is expressed in international units (I.U.) which is equivalent to the number of micromoles of sedoheptulose-7-phosphate produced per minute per liter of erythrocytes.

$$\text{ETKA} = \frac{K \times \Delta A \text{ sample}}{30} \cdot \frac{1000}{\frac{X(0.005)}{100}} \text{ µmole/min./LRBC or I.U.}$$

in which :-

$K = \frac{\text{Standard (µmole)}}{\Delta A \text{ standard}}$

X = hematocrit reading of washed erythrocyte

ΔA = difference in absorbance reading between 510 and 540 nm.

30 = incubation time in minutes

$\frac{X(0.005)}{100}$ = true red blood cells used in assay tube

1000 = conversion factor to 1 liter of unwashed erythrocytes

Thiamin pyrophosphate effect (TPPE) was expressed in the percentage increase of sedoheptulose-7-phosphate formation after the addition of thiamin pyrophosphate.

$$\text{TPPE (\%)} = \frac{\text{ETKA with added TPP} - \text{ETKA without added TPP} \times 100}{\text{ETKA without added TPP}}$$

APPENDIX XI

Determination of erythrocytes glutathione reductase activity (EGRA) and activity coefficient (AC)

Principle

Glutathione is a flavoenzyme with FAD as a prosthetic group, a coenzyme form of riboflavin, which catalyzes the reduction of oxidized glutathione (GSSG) by the following reaction:

$$GSSG + NADPH + H^{+} \rightleftharpoons 2\,GSH + NADP^{+}$$

EGRA was determined by the method modified from Glatzle et al (Glatzzle, 1971), which is based on the assay of reduced nicotinamide adenine dinucleotide phosphate (NADPH) dependent on glutathione reductase activity, with and without incubation with saturating amount of FAD in vitro. If there is insufficient FAD in EGR, the addition of FAD to the hemolysate can stimulate the enzyme activity and indicates the saturated enzyme activity. This can be checked by measure the diminution of NADPH in the presence of oxidized glutathione. The rate of decreased absorbance at 334 nm provides the measurement of the diminution of NADPH, which indicates the enzyme activity.

Preparation of blood samples

One part of packed washed erythrocytes was added to 19 parts of distilled water and the hemolysated was kept frozen at -20 °C and the determination of EGRA was carried out within 2 week after the hemolysate preparation.

Reagents

1. Buffer, 0.2 M potassium phosphate (K_2HPO_4)

   8.71 g of K_2HPO_4 was dissolved in 400 mL distilled water was added to make 500 mL solution.

2. Nicotinamide adenine dinucleotide phosphate (NADPH)

   16.67 mg of the tetrasodium salt of NADPH in 5 mL of 1 % sodium hydrogen carbonate was protected from light and kept in ice.

3. Dipotassium ethylene diamine tetraacetate (EDTA-K_2)

   0.75 g of EDTA-K_2 was dissolved in distilled water to make 25 mL solution. it was prepared weekly and kept in the refrigerator.

4. Flavin adenine dinucleotide, monosodium salt (FAD-Na)

   1.18 mg of FAD-Na was dissolved in distilled water to make 5 mL solution which was kept in ice and protected from light.

5. Glutathione, oxidized (GSSG)

   23 mg of GSSG was dissolved in distilled water to make 5 mL solution and then 0.04 mL of 1 N NaOH was then added to the solution.

Procedure

The test was done in 2 mL quartz cuvettes of 0.5 cm width, at 37°C. To 1.4 mL of 0.1 M K_2HPO_4 pH 7.4, 0.1 mL of hemolysate, 0.1 mL NADPH and 0.1 mL EDTA-K_2 solution were added. The mixture was incubated at 35°C for 5 minutes. Then 0.1 mL of oxidized form of glutathione was added. The solution was mixed well. The reaction rate was measured by recording the absorbance at 334 nm by Spectrophotometer for 5 minutes at 35 °C. For the assay of saturated enzymatic activity in vitro, 1.35 mL K_2HPO_4 solution plus 0.05 mL of FAD-Na solution was used instead of the 1.4 mL of K_2HPO_4 solution. 1.8 mL of K_2HPO_4 solution was used as reference.

Calculation

EGRA is expressed in international units (I.U.) which is equivalent to number of micromoles of NADPH consumed per minute per liter of erythrocytes.

$$\text{EGRA} = \frac{\Delta A334}{5} \times \frac{10^6}{6200} \times \frac{1}{0.5} \times 1.8 \times \frac{1}{\frac{X \times 0.1}{100 \times 20}} \quad \mu\text{mole/min./LRBC or I.U}$$

in which:-

$\frac{\Delta 334}{5}$ = decrease in absorbance at 334 nm per minute

$\frac{6200}{10^6}$ = molar extinction coefficient of NADPH at 334 nm

0.5 = light path through the cuvett in cm

1.8 = final volume

$\frac{X \times 0.1}{100 \times 20}$ = true red blood cells used in assay tube in mL

$$\text{Activation coefficient (AC)} = \frac{\text{EGRA with added FAD}}{\text{EGRA without added FAD}}$$

APPENDIX XII

Determination of plasma ascorbic acid

Ascorbic acid was determined as the derivative of 2,4-dinitrophenylhydrazine using the method of Stanley et al (Stanley, 1979).

Principle

Ascobic acid is oxidized by copper to form dehydroascorbid acid and diketogluconic acids. These products are treated with 2,4-dinitrophenylhydrazine to form the derivative bis-2-4-dinitrophenylhydrazone. This compound, in strong sulfuric acid, undergoes a rearrangement to from a product with an absorption band that is measured at 520 nm. The reaction is run in the presence of thiourea to provide a mildly reducing medium, which helps to prevent interference from nonascorbic chromogens.

Reagents

All stable for at least one week.

1. Trichloroacetic acid (TCA), 5% and 10% solution in distilled water
2. 2,4-Dinitrophenylhydrazine/thiourea/copper (DCT) solutions in distilled water, add 0.4 g thiourea, 0.05 g $CuSO_4 \cdot 5H_2O$, and 3.0 g 2,4 dinitro-phenylhydrazine and bring to a total volume of 100 mL with 9 $N H_2SO_4$
3. 65% H_2SO_4

procedure

1 mL of plasma was added to 1.0 mL of ice-cold 10% TCA, mixed thoroughly, and centrifuged for 20 min. at 3500 g. In order to form the bis-2-4-dinitrophenylhydrazone, 0.5 mL of supernatant was mixed with 0.1 mL of DTC and incubated for 3 hr at 37°. To convert this to the rearranged products, which were measures spectrophotometrically, 0.75 mL of ice-cold 65% H_2SO_4 was added and mixed well, and the solutions were allowed to stand at room temperature for an additional 30 min. Absorbances were determined at 520 nm. Standards L-ascorbic acids were made in 5% TCA in the same procedure and rage from 0 to 20 μg/mL.

APPENDIX XIII

Determination of serum calcium and ionized calcium

: NOVA 7

Principle

The ions exchange phenomena occurs at the membrane of the ion selective electrode. The ions move from the solution on either side of the membrane. Overtime, the ions diffuse back and forth across the membrane until an equilibrium is reached and the salt concentrations in both solutions are equal. During the equilibration process, the net flow for each ion occurs in the direction which promotes equilibration. After equilibration, the ions continue to move back and move across the membrane, but the net effect of the ionic diffusion is zero, and the concentration in the solution remains unchange (Jack, 1979).

Reference range for serum calcium: 2.20-2.70 mmol/L.

Reference range for serum ionized calcium: 1.14-1.34 mmol/L.

Reagents

Fluid pack

- Internal standard A
- Internal standard B
- Reference solution
- Waste bottle.

Procedure

1. The "calibrate" botton: Calibrate botton was pressed. Initiates automated calibration cycle was performed with internal standards and drawn from NOVA 7 fluid pack.

2. The "analyze" botton: The analyze botton was pressed once. The probe moved to await position of the head-hold sample.

3."Analyze" botton was pressed again with in 30 seconds: Sample was aspirated and analysis was performed.

APPENDIX XIV

Determination of phosphorus

Determination of serum phosphorus was determined by method of Golddenberg and Fernandez (Goldenberg, 1966).

Reference values for serum : 0.8-1.4 mmol/L.

Reagent

1. Iron-trichloroacetic acid, stabilized: 50 g of trichloroacetic acid (CCl COOH), (May-Baker Ltd. Dagenham, England) was transferred to a 500 ml volumetric flask in the presence of 300 ml of water. 5 g of thiourea [$(cs(NH_2)_2)$] (May-baker Ltd. Dagenham, England) and 15 g of Mohr's salt (ferrous Ammonium sulfate hexahydrate [$Fe(NH_4)_2$ $(SO_4).6H_2O$] (May-Baker Ltd. Dagenham, England) were added. Water was added to 500 ml. The solution was stored in a amber bottle.

2. Ammonium molybdate, 0.0355 M: 45 ml conc. H_2SO_4 with cooling was added to a 500 ml volumetric flask which contained 200 ml of cold water. 22 g of ammonium molybdate [$(NH_4)_2$ Mo O. $4H_2O$] (Mallinckrodt chemical Work St. Louis) was added to 500 ml.

3. Phosphorus standard was contained 5 ml phosphorus per dl.: 0.220 g of potassium monbusic (KH_2PO_4) (Mallinckrodt chemical Works) was dried for 1 hour at 110°C and dissolved in water in a 1 liter volumetric flask. Water was added to 1 liter. A few drops of chloroform was added as the preservation and stored in a polyethylene bottle.

4. HCl, 6N: 10 ml of conc. HCl was added to 10 ml water.

Procedure

Phosphorus was determined by the method of Golddenberg and Fernandez (Golddenberg, 1966). The serum was deproteinized by an iron-Trichloracetic acid reagent. The supernate was mixed with molybdie acid to form molybdiphosphate, which was reduced by Fe^{++} to produce molybdenum blue. Absorption was measured at 660 nm.

APPENDIX XV

Determination of magnesium

Principle

Magnesium was determined by the method of Hausen and Frier (Hausen, 1967) using a flame atomic absorption spectrophotometer. The serum magnesium was diluted sufficiently with lanthanum oxide solution, the absorbance of hollow-cathode magnesium lamp at 285.20 nm was recorded.

Reference values for serum: 1.8-3.0 mg/dl (0.7-1.23 mmol/L)

Reagents

1. Stock lanthanum oxide (5% lanthanum ion solution in 4N HCl): 58.7 g lanthanum oxide (LaO) was in a 1-litre volumetric flask. Then 250 mL of concentrated HCl was added very slowly to it until the material dissolved. Water was added to make a total amount of 1 litre.
2. Working lanthanum solution (0.1% w/v): 10 mL of stock solution was diluted to 500 mL with water.
3. Stock magnesium standard solution, (10 mg/dL): 1 mL of 1 g/L Titrisol Magnesium standard (9949 Titrisol; E Merck) was diluted to 1000 mL with 0.1 mL lanthanum oxide.

4. Working magnesium standards: 1, 2, 3, 4 and 5 mL of stock magnesium standard were diluted to 10 mL with 0.1% lanthanum oxide in volumetric flask to obtain magnesium concentrations of 0.1, 0.2, 0.3, 0.4 and 0.5 mg/L respectively.

Procedure

1. The serum sample was diluted to 1: 50 with a 0.1% (w/v) lanthanum oxide diluent.
2. The magnesium content in the samples and standards was assayed by a PERKIN-ELMER 1100B atomic absorption spectrophotometer using the following conditions.

Flame	air/acetylene
Magnesium cathod lamp current	6 mA
Spectral band pass	0.7 nm
Wave-length	85.2 nm

3. A standard curve using magnesium standard in 0.1% lanthanum oxide was constructed at a range of 0.2 to 0.8 mg/L. Concentration of the samples were calculated from the standard curve.

APPENDIX XVI

Determination of serum zinc and copper

All glasswares, plastic tubes and Eppendorf pipette tips used in the analysis of zinc and copper were soaked for 48 hrs in 30% nitric acid and were rinsed twice with deionized water before use.

Serum zinc and copper were measured by flame-atomic absorption spectrometry according to the method of model 1100B; perkin-Elmer. The instrument was operated according to the instruction (Analytical methods, 1974). Calibration curves were prepared by using standard solution (E. Merck; F.R. Germany). A quality control human serum (Assayed Chemistry control, level I and II; Biorad, Placentia, CA, USA) for zinc were analyzed by the same analytical techniques, yielding value of 0.84 ± 0.14 and 0.61 ± 0.08 μg/L (mean ± SD) within the range of the certified value (0.62-0.92 and 0.46-0.68 μg/L). For copper, the value obtained were 1.11 ± 0.13 and 0.79 ± 0.13 which was within the certified value of 0.79-1.19 and 0.60-0.89 μg/L, respectively.

Reagent

1. Stock standard zinc solution

Stock standard solution (Titrisol® Merck Art 9953) containing 1 g of zinc chloride was diluted to 1000 mL. Thus 1000 ppm of zinc was used.

Working standard of 0.10, 0.20, 0.40, 0.80, ppm of zinc were prepared by diluting with 5% glycerol.

2. Stock standard copper solution

Copper stock standard solution containing 1000 ppm were prepared from Titrisol® Merck Art 9953 (1 g copper in 1000 mL). Intermediate standard of 1000 ppb and 100 ppb were prepared by dilution with 0.1% HNO_3

Working standard of 10, 20, 30, 40 ppb were prepared from intermediate standard 100 ppb by diluting with 0.1%HNO_3

Procedure

Serum sample were diluted with deionized water (serum dilution 1:1 for copper, 1:5 for zinc). The concentration of serum zinc and copper were calculated from the standard curve.

APPENDIX XIII

(Tables i-xx)

APPENDIX XVII

Table i. Baseline characteristic of patients

Fybogel	Sex	Age (yr)	BW (kg)	Ht (cm)	Placebo	Sex	Age (yr)	BW (kg)	Ht (cm)
No. 1	F	59	82.6	160	**No. 1**	F	40	60.80	157
2	F	60	63.4	154	**2**	F	60	73	146
3	F	58	72.5	156	**3**	F	54	80	154
4	F	42	66.2	158	**4**	F	57	60	153
5	F	62	61.6	154	**5**	F	56	57.8	152
6	F	58	66.8	152	**6**	F	54	60.1	152
7	F	53	66.5	158	**7**	F	54	64.3	156
8	F	57	89.9	159	**8**	F	67	71.0	160
9	M	49	80.6	165	**9**	F	67	65.3	154
10	F	40	105.7	158	**10**	F	43	85.2	156.5
11	F	56	69.0	152	**11**	F	55	88.4	160
12	F	51	97.1	160	**12**	F	42	66.2	158
13	F	57	63.3	158	**13**	F	58	72.5	156
14	M	48	72.6	167	**14**	F	60	63.4	154
15	F	48	68.2	156	**15**	M	43	85.1	171.5
16	F	43	85.2	156.5	**16**	F	66	80.6	155
17	F	54	80.0	154	**17**	M	59	70.8	165
18	F	56	57.8	152					

Table ii. Total energy intake of patients (kcal/day)

Fybogel	Wk 0	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
No. 1	1642	1232	1340	1134	1296	1320	1301
2	1554	1164	1148	1206	1305	1295	1265
3	1550	1230	1298	1348	1368	1268	1278
4	1632	1056	1023	1126	1269	1125	1230
5	1670	1234	1163	1204	1284	1296	1120
6	1780	1120	1453	1453	1485	1532	1302
7	1850	1423	1369	1267	1369	1241	1198
8	1762	1320	1325	1289	1120	1230	1126
9	1465	1320	1268	1269	1346	1239	1247
10	1840	1220	1130	1245	1253	1325	1269
11	1552	1130	1430	1024	1109	1036	1203
12	1630	1240	1320	1346	1452	1043	1120
13	1764	1320	1296	1098	1306	1236	1138
14	1687	1322	1358	1153	1286	1124	1204
15	2150	1432	1326	1356	1341	1432	1365
16	1680	1203	1189	1278	1302	1298	1304
17	1637	1147	1035	1053	1232	1274	1257
18	1850	1342	1247	1108	1284	1312	1301
Placebo							
No. 1	1740	1320	1348	1236	1324	1260	1198
2	1684	1201	1233	1234	1304	1240	1243
3	1630	1210	1365	1463	1469	1204	1245
4	1852	1102	1612	1344	1238	1107	1328
5	1639	1140	1106	1069	1254	1047	1152
6	1630	1147	1121	1205	1320	1324	1280
7	1697	1005	1123	1158	1301	1206	1296
8	1870	1270	1204	1146	1120	1203	1287
9	1743	1208	1196	1153	1206	1196	1206
10	1850	1029	1038	1028	1264	1102	1069
11	1874	1002	1205	1153	1246	1356	1269
12	1750	1320	1204	1320	1365	1205	1193
13	1630	1230	1132	1206	1366	1355	1269
14	1698	1204	1156	1304	1402	1393	1388
15	2164	1423	1398	1284	1204	1204	1306
16	1843	1042	1265	1156	1269	1163	1012
17	1965	1320	1297	1305	1374	1420	1320

Table iii Percentages of carbohydrate as energy intake of patients

Evbogel	Wk 0	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
No. 1	40	52	53	53	52	52	53
2	45	54	52	52	52	53	53
3	56	53	51	49	51	51	52
4	40	49	51	52	52	54	54
5	42	47	53	49	50	52	51
6	41	53	51	49	53	54	56
7	46	52	49	51	52	53	54
8	57	48	50	53	53	51	53
9	43	53	50	55	54	52	50
10	55	49	51	53	51	50	53
11	43	54	51	54	53	52	50
12	42	53	54	54	53	53	55
13	40	52	53	54	54	55	54
14	51	47	49	52	52	52	53
15	52	56	54	51	54	50	51
16	46	54	52	50	51	51	51
17	48	52	52	48	50	52	51
18	46	50	52	51	50	49	51
Placebo							
No. 1	50	50	51	53	53	50	53
2	45	43	40	47	46	45	39
3	47	50	50	55	53	55	54
4	60	59	48	64	41	52	56
5	42	53	48	51	54	51	52
6	41	52	52	54	53	53	55
7	42	52	50	48	50	52	53
8	49	52	51	50	51	52	53
9	47	51	51	51	51	52	52
10	47	54	52	52	53	55	56
11	46	52	52	54	56	55	55
12	43	49	50	51	51	52	51
13	47	49	49	51	53	53	53
14	43	54	52	54	52	53	54
15	53	54	53	51	52	53	52
16	56	53	50	52	52	53	53
17	45	50	52	52	53	52	54

Table iv. Percentages of fat as energy intake of patients

Evbogel	Wk 0	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
No. 1	36	27	32	28	29	30	31
2	31	29	27	29	30	27	29
3	27	30	30	30	31	30	30
4	36	28	31	33	31	29	28
5	35	24	28	28	27	27	30
6	38	29	29	25	29	30	27
7	32	26	29	35	32	32	30
8	25	28	31	30	32	33	30
9	39	29	29	27	27	27	29
10	28	32	30	27	27	26	28
11	36	32	32	30	28	28	30
12	36	26	31	31	31	32	30
13	38	28	30	34	35	33	32
14	30	31	33	35	33	32	33
15	30	30	26	27	26	28	28
16	34	32	30	28	27	28	26
17	32	32	29	30	28	28	29
18	33	34	30	34	29	28	30
Placebo							
No. 1	31	29	31	33	32	32	30
2	22	19	18	17	18	17	17
3	32	25	30	28	30	33	30
4	29	29	44	24	44	34	33
5	36	32	31	30	32	33	30
6	37	30	31	31	31	32	31
7	37	28	29	33	29	28	27
8	29	30	30	34	33	33	31
9	29	30	31	32	31	32	32
10	31	29	30	32	30	31	30
11	34	34	32	35	33	32	27
12	40	27	31	30	31	28	30
13	32	27	28	27	26	27	31
14	33	29	27	26	28	27	29
15	27	28	31	32	32	29	29
16	22	30	28	27	30	30	29
17	31	29	31	29	27	27	29

Table v. Percentage of protein as energy intake of patients

Evbogel	Wk 0	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
No. 1	24	21	15	19	20	18	16
2	24	17	21	19	19	19	19
3	17	17	19	21	18	19	18
4	24	23	18	16	17	17	19
5	23	29	19	23	23	21	19
6	21	18	20	26	18	16	17
7	22	22	22	14	16	15	17
8	18	24	19	17	15	16	18
9	18	18	21	19	19	21	22
10	17	19	19	20	22	23	20
11	21	14	17	16	18	20	21
12	22	21	15	16	17	15	14
13	22	20	17	22	12	12	14
14	19	22	17	13	16	16	14
15	18	14	19	22	20	22	21
16	20	14	18	23	22	22	23
17	20	16	19	23	22	19	20
18	21	15	18	15	20	23	19
Placebo							
No. 1	19	21	19	15	15	18	17
2	22	19	18	17	18	17	17
3	21	26	20	17	17	13	15
4	12	12	7	13	15	14	11
5	22	15	22	20	14	16	18
6	23	19	17	15	16	14	14
7	21	20	21	20	21	20	19
8	22	17	18	16	17	15	16
9	24	19	18	17	19	16	16
10	22	17	18	17	17	15	14
11	20	14	16	11	11	13	19
12	17	24	20	19	18	20	19
13	21	24	23	22	21	20	17
14	24	17	21	20	19	21	17
15	20	18	16	17	16	17	19
16	22	18	22	20	19	16	18
17	24	21	17	19	20	22	17

Table vi. Body weight of patients

Fybogel	Wk 0	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 32
No. 1	63.4	61.7	61.2	61.0	60.6	60.4	61.8	62.2
2	82.6	82.0	82.5	79.0	78.5	78.0	78.0	77.8
3	72.5	70.9	71.4	71.4	71.4	71.4	69.8	70.8
4	61.6	62.0	62.1	61.1	59.4	59.4	59.0	0.0
5	66.8	66.8	67.0	67.7	68.0	66.7	67.9	67.3
6	66.5	66.7	65.5	65.0	65.7	65.5	66.0	67.0
7	89.9	87.2	87.3	86.2	85.6	84.6	84.4	87.8
8	66.2	66.0	65.7	66.1	66.7	66.7	67.6	67.8
9	105.7	103.2	103.0	100.8	101.4	101.8	99.0	100.8
10	80.6	80.4	78.0	78.4	79.7	77.4	77.9	77.8
11	69.0	68.1	67.2	65.7	65.1	64.7	63.4	63.8
12	97.1	96.0	96.7	97.7	96.7	95.0	94.0	0.0
13	63.3	64.0	63.0	63.0	63.0	63.0	61.8	63.0
14	68.2	66.9	68.0	69.0	68.0	69.7	67.6	68.0
15	72.6	73.0	71.6	71.3	73.0	72.2	73.0	73.0
16	80.0	81.7	81.0	80.5	81.0	80.8	80.5	81.2
17	57.8	57.7	59.3	56.0	56.8	57.3	56.8	57.8
18	85.2	87.2	87.8	87.0	87.0	87.8	86.8	88.0
Placebo								
No. 1	60.8	60.2	60.2	59.8	60.5	60.0	59.2	60.6
2	73.0	73.5	74.5	74.2	76.0	75.0	75.0	75.1
3	80.0	81.7	81.7	81.7	81.1	81.5	81.7	81.0
4	60.0	60.0	59.2	58.7	60.0	60.2	60.6	61.9
5	57.8	57.7	59.1	58.6	57.7	57.5	59.3	
6	60.1	57.4	55.4	55.7	55.4	54.8	56.2	56.4
7	64.3	63.6	64.6	65.2	64.3	65.3	63.5	64.7
8	71.0	69.0	71.1	71.0	72.5	74.0	75.5	74.0
9	65.3	65.2	65.4	63.7	64.3	65.1	65.4	65.1
10	87.2	90.2	89.0	89.6	89.1	88.3	89.2	89.0
11	88.4	87.5	86.7	85.7	87.8	87.0	88.8	91.2
12	66.2	66.0	65.7	66.3	67.0	67.0	67.1	66.0
13	72.5	70.9	70.8	70.1	70.5	70.7	72.6	72.2
14	63.4	61.7	61.6	61.2	61.5	62.0	62.5	64.1
15	85.1	82.4	79.9	80.2	80.4	81.0	82.2	82.5
16	80.6	79.0	80.3	80.3	79.3	80.6	80.7	80.8
17	70.8	68.7	70.3	70.6	71.2	70.5	71.1	71.5

Table vii. Fasting blood glucose levels of 35 patients

Fybogel	Wk 0	Wk 4	Wk 8	Wk 16	Wk 24	Wk 32
No. 1	207	173	202	141	135	130
2	169	153	250	202	157	186
3	279	281	224	294	265	288
4	169	155	205	216	151	.
5	173	182	187	173	180	184
6	151	133	196	200	247	220
7	220	196	177	159	164	173
8	171	182	231	159	155	189
9	216	245	231	249	216	220
10	213	151	222	180	250	299
11	288	249	253	101	115	198
12	191	101	182	198	92	.
13	259	238	241	214	214	260
14	227	250	220	243	238	245
15	211	135	195	162	175	195
16	195	140	148	139	83	169
17	220	169	202	191	168	422
18	300	283	321	283	252	310
Placebo						
No. 1	319	346	360	252	314	285
2	160	288	247	214	238	250
3	195	140	160	141	187	148
4	157	135	141	191	184	272
5	220	169	177	182	202	.
6	184	79	106	171	169	265
7	227	141	180	166	135	126
8	94	101	88	160	115	123
9	173	153	182	222	150	205
10	200	333	290	249	204	216
11	211	117	144	193	133	216
12	171	182	189	225	240	251
13	279	281	288	346	305	292
14	207	173	130	200	160	90
15	256	207	187	213	252	283
16	146	160	177	155	169	159
17	245	205	13	128	180	168

Table viii. HbA1c levels of patients

Fybogel	Wk 0	Wk 8	Wk 16	Wk 24	Wk 32
No. 1	13.2	10.5	8.2	6.5	7.0
2	10.3	10.5	9.4	8.8	8.7
3	11.6	12.0	11.9	10.8	13.0
4	7.6	8.6	8.6	7.4	.
5	9.3	8.4	7.8	8.2	8.6
6	10.7	10.3	9.0	9.0	9.8
7	9.3	8.8	7.8	7.5	8.0
8	12.0	11.0	9.5	9.7	10.7
9	9.9	10.8	11.6	11.5	11.3
10	10.5	9.7	11.3	9.4	11.4
11	14.6	13.3	10.9	8.8	10.1
12	9.0	7.9	8.6	7.8	.
13	10.6	10.8	11.0	10.4	11.3
14	10.3	10.0	10.8	9.1	10.8
15	9.4	10.2	9.5	9.0	10.2
16	9.1	9.0	8.0	8.0	8.8
17	10.2	8.9	9.0	8.6	12.2
18	10.1	10.9	12.6	11.8	12.8
Placebo					
No. 1	12.6	12.5	12.1	11.6	11.6
2	9.2	11.5	10.2	10.8	12.9
3	9.1	7.8	8.1	8.5	9.0
4	8.7	7.5	11.4	10.0	9.5
5	10.2	10.5	9.5	8.9	.
6	10.5	7.5	7.9	9.2	9.6
7	13.6	11.2	8.6	7.7	9.0
8	9.2	9.2	13.2	10.0	9.8
9	11.4	9.6	11.5	9.6	10.2
10	10.1	11.9	11.3	11.1	10.9
11	8.9	8.6	8.8	8.3	9.3
12	12.0	11.0	10.1	11.1	10.8
13	11.6	13.0	12.4	12.1	12.8
14	13.2	7.0	7.7	7.7	8.7
15	10.5	8.0	8.3	9.9	9.4
16	9.1	8.5	10.0	8.9	9.4
17	8.6	9.9	8.2	8.9	10.2

Table ix. Fasting triglycerides levels of patients

Fybogel	Wk 0	Wk 4	Wk 8	Wk 16	Wk 24	Wk 32
No. 1	107	165	210	228	209	228
2	157	199	227	189	186	152
3	131	119	146	152	135	199
4	149	102	127	119	120	.
5	342	389	391	360	373	429
6	199	126	251	142	119	296
7	171	137	205	168	140	193
8	90	82	83	127	96	121
9	167	181	192	135	88	158
10	326	410	289	511	587	436
11	134	104	119	60	81	117
12	101	85	107	99	88	.
13	104	236	139	122	112	148
14	134	116	127	173	158	142
15	242	239	210	173	188	342
16	194	135	153	165	178	155
17	180	223	170	161	122	222
18	334	127	152	215	142	218
Placebo						
No. 1	122	174	110	84	115	108
2	258	380	458	387	443	615
3	194	135	164	188	187	153
4	171	213	200	295	201	290
5	180	223	296	159	170	.
6	94	83	108	96	95	99
7	551	512	478	478	387	550
8	164	242	161	745	709	766
9	174	202	202	160	173	227
10	334	127	241	141	204	152
11	137	119	81	80	91	148
12	90	82	121	104	90	88
13	131	119	199	183	196	183
14	107	165	216	333	256	312
15	277	156	123	173	150	206
16	144	104	154	141	147	152
17	288	280	186	135	255	232

Table x. Fasting total cholesterol levels of patients

Fybogel	Wk 0	Wk 4	Wk 8	Wk 16	Wk 24	Wk 32
No. 1	251	278	340	332	290	332
2	297	282	239	278	259	205
3	228	212	228	239	212	263
4	293	336	313	263	286	
5	228	170	216	189	216	224
6	324	239	170	290	317	344
7	297	205	216	212	232	216
8	243	251	220	239	247	278
9	208	224	212	193	212	228
10	185	147	220	228	259	228
11	216	243	293	181	309	305
12	236	178	220	193	193	
13	243	159	255	212	224	243
14	259	263	274	239	239	205
15	228	197	224	189	239	212
16	290	259	286	236	247	239
17	282	255	278	228	228	286
18	270	278	243	263	224	248
Placebo						
No. 1	201	208	201	193	185	193
2	336	351	344	382	336	378
3	290	259	247	220	216	286
4	224	220	270	270	224	282
5	282	255	278	282	278	
6	274	205	216	220	251	286
7	367	305	313	255	220	255
8	239	220	185	317	297	274
9	274	263	301	282	266	297
10	270	278	259	282	243	243
11	282	239	255	301	297	347
12	243	251	278	243	263	263
13	228	212	263	232	224	251
14	251	278	332	344	320	293
15	286	247	266	313	290	283
16	270	270	278	263	278	280
17	216	208	232	232	259	236

Table xi. Vitamin A,E,C levels of patients

Fybogel	Vitamin A, serum (µg/dl)			Vitamin E, serum (mg/dl)			Vitamin C, serum (mg/dl)		
	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	54.71	50.08	50.06	1.06	1.17	1.04	0.79	0.92	1.18
2	83.40	104.16	82.56	1.07	1.59	1.18	0.79	1.05	0.80
3	83.36	46.12	54.31	1.08	1.49	1.45	0.67	0.56	0.24
4	68.07	60.25	69.55	1.14	1.26	1.26	0.93	0.97	1.35
5	120.11	106.08	126.24	1.78	1.70	1.85	1.41	1.52	1.64
6	55.49	62.46	54.00	1.08	1.15	0.85	1.11	1.09	1.04
7	52.90	29.66	45.13	1.11	0.75	1.67	1.19	0.76	0.83
8	91.21	87.02	51.90	1.25	2.19	0.91	0.80	1.98	1.41
9	77.11	66.61	94.21	1.26	0.95	2.76	0.89	0.99	1.17
10	86.01	81.99	53.16	1.43	0.95	1.36	1.01	0.64	0.86
11	62.04	45.90	48.28	1.11	1.11	1.78	1.28	0.92	0.92
12	50.26	47.51	52.46	1.05	0.81	0.94	0.54	0.36	0.84
13	41.14	41.32	32.23	0.82	1.41	1.04	0.71	1.00	1.39
14	72.60	64.34	54.88	1.34	1.61	1.79	0.67	0.98	0.53
15	63.24	49.20	67.10	1.12	1.25	1.71	1.37	0.77	1.29
16	73.94	65.42	55.05	1.46	1.60	1.57	0.58	0.76	1.41
17	62.08	62.13	65.68	1.86	1.87	2.00	1.30	1.47	1.10
18	57.02	67.30	61.84	1.91	2.17	2.24	0.71	1.07	0.58
Placebo									
No. 1	67.86	59.10	52.44	1.07	0.80	1.44	1.16	1.19	1.33
2	138.25	149.74	124.88	1.63	1.39	1.54	0.70	1.22	1.15
3	73.94	67.05	65.42	1.46	1.22	1.60	0.58	0.57	0.76
4	62.26	58.78	74.32	0.80	2.22	1.78	0.66	1.20	0.87
5	62.08	80.84	62.13	1.86	2.32	1.87	1.30	0.99	1.15
6	45.34	37.22	47.36	0.88	1.55	1.56	0.39	0.75	0.88
7	126.66	182.70	182.05	2.01	2.83	1.45	0.50	0.33	0.22
8	49.22	54.71	64.75	2.19	2.13	2.25	1.41	1.01	1.70
9	57.02	61.17	67.30	1.91	2.29	2.17	0.71	1.04	1.07
10	43.32	54.26	79.08	0.90	1.10	1.45	0.75	0.83	0.31
11	52.90	45.13	38.83	1.11	1.67	1.72	1.19	0.83	0.62
12	68.07	69.55	65.42	1.14	1.26	1.82	0.93	1.35	1.07
13	83.40	82.56	88.38	1.07	1.18	1.66	0.79	0.80	0.76
14	85.91	79.38	67.32	1.23	0.97	1.29	0.44	0.49	0.26
15	68.78	70.27	55.31	1.36	1.59	1.38	0.42	0.58	0.30
16	66.02	52.43	68.96	0.79	2.20	2.27	0.78	0.61	0.57
17	87.77	89.68	79.65	0.95	1.33	1.25	1.01	0.89	0.96

Table xii. Vitamin B_1 and B_2 levels of Fybogel group

	B_1						B_2					
	ETKA			TPPE			EGRA			AC		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	258.40	260.80	245.23	0.0	0.0	0.0	3367.74	940.8	2269.79	1.07	1.38	1.05
2	207.80	236.70	232.29	0.0	0.0	0.0	2961.29	2095.37	1780.65	1.02	0.9	1.04
3	248.00	236.40	184.98	0.0	6.0	0.0	1357.35	1524.19	1531.91	1.22	1.06	1.2
4	218.50	182.04	101.88	0.0	0.0	0.0	1527.18	1790.91	2035.84	1.48	1.31	1.08
5	260.40	253.10	241.54	0.0	3.3	0.0	3329.97	3741.90	3462.09	0.82	0.97	1.02
6	201.70	229.40	211.54	0.0	0.0	4.5	2583.6	2927.41	3454.09	1.28	0.98	1.19
7	215.50	229.80	260.23	0.0	0.0	0.0	1729.6	1531.91	2297.34	1.09	1.1	1.05
8	226.20	273.50	239.79	0.0	0.0	0.0	1694.1	2082.31	1784.72	1.08	1.01	1.05
9	212.10	164.10	189.08	0.0	5.1	0.0	2158.63	2399.14	1135.48	0.99	1.01	1.3
10	273.90	293.96	211.50	0.0	0.0	0.0	2133.53	2747.13	1722.36	1.06	0.98	1.09
11	198.40	212.10	271.26	0.0	0.0	0.0	2379.23	2971.90	2106.53	1.04	0.93	1.08
12	154.56	186.87	167.50	0.0	0.0	0.0	1882.51	1248.69	1464.70	1.1	1.36	1.05
13	252.40	327.80	267.58	0.0	0.0	0.0	1943.90	2259.80	1960.62	1.13	1.04	1.2
14	183.10	139.29	150.82	0.0	0.0	0.0	1327.19	1858.06	1417.99	1.27	1.06	1.19
15	229.20	151.97	218.44	1.6	0.0	0.0	1907.83	2100.21	1593.40	1.2	0.96	1.15
16	316.10	230.20	240.42	0.0	0.0	0.0	1788.65	1912.71	1287.52	1.09	1.04	1.24
17	119.60	167.57	198.65	0.0	0.0	0.0	1798.13	1344.65	1408.37	1.08	1.11	1.16
18	173.61	150.45	269.95	0.0	0.0	0.0	2547.35	1364.82	1304.82	0.93	1.12	1.22

Table xiii. Vitamin B_1 and B_2 levels of placebo group

	B_1						B_2					
	ETKA			TPPE			EGRA			AC		
Placebo	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	177.7	187.4	132.95	0.0	0.0	9.4	1715.54	2270.39	1947.97	0.98	1.02	1.04
2	239.1	298.1	265.82	0.0	0.9	0.0	1972.94	3200	3086.97	1.01	0.94	0.98
3	316.1	128.45	230.2	0.0	0.0	0.0	1788.65	1590.46	1912.71	1.09	1.08	1.04
4	268.7	241.63	337.16	1.1	0.0	9.9	2347.03	2434.36	1790.32	1.05	1.01	1.04
5	119.6	155.13	167.58	0.0	12.2	0.0	1798.13	1606.04	1344.65	1.08	1.15	1.11
6	167.5	241.9	227.18	0.0	0.0	0.0	2588.7	1666.2	1296.33	1.08	1.2	1.25
7	250	196.44	216.83	0.0	3.9	0.0	2963.29	1680.16	2197.71	1.16	1.1	1.1
8	154.25	238.3	103.35	0.0	0.0	12.1	2273.16	1348.59	1647.41	0.98	1.17	1.25
9	173.61	182.9	150.45	13.3	14.3	0.0	2547.35	2274.19	1364.82	0.93	1.01	1.12
10	261.83	260.23	203.63	0.0	0.0	0.0	2513.85	2297.34	1566.39	1.07	1.05	1.17
11	215.5	260.23	158.07	0.0	0.0	0.0	1729.6	2297.34	1581.33	1.09	1.05	1.23
12	218.5	101.88	110.05	0.0	0.0	0.0	1527.18	2035.84	1598.34	1.48	1.08	1.19
13	207.8	232.29	166.54	0.0	0.0	0.0	2961.29	1780.65	1606.04	1.02	1.04	1.02
14	211.7	123.46	107.89	0.0	0.0	0.0	1523.42	2798.29	742.27	1.33	0.93	1.55
15	246.97	193.54	204.42	0.0	0.0	0.0	592.5	1120.3	1100.17	1.28	1.29	1.29
16	280.2	264.43	289.44	0.0	0.0	0.0	2520.85	1852.85	2148.39	0.97	0.89	1.14
17	277.8	194.2	254.2	0.0	0.0	0.0	2008	2249.24	2154.5	0.97	1.01	1.06

Table xiv. Vitamin B_{12} and folate levels of patients

	B_{12}, serum (ng/ml)			Folate, serum (ng/ml)			Folate, red cell (ng/ml cells)		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	348	798	424	11.64	6.48	20.40	267	201	160
2	235	474	338	10.20	9.12	5.04	382	121	210
3	351	360	884	15.60	10.80	17.40	356	109	98
4	265	244	252	6.24	5.40	8.64	126	152	105
5	253	296	299	6.84	3.60	8.40	376	167	256
6	324	381	825	13.92	8.16	7.92	286	187	185
7	309	258	263	15.60	17.28	18.96	160	762	192
8	128	119	768	16.08	15.36	22.56	156	107	317
9	206	169	313	16.44	11.64	15.12	107	178	219
10	521	707	525	6.48	17.76	16.56	98	299	277
11	402	415	439	18.96	6.00	19.80	167	163	309
12	378	337	940	7.32	9.60	18.72	140	167	271
13	142	410	740	15.48	20.40	13.20	158	114	226
14	148	173	467	11.52	12.72	12.48	307	522	215
15	392	760	655	11.04	14.16	11.28	134	412	292
Placebo									
No. 1	854	553	480	20.20	18.20	23.30	166	104	109
2	1056	1895	1831	8.16	10.20	10.08	246	393	341
3	392	823	760	11.04	4.08	14.16	134	210	412
4	522	744	874	4.50	11.80	8.88	192	280	244
5	359	1182	763	4.44	5.16	22.32	185	210	279
6	731	466	471	7.32	7.44	9.48	227	221	228
7	638	364	368	16.32	12.48	16.56	155	238	229
8	551	260	644	16.44	17.52	24.60	208	262	174
9	422	440	596	7.32	7.20	4.56	178	182	190
10	309	263	777	15.60	18.96	6.60	160	192	248
11	265	244	723	6.24	8.64	9.48	126	105	256
12	235	338	566	10.20	5.04	7.92	382	210	258
13	580	682	551	9.48	5.52	5.54	267	192	164
14	470	561	555	5.98	6.72	5.16	124	127	238
15	740	756	897	4.20	9.84	6.44	251	220	199

Table xv. Iron and calcium levels of patients

	Iron, serum (µg/dl)			TIBC, serum (µg/dl)			Calcium, serum (mmol/l)			Ionized calcium, serum		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	50	78	70	250	267	290	2.23	2.17	2.29	1.25	1.21	1.33
2	75	118	92	275	212	260	2.17	2.10	2.27	1.22	1.19	1.22
3	63	88	95	250	250	250	2.23	2.36	2.34	1.20	1.33	1.24
4	88	113	117	275	225	275	2.22	2.01	2.20	1.19	1.17	1.19
5	94	88	92	282	275	264	2.17	2.32	2.26	1.20	1.27	1.24
6	113	100	82	325	300	336	2.20	2.34	2.27	1.22	1.26	1.24
7	106	87	73	306	325	230	2.33	2.43	2.42	1.24	1.35	1.13
8	118	113	175	306	238	240	2.12	1.98	2.16	1.12	1.11	1.17
9	82	75	146	259	225	269	2.15	2.35	2.32	1.22	1.33	1.24
10	100	87	100	275	375	290	2.09	2.20	2.45	1.21	1.23	1.21
11	71	87	78	257	275	268	2.31	1.98	2.25	1.22	1.19	1.19
12	64	92	94	251	274	266	2.34	2.38	2.24	1.31	1.23	1.24
13	71	92	94	329	278	315	2.16	2.43	2.19	1.26	1.25	1.21
14	67	66	98	267	259	287	2.01	2.00	2.14	1.22	1.15	1.20
15	150	113	129	300	325	271	2.08	2.28	2.19	1.11	1.25	1.22
16	75	100	107	300	294	294	2.15	2.24	2.31	1.23	1.19	1.20
17	87	107	90	250	259	332	2.13	2.17	2.24	1.20	1.13	1.24
18	59	79	59	235	280	252	2.18	2.28	2.22	1.19	1.22	1.26
Placebo												
No. 1	89	100	80	289	250	293	2.30	2.24	2.24	1.23	1.20	1.24
2	100	100	62	275	350	241	2.36	2.48	2.42	1.27	1.26	1.23
3	75	67	100	300	240	294	2.15	2.24	2.43	1.23	1.19	1.18
4	58	38	78	279	282	280	2.21	2.22	2.31	1.15	1.24	1.18
5	87	107	90	250	259	332	2.13	2.17	2.31	1.20	1.13	1.24
6	100	55	74	200	240	220	2.10	2.19	2.21	1.25	1.32	1.28
7	78	76	99	289	272	338	2.46	2.80	2.82	1.43	1.55	1.54
8	50	43	56	225	219	216	2.19	2.10	2.12	1.25	1.12	1.16
9	70	100	112	220	289	271	1.96	2.25	2.12	1.33	1.25	1.24
10	59	68	79	235	249	280	2.18	2.28	2.34	1.19	1.22	1.24
11	75	68	32	250	248	241	2.22	2.39	2.33	1.25	1.22	1.19
12	118	113	74	306	238	144	2.12	1.98	2.13	1.12	1.11	1.12
13	63	88	94	250	250	277	2.23	2.36	2.28	1.20	1.33	1.24
14	50	78	98	250	267	278	2.23	2.17	2.18	1.25	1.21	1.24
15	200	192	185	325	333	272	2.37	2.31	2.25	1.25	1.24	1.22
16	58	56	68	238	251	267	2.40	2.48	2.19	1.29	1.28	1.22
17	150	72	98	375	227	324	2.22	2.28	2.24	1.20	1.22	1.24

Table xvi. Mineral levels of patients

	Phosphorus, serum (mmol/l)			Sodium, serum (mmol/l)			Potassium, serum (mmol/l)			Chlorides, serum (mmol/l)		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	1.12	1.20	1.24	135	139	137	4.91	4.84	4.54	103	103	110
2	1.10	1.14	1.20	138	139	138	3.92	4.77	3.88	105	105	108
3	1.12	1.14	1.20	141	137	139	5.20	4.90	4.20	103	99	109
4	1.26	1.23	1.50	142	140	143	3.85	4.61	4.02	108	102	111
5	1.18	1.24	1.27	137	131	131	5.27	5.05	4.79	98	94	97
6	1.07	1.38	1.28	141	146	142	4.86	3.22	4.89	104	107	108
7	1.38	1.26	1.30	140	142	141	5.02	4.44	4.51	101	105	108
8	0.98	1.02	1.12	140	137	139	4.75	4.19	3.91	105	107	103
9	1.20	1.23	1.27	138	140	138	4.24	4.53	4.76	105	105	108
10	0.99	1.01	1.25	132	133	138	4.37	3.92	5.33	95	102	105
11	0.81	0.92	1.01	138	142	144	5.03	4.71	4.26	101	107	110
12	1.07	1.30	1.28	142	139	140	5.43	5.17	5.20	107	107	107
13	1.42	1.63	1.05	142	142	142	4.28	4.25	4.82	108	108	110
14	1.02	0.83	1.11	142	139	139	4.46	3.93	4.44	109	106	104
15	1.08	1.10	1.11	137	135	140	4.22	4.15	4.29	103	106	102
16	1.36	1.38	1.48	138	142	141	5.18	4.97	4.89	102	105	109
17	1.12	1.08	1.07	138	139	137	4.01	4.65	4.31	106	109	105
18	1.00	0.97	1.10	143	136	135	4.12	4.70	4.59	104	106	99
Placebo												
No. 1	0.98	1.01	1.06	136	136	136	5.07	4.43	4.38	97	96	103
2	1.06	1.20	1.12	144	140	141	5.91	4.46	3.99	105	107	106
3	1.53	1.48	1.47	138	146	142	5.18	4.41	4.97	102	106	105
4	1.12	1.10	1.10	138	142	141	3.98	3.21	4.10	100	99	109
5	1.06	0.98	1.01	138	139	138	1.04	4.65	4.32	106	109	107
6	1.34	1.26	1.27	138	140	139	4.06	4.33	4.48	106	110	104
7	1.24	1.30	0.70	134	140	138	4.96	5.36	5.61	100	111	107
8	1.26	1.31	0.93	141	142	141	3.99	4.27	3.61	105	111	111
9	1.34	1.20	1.22	141	143	144	4.91	4.54	4.38	114	112	115
10	1.19	0.97	1.10	143	137	136	4.12	4.61	4.70	104	107	106
11	0.75	1.33	1.09	141	142	144	4.35	4.65	4.25	106	104	108
12	0.98	1.02	1.07	140	137	141	4.75	4.19	4.41	105	107	105
13	1.12	1.14	1.35	141	137	135	5.20	4.94	5.35	103	99	98
14	1.20	1.28	1.30	135	139	140	4.91	4.84	4.67	103	103	106
15	1.12	1.16	1.09	137	138	137	4.73	4.60	4.11	99	104	104
16	1.10	1.14	1.09	141	139	145	4.44	4.63	4.16	107	107	109
17	0.95	1.05	0.83	139	137	142	4.57	3.97	4.37	106	108	113

Table xvi. (continue) Mineral levels of patients

	Magnesium, serum (mmol/l)			Zinc, serum (g/dl)			Copper, serum (g/dl)		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	0.787	0.817	0.775	1.080	1.000	1.100	1.339	1.242	1.322
2	0.647	0.858	0.843	1.273	1.140	0.825	1.428	1.212	1.926
3	0.772	0.829	0.804	0.970	1.190	1.055	1.066	1.158	1.086
4	0.587	0.732	0.775	1.065	0.855	1.065	1.361	1.296	0.670
5	0.607	0.788	0.798	1.523	1.315	1.215	1.020	1.340	1.270
6	0.645	0.736	0.761	1.180	1.655	0.895	1.396	1.540	1.390
7	0.607	0.753	0.728	0.865	0.975	1.035	1.041	1.274	1.244
8	0.960	0.870	1.002	0.845	0.905	1.075	1.166	1.172	1.164
9	0.716	0.603	0.796	1.110	0.980	1.170	0.995	0.908	0.966
10	0.734	0.574	0.831	1.025	0.845	0.895	0.998	1.396	1.568
11	0.703	0.738	0.798	0.825	1.125	0.925	1.178	1.278	1.154
12	0.792	0.802	0.814	1.110	0.945	0.925	1.240	1.374	1.350
13	0.697	0.841	0.880	0.890	1.150	1.155	0.940	1.266	1.222
14	0.595	0.891	0.815	0.895	1.075	0.820	0.936	1.256	1.066
15	0.833	0.858	0.981	0.875	1.120	0.875	0.816	0.894	1.004
16	0.726	0.718	0.560	0.810	0.975	0.960	1.114	1.316	1.382
17	0.656	0.804	0.794	0.860	0.755	0.960	0.874	0.988	0.978
18	0.720	0.525	0.703	1.050	0.680	0.765	1.374	1.670	1.390
Placebo									
No. 1	0.676	0.710	0.784	0.965	1.180	1.015	0.920	1.030	1.140
2	0.639	0.749	0.770	1.245	0.945	1.005	1.252	1.456	1.566
3	0.726	0.660	0.718	0.810	0.960	0.975	1.114	1.178	1.316
4	0.547	0.712	0.817	0.835	0.435	0.760	0.960	0.520	0.990
5	0.656	1.043	0.804	0.860	1.115	0.755	0.874	1.246	0.988
6	0.794	0.675	0.730	1.115	1.000	0.985	1.530	1.020	0.472
7	0.794	0.887	0.837	0.825	1.005	0.920	1.514	1.504	1.300
8	0.841	0.965	0.669	0.965	0.890	0.780	0.790	1.286	1.162
9	0.720	0.599	0.525	1.050	0.615	0.680	1.374	1.150	1.670
10	0.656	0.645	0.660	0.865	0.930	0.765	0.886	0.960	1.460
11	0.607	0.728	0.724	0.865	1.035	1.165	1.041	1.244	1.256
12	0.587	0.775	0.831	1.065	1.065	0.890	1.361	0.670	1.460
13	0.674	0.843	0.821	1.273	0.825	1.125	1.428	1.926	1.472
14	0.687	0.759	0.689	0.820	0.865	0.750	1.292	1.118	1.116
15	0.800	0.761	0.582	0.705	0.955	0.910	1.158	1.324	1.136
16	0.753	0.751	0.954	0.935	0.840	0.960	1.340	1.164	1.246
17	0.616	0.909	0.867	1.095	0.925	1.020	0.779	0.988	0.860

Table xvii. Liver function tests of patients

	SGOT (U/L)			SGPT (U/L)			GGT (U/L)			AP (U/L)		
Fybogel	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	21	19	32	20	28	28	67	68	79	91	88	93
2	35	40	31	34	34	29	38	35	33	50	50	55
3	22	21	18	19	23	17	28	41	25	137	157	130
4	33	28	14	52	22	15	21	14	10	118	137	103
5	40	39	45	58	45	68	56	69	52	74	72	77
6	20	43	22	10	63	33	26	72	37	96	110	70
7	12	12	15	16	17	17	23	25	28	48	55	65
8	28	23	25	31	28	34	24	17	21	73	89	70
9	15	13	18	17	16	15	17	21	26	52	49	47
10	20	16	21	18	22	16	42	35	37	74	57	59
11	15	23	16	11	23	19	45	55	40	111	123	79
12	29	30	28	21	21	21	14	20	16	101	102	101
13	18	20	19	22	21	27	38	41	33	64	54	76
14	27	27	26	26	24	23	38	32	25	55	75	72
15	34	27	18	36	29	26	67	45	44	124	103	107
16	33	34	17	54	58	22	63	90	45	100	107	78
17	19	23	15	21	32	20	27	43	19	74	74	59
18	19	22	25	14	15	30	58	67	70	40	43	62
Placebo												
No. 1	14	20	16	21	23	15	20	19	17	38	43	49
2	31	22	20	21	19	11	47	49	47	57	69	59
3	33	26	34	54	40	58	63	71	90	100	97	107
4	18	17	17	18	17	17	12	13	15	51	57	45
5	19	23	19	21	32	19	27	43	21	74	74	70
6	25	16	26	19	15	20	20	15	19	58	66	78
7	17	25	20	20	15	9	90	30	19	96	34	32
8	21	30	23	16	30	25	20	56	30	55	56	66
9	28	18	26	20	19	19	24	25	27	113	110	109
10	19	22	22	14	22	15	58	53	67	40	46	43
11	17	23	15	13	20	14	16	19	25	78	64	73
12	28	23	22	31	22	27	24	17	18	73	89	79
13	22	21	20	19	23	23	28	41	55	137	157	147
14	21	19	21	20	28	27	67	68	55	91	88	80
15	96	93	86	84	79	84	81	63	74	95	88	73
16	24	14	21	15	12	19	39	52	42	93	92	71
17	44	41	59	40	37	54	62	68	62	54	90	96

Table xviii. Renal function tests and protein levels of patients

Fybogel	BUN (mg/dL)			Creatinine (mg/dL)			Total protein (g/L)			Albumin (g/L)		
	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	25	18	25	1.3	1.2	1.0	72.7	69.3	80.1	41.6	43.3	49.4
2	13	15	16	0.3	0.7	0.9	68.5	76.0	71.3	40.6	41.8	45.3
3	16	18	15	1.1	1.1	1.1	73.4	76.9	68.1	40.9	42.8	39.7
4	11	14	12	0.9	0.7	0.8	72.0	67.3	72.5	39.6	37.6	40.9
5	18	20	15	1.0	1.0	0.7	69.3	67.1	68.6	46.7	44.8	48.2
6	16	15	16	0.9	0.8	1.0	67.5	89.6	67.7	38.7	52.8	37.7
7	15	13	17	0.9	0.7	0.7	72.4	73.5	74.9	43.8	47.5	46.2
8	13	10	14	0.8	0.8	0.5	68.2	64.7	77.4	39.3	36.8	43.6
9	12	11	17	0.6	0.7	1.1	82.7	78.8	76.9	40.7	43.4	33.7
10	11	10	10	0.9	0.6	0.7	73.7	76.7	86.8	41.5	43.2	55.2
11	8	11	11	0.7	0.9	1.0	72.8	79.4	71.0	44.4	50.3	40.1
12	14	24	18	1.2	1.5	1.1	78.4	76.1	77.2	43.8	42.4	42.2
13	18	19	14	0.4	0.4	0.5	80.5	81.4	78.8	42.6	42.0	43.2
14	15	17	15	1.1	1.3	0.8	73.9	80.0	76.9	42.2	50.1	46.3
15	13	11	13	1.0	0.9	1.3	66.3	63.5	69.9	44.4	42.6	46
16	13	18	17	0.9	0.8	0.7	68.3	79.9	75.6	42.1	48.3	45.1
17	13	22	13	0.7	0.8	0.6	68.3	58.8	69.0	44.0	40.1	48.1
18	11	9	8	1.0	0.7	0.8	73.2	76.7	84.2	41.7	43.3	48
Placebo												
No. 1	10	11	11	0.8	0.7	0.9	71.6	66.3	72.7	47.1	43.2	47.7
2	21	28	24	1.0	1.1	1.2	76.2	76.6	73.2	44.1	44.7	43.1
3	13	18	18	0.9	1.1	0.8	68.3	69.1	79.9	42.1	40.9	48.3
4	17	18	24	1.1	0.8	0.7	62.7	68.1	67.2	42.1	44.1	43.3
5	13	22	13	0.7	0.8	0.8	68.3	58.8	63.2	44.0	40.1	42.3
6	18	14	17	1.1	1.0	0.9	75.0	69.8	74.9	41.5	38.6	40.1
7	21	25	26	1.4	1.8	1.3	70.9	70.2	73.8	37.8	39.6	43.9
8	24	29	22	0.9	1.1	1.0	63.0	55.6	54.5	41.4	34.0	30.1
9	16	13	16	1.1	0.8	0.7	62.3	72.2	68.9	39.5	44.3	44.8
10	11	12	9	1.0	0.7	0.7	73.2	78.0	76.7	41.7	44.9	43.3
11	10	15	17	0.7	1.1	0.6	48.7	68.8	72.6	26.4	39.7	45
12	13	10	12	0.8	0.8	0.6	68.2	64.7	77.2	39.3	36.8	44.6
13	16	18	10	1.1	1.1	0.8	73.4	76.9	70.6	40.9	42.8	37.7
14	25	18	18	1.3	1.2	1.1	72.7	69.3	72.2	41.6	43.3	42.6
15	11	8	6	0.9	0.7	0.6	79.2	81.1	77.6	40.3	44.3	42.3
16	17	16	18	1.0	0.9	1.0	73.6	80.4	73.6	41.4	47.8	40
17	19	14	17	1.3	1.4	1.4	70.4	72.4	76.9	39.4	39.8	39.8

Table xix. Hematological levels of patients

Fybogel	Hematocrit (%)			WBC ($x10^3/mm^3$)			RBC ($x10^6/mm^3$)			Platelet count ($x10^3/mm^3$)		
	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24	Wk 0	Wk 8	Wk 24
No. 1	41.5	42.6	41.6	7.00	9.83	10.1	4.82	4.99	4.94	370	386	358
2	39.3	45.1	41.0	7.70	7.58	6.62	4.47	4.78	4.79	290	260	406
3	44.7	43.2	42.0	10.65	9.94	8.64	5.22	5.72	5.85	293	293	316
4	40.0	40.0	40.3	8.01	6.51	6.43	4.27	4.52	4.36	279	254	256
5	41.0	40.0	42.0	9.95	8.71	8.40	4.42	4.76	4.84	238	292	290
6	45.0	51.0	44.0	11.40	12.86	8.83	4.59	5.36	4.68	338	308	291
7	40.1	41.1	41.8	8.84	8.52	8.43	4.61	4.89	4.91	313	322	277
8	43.5	46.1	44.0	9.09	7.22	8.24	4.58	4.92	4.87	183	168	182
9	42.5	43.0	43.0	7.31	7.21	7.23	5.17	5.31	5.4	301	289	292
10	42.9	45.0	42.2	5.54	5.66	5.94	5.06	5.66	6.32	293	227	352
11	42.7	42.4	40.0	6.15	6.09	6.40	4.98	5.03	6.4	223	233	225
12	42.9	44.0	45.0	7.33	7.85	7.64	4.82	4.94	4.97	350	328	330
13	40.9	39.0	40.0	6.82	10.4	7.20	4.42	4.97	4.78	224	261	240
14	44.0	42.0	45.6	6.05	5.25	5.25	5.32	5.38	5.34	267	225	215
15	51.0	45.6	48.0	6.04	7.10	8.10	6.36	5.69	5.59	289	277	249
16	48.6	41.1	40.0	11.99	11.56	9.69	4.96	4.77	4.46	380	432	410
17	42.2	42.0	40.1	7.45	6.95	6.35	4.24	4.11	4.21	283	261	333
18	45.0	39.8	40.8	9.46	8.76	10.9	4.86	4.54	4.8	282	209	304
Placebo												
No. 1	42.3	43.7	44.4	9.65	8.97	8.59	5.02	5.59	5.64	417	336	379
2	43.0	43.0	46.0	10.10	12.92	7.89	4.38	4.94	5.09	272	298	231
3	48.6	41.1	42.0	11.99	11.56	10.9	4.96	4.77	4.64	380	432	396
4	39.7	39.0	40.6	9.18	6.54	8.33	4.11	4.41	4.43	379	341	300
5	42.2	38.0	42.0	7.45	6.95	8.20	4.24	4.11	4.00	283	261	293
6	42.7	41.0	0.0	6.81	5.69	6.70	4.84	4.63	4.62	311	244	289
7	42.0	37.6	36.8	9.04	7.53	6.58	4.8	4.67	4.26	272	346	368
8	47.8	51.8	0.0	13.40	11.69	10.12	5.02	5.27	5.3	226	196	214
9	43.0	43.0	43.4	9.56	8.63	8.62	5.21	4.87	5.23	299	356	328
10	45.0	43.0	39.8	9.46	7.91	8.76	4.86	5.04	4.54	282	285	209
11	39.8	40.2	41.0	7.21	7.20	6.70	4.72	4.78	4.63	188	212	234
12	43.5	46.1	45.0	9.09	7.22	5.63	4.58	4.92	4.97	183	168	155
13	44.7	43.2	42.0	10.65	9.94	7.90	5.22	5.72	5.35	293	293	314
14	41.5	42.6	45.0	7.00	9.83	9.02	4.82	4.99	5.03	370	386	354
15	42.0	44.1	38.0	11.38	9.77	8.28	4.45	4.56	4.28	159	185	179
16	48.6	44.0	44.8	6.72	8.11	7.13	5.09	5.01	4.98	260	278	273
17	47.0	44.1	43.0	10.67	7.93	7.84	5.35	4.92	5.14	195	187	192

Table xx. Thyroid function tests of patients

Fybogel	Thyroid function test			
	T_3(ng/dL)	Total T_4 (µg/dL)	Free T_4 (ng/dL)	TSH (mU/L)
No. 1	111	8	2	1.3
2	153	12	3	1.4
3	81	7	3	1.3
4	113	7	1	1.1
5	143	11	4	1.5
6	81	5	1	0.8
7	142	13	1	1.8
8	98	9	2	1.1
9	107	9	1	1.8
10	74	6	2	1.6
11	68	5	2	0.8
12	101	8	1	1.2
13	163	8	1	1.4
14	160	10	1	1.6
15	97	6	2	1.7
16	114	9	4	1.6
17	95	6	3	1.4
18	128	8	2	1.9
Placebo				
No. 1	136	9	3	1.6
2	114	9	4	1.6
3	64	5	1	0.9
4	95	6	3	1.4
5	115	8	1	1.2
6	86	7	2	1.2
7	145	6	6	1.2
8	106	7	2	1.2
10	109	8	2	1.2
11	98	9	2	1.1
12	81	7	3	1.3
13	111	8	2	1.3
14	141	9	2	1.5
15	196	11	2	1.7
16	152	11	1	2.0

BIOGRAPHY

NAME Miss Orapin Choothawornchaikul

DATE OF BIRTH 17 November 1969

PLACE OF BIRTH Bangkok, Thailand

INSTITUTIONS ATTENDED

Thai Red Cross College of Nursing, 1987-1991

Bachelor of Nursing

Mahidol University, 1994-2000.

Master of Science (Nutrition)