A Review :
Dietary Fiber Biochemical Inductions and Its Hypocholesterolemic Effects

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ABSTRACT

Most people already know that dietary fiber can have detrimental or beneficial effects on health, primarily with regard to nutritional status. In this writing one of the beneficial effects of the consumption of dietary fiber especially its hypocholesterolemic effect will be discussed. Many research papers have already showed regarding the connection between the biochemical induction of soluble fiber and the hypocholesterolemic effect of soluble fiber. In these investigations treatments were given to various kinds of experimental animals and to humans as experimental subjects. Kinds of foods were used as sources of fiber. The researchers were able to discover a variety of biochemical inductions that led to a hypocholesterolomic effect and were able to lower the cholesterol concentration in various kinds of lipoprotein fractions. Biochemical inductions discovered were, among others: fiber making food difficult to be digested, thereby inhibiting lipid absorption, decreasing cholesterol synthesis, increase of cholesterol excretion through the bile, decreasing of Apo B synthesis in the liver, decrease of the mRNA Apo B concentration of the liver, decrease in mRNA Apo A-I and mRNA Apo A-IV concentration in intestinal cells, decrease in HMG-CoA reductase activity and decrease in insulin secretion. Every soluble fiber from specific sources of dietary fiber produced a certain biochemical induction and also hypocholesterolemic effect to a certain lipoprotein fraction. The concentration of total cholesterol and cholesterol in lipoproteins containing Apo B, and the LDL-C: HDL-C ratio are all lowered. Thus the patient is able to choose as a source of fiber, the food of his or her preference appropriate to his or her kind of hypercholesterolemic disorder, with the goal of reduction of cholesterol concentration.

Key Words: Bile, HMG-CoA Reductase, Apo A I-mRNA, Apo A II-mRNA, LDL receptor mRNA

INTRODUCTION

Dietary fiber is a polysaccharide that comes from plants or which can be found in phytogenic foodstuffs and is indigestible. Fiber is found in fruits, vegetables, and seeds. Fiber is used in the food industry and likewise is used as a laxative. In the 1970's much research was done on fiber. This research concerned the chemical and physical characteristics of fiber, total fiber content of various kinds of diets, physiological effects and the relationship of quantity and quality among various types of fiber with various types of diseases (Passmore & Eastwood, 1986). Consumption of fiber has decreased since the 19th Century, while people complain that the incidence of diseases such as diverculitis, cardiovascular diseases and diabetes have an inverse relationship with dietary fiber consumption. Dietary fiber plays a preventive role for diseases like diverculitis, gallstones, carcinoma and also lowers plasma cholesterol concentrations (Poleman & Capra, 1984). Furthermore, research in causes and effects of hypocholesterolemia of dietary fiber continues to appear. Remembering that hypercholesterolemic status is a risk factor for atherosclerosis, and that atherosclerosis normally is encountered in elderly, this constitutes a development that will require several years' time (Mannen *et al.*, 1997), whose prevention needs to be done at a young age. It is already known that soluble dietary fiber has a hypocholesterolemic effect (Olson *et al.*, 1997). Some researchers have already conducted their

respective research using fiber from various sources and various methods. They explain some of the mechanisms that cause the hypocholesterolemic effect appropriate to their respective expertise and discipline. The fruits of these researchers' investigations are formed by a variety of biochemical inductions, which creates a mediating hypocholesterolemic effect from soluble fiber. Thus the results of the studies were lowered cholesterol concentration in different lipoprotein fractions. It is already known that the soluble fibers from various types of sources differ in their structure and chemical composition resulting in differences effect of biochemical processes. Thus it is hoped that new suggestions will be made regarding the consumption of soluble fiber from specific sources appropriate to the biochemical process that cause hypercholesterolemia and also acceptable to consumers as a food or mixture for food. Advice for dietary fiber consumption is expanding. That is why it is necessary to study the influence or biochemical induction that makes it possible for fiber to lower cholesterol in individual suffer from hypercholesterolemia which the cause is already known. And it can also provide the patient with a choice for a source of fiber to be consumed according to the type of hypercholesterolemia.

DISCUSSION

The hypocholesterolemic effect of dietary fiber constitutes an effect of various biochemical responses to fiber induction. These changes comprise, among others, decrease in metabolizable energy content, food's digestibility (Baer *et al.*, 1997), lipid absorption from the intestines, intestinal or pancreatic hormone secretion, lipoprotein metabolism, bile acid metabolism, fermentation byproducts and influence on hepatic cholesterol synthesis (Kay, 1982 cit Fukushima *et al.*, 2000). At the end of the 20th Century researchers reported the decreased hepatic levels of low density lipoprotein (LDL) receptor mRNA, intestine Apo A-I mRNA, and intestine Apo A-IV mRNA by soluble dietary fiber. The results of this researches showed that fiber creates a hypocholesterolemic effect if soluble fiber is consumed. Humans and various species of experimental animals were used in those researches. The researchers used various kinds of foodstuffs as sources of soluble fiber. These foodstuffs include, among others, oats, barley, guar gum, beans, psyllium (Dwyer, 1995), cantaloupe, grapefruit, orange, papaya, raisins, lima beans, okra, sweet potato, winter squash, zucchini, granola, oat bran, oatmeal (Chandalia *et al.*, 2000), pea fiber, sugar beet fiber (Hamberg *et al.*, 1981), soybean protein component products (Potter *et al.*, 1995), and various types of bisodiomycotina mushrooms (Fukushima *et al.*, 2000). The structure and chemical composition of soluble fiber from various sources can be distinct, with the result that its biochemical induction can be different as well.

CHOLESTEROL METABOLISM

Cholesterol is one of the kinds of lipids that are only produced in the bodies of humans and animals. As a building block for cholesterol biosynthesis is acetyl-coenzyme A (acetyl-CoA). Acetyl-CoA is a product of fat, carbohydrate, as well as protein or ketogenic amino acid metabolism. Cholesterol synthesis is lowered when a high-cholesterol diet is consumed. Cholesterol concentration in the blood is influenced by cholesterol intake from food. Its primary synthesis is in the liver, which is also responsible for its used and excretion. Cholesterol from absorbed food already contained in chylomicron molecules, leaves the intestine, following the flow of lymph toward the heart, henceforth entering into blood circulation. Cholesterol which is the product of synthesis within the liver, secreted as component of very low density lipoprotein (VLDL) molecules into blood circulation.

Cholesterol in blood plasma exists in various kinds of lipoproteins Those lipoproteins are chylomicron, VLDL, intermeiate density lipoprotein (IDL), LDL, and high density lipoprotein (HDL). Lipoproteins are complex compounds formed by various kinds of lipids and proteins (apolipoproteins). Every component in every lipoprotein possesses a certain physiological functions. The characteristics and composition of these lipoproteins can be seen in Table 1 and Table 2.

The combination of lipids with apolipoproteins causes a change in the physical characteristics of the lipids. Lipids that cannot be dissolved in watermedium form a compound that dissolves in plasma, namely a lipoprotein. Besides this, each apolipoprotein has its

Table 1 : **Characteristics and Composition of Lipoproteins (Mayes , 1993 a)**

Lipoprotein Fraction		Characteristic of Lipoproteins				Composition	
Separation by Ultra-centrifuge	Separation by Electro phoresis	Sources	Diameter (nm)	Density	Sf	Protein (%)	Total Lipid (%)
Chylomi-cron	—	Intestine	90-1000	<0,95	>400	1-2	98-99
Very low density lipoproteins (VLDL)	Prebeta	Liver and Intestine	30-90	0.95-1.006	20-400	7-10	90-93
Intermidi-ate-density lipoprotein (IDL)	—	VLDL and chylomi-cron	25-30	1.006-1.019	12-20	11	89
Low-density lipoprote-ins (LDL)	Beta	VLDL	20-25	1.019-1.063	2-12	21	79
High-den-sity lipo-proteins HDL_2	Alfa	Liver and intestine VLDL? Chylomi-crones?	10-20	1.063-1.125		33	67
HDL_3			7.5-10	1.125-1.210		57	43
Albumin-FFA		Adipose tissue		>1.2810		99	1

specific biochemical role, in Table 3 can be seen the biochemical roles of each apolipoprotein.

Total cholesterol is the sum of cholesterol found in all lipoproteins in the blood plasma, that is, chylomicron, VLDL, IDL, LDL, and HDL. Chylomicron is a lipoprotein secreted by the digestive organs. This lipoprotein contains lipids, those lipids are cholesterol, phospkolipids and mayor lipid in chylomicron is triacylglycerol, which comes from absorption in the intestine. The mayor lipid in VLDL is also triacylglycerol in blood plasma chylomicron and VLDL undergoes metabolism. Triacylglycerol in the central part of the chylomicron and VLDL undergoes lipolysis or fat hydrolysis by an enzyme, lipoprotein-lipase becomes the triacylglycerol glycerol and free fatty acids. Once triacylglycerol lipolyzed, the volume of chylomicron and VLDL reduced with the result that their walls become wrinkled, protrusions appeared. Then the protrusions free to form HDL while the VLDL component left behind forms IDL and afterward changes to form LDL. The remainder of the chylomicron that is chylomicron remeand enters the liver cells through a receptor.

LDL undergoes metabolism through LDL receptors that can bind Apo B_{100} and Apo E. LDL receptor is a protein, which is found in the target cell wall. Here target cell means a cell, which needs cholesterol as a substrate for physiological compound biosynthesis. Physiological compounds synthesized from cholesterol are, among others, bile acid and steroid hormones including vitamin D. The shortage or nonexistence of LDL

Table 2 : **Percentages of lipid and apolipprotein contained in lipoproteins (Mayes 1993 a)**

Lipoproteins	Percentages of lipids					Apolipoproteins
	Triacyl-glycerol	Pho Phos-lipid	Choles-terol (ester)	Choles-erol (free)	Free Fatty Acids	
Chylomicrons	88	8	3	1	...	AI, AII, AIV, B48, CI, CII, CIII, E
VLDL (prebeta)	56	20	15	8	1	CI, CII, CIII, B100, E
LDL (Beta)	13	28	48	10	1	B100
HDL (Alfa)	13-16	43-46	29-31	6-10	6	AI, AII, AIV, D, E
Albumin-FFA	0	0	0	0	100	Albumin

receptor results in hypercholesterolemic status. Hypercholesterolemic status can also happen if LDL undergoes a transformation and can no longer bind to its receptor. With this condition cholesterol's characteristics can easily change to become atherogenic (Mayes, 1993b).

HDL contains many phospholipids. These phospholipids react with free cholesterol (unesterified), with the LCAT enzyme whose activator is Apo A-I. In this way HDL takes cholesterol from other lipoproteins and also from endothelial cells of the blood vessels. This cholesterol is carried to the liver or intestines by HDL for, namely a locale degradation for HDL. This is why HDL is known as an antiatherogenic lipoprotein. A high LDL cholesterol to HDL cholesterol ratio also constitutes a risk factor for atherosclerosis (Mayes, 1993a)

Some researches looking into the effect of fiber on cholesterol content has already been implemented. The researchers used different kind of souce and they also looked at cholesterol found in different lipoproteins. Potter *et al.*, (1993), Bakhit *et al.*, (1994) and Potter *et al.*, (1995) used soybean products as a source of fiber. Bakhit *et al.*, (1994) used soy cotyledone fiber. The results of their research showed decrease of LDL, HDL and total cholesterol concentration for subjects with hypercholesterolemic status whose total cholesterol concentration was greater than 5.7 mmol/L. Soy protein is a processed soy product that still contains fiber. Yet soy protein also has a lowering effect on cholesterol through a mechanism other than fiber. This effect of soy protein can obscure the effects of fiber, so that the addition of soy fiber to the subject who is consuming soy proteins may not be observed (Potter *et al.*, 1993). Soy protein influences cholesterol metabolism, while fiber binds or absors bile acids and neutral steroids and increases waste disposal from enterohepatic circulation (Ilman & Topping, 1985, and Story & Kritchevsky, 1976 cit Stark & Madar, 1993). Bile aside and neutral steroids are products of cholesterol metabolism (Mayes 1993 a) from this, fiber in the gastrointestinal tract increases viscosity of gastrointestinal contents and inhibits the formation of micel, thus inhibiting lipid digestion and absorption. Sandstrom *et al.*, (1994) used pea as a fiber source for their research. The goal of their research was to monitor the influence of pea fiber on cholesterol concentrations. They also observed other beneficial effects, such as reducing the contrations of total cholesterol and LDL cholesterol, increasing HDL cholesterol and the ratio of HDL cholesterol concentration to total cholesterol concentration significantly. All of those changes decrease in the risk factor of atherosclcrosis. With the consumption of pea fiber cause significantly reduction insulin concentration. Insulin hormone increases the activity of hydroxymethyl CoA reductase (HMG-CoA reductase), an enzyme which plays a role in cholesterol synthesis. The decrease in insulin content causes a decrease in HMG-CoA reductase activity and also a decrease in cholesterol synthesis (Mayes, 1993b), and this is consistent with a decrease in cholesterol content.

Some possible mechanisms for decreasing cholesterol concentration.

1. Dietary fiber inhibits the absorption of cholesterol.

The existence of soluble fiber in the gastrointestinal tract increases viscosity and inhibits the formation of micel and lipid absorption (Gallaher *et al.*, 1993 and Superko 1988 cit Stark & Madar 1993) and cholesterol is one component of lipids that undergo absorption. In the process of lipid absorption, chylomicron needs to be formed. As the component, chylomicron, among others are Apolipoprotein A-I and Apolipoprotein A-IV (Mayes, 1993a). mRNA Apolipoprotein A-I and mRNA Apolipoprotein A-IV decreased in the ileums of rats fed 150g/kg of dietary beet fiber, as compared to those rats fed a fiber-free diet (Sonoyama *et al.*, 1995). Apparently the increased of the viscosity of gastrointestinal and the inhibition of the formation of chylomicron interfere with the digestion and absorption of lipids, including cholesterol.

2. Dietary fiber lowers insulin concentration

Lipid absorption is regulated by the insulin hormone. Dietary fiber affects insulin consentration. A research had been conducted on healthy humans, the subjects were given a control diet which contained cellulose powder and a diet which contained such fibers as pea fiber, wheat bran , and beet fiber , each containing 50g glucose. For those given pea fiber the area below-the-curve decrease for insulin content had already begun by the 30th minute while for the other groups the moment of their decrease was less, although insignificant if compared with those given pea fiber (Hamberg *et al.*, 1989). In cholesterol metabolism, insulin influences the activity of HMG-CoA reductase activity. HMG-CoA reductase is an enzyme that controls cholesterol synthesis. HMG-CoA reductase can undergo reversible modification, becoming active or becoming inactive with the phosphorilation dephosphorilation mechanism catalyzed by the reductase-kinase enzyme. The reductase-kinase enzyme, whose activity is regulated by cAMP, a 2nd messanger for hormone insulin, thyroid and glucagon (Mayes *et al.*, 1993b). Laws *et al.*, (1991) conducted research on 83 men between 50 and 65 years of age free from coronary heart disease or diabetes, and investigated their fasting insulin concentration, body mass index and waist hip ratio. The subjects were further divided into 3 groups (tertile). HDL cholesterol and triglyceride content were also investigated as dependant variables. It is possible that fasting insulin levels is a predictor for HDL cholesterol and triglyceride contentrations.

The results of other research conducted on diabetes mellitus type-II sufferers found a below-the-curve decrease in insulin content of up to 12% for 24 hours. Insulin constitutes one of the hormones, which regulates metabolism. In this investigation fiber was given not as a supplement but as a component of a fiber-rich diet that was served to the subjects from a variety of menu choices (Chandalia *et al.*, 2001). Hyperinsulinism is one of the conditions that precede the onset of diabetes mellitus type-II (Non Insulin Dependent Diabetes Mellitus = NIDDM) and cardiovascular disease (CVD). Hyperinsulinism affects the insulin resistant, and this condition can lead to insulin resistance syndrome (IRS). Other symptoms of IRS are hypertension, low HDL cholesterol and high triacylglycerol, and all three are factors for CVD. It is likely that giving soluble dietary fiber to a NIDDM patient will lower their cholesterol concentration, thus preventing the onset of IRS.

Table 3 : **Apolipoprotein of human plasma lipoproteins (Mayes, 1993 a)**

Apolipoprotein	Molecular Mass (DA)	Additional Remaks
A-I	28,000	Activator of lecithin:cholesterol acyltransferase (LCAT). Ligand for HDL receptor.
A-II	17,000	Structure is two identical monomers joined by a disulfide bridge, Inhibitor of LCAT?
A-IV	46,000	Assiociated with the formation of the triacylglicerol rich lipoproteins. Function unknown. Synthetized by intestine
B-100	550,000	Synthesized in liver. Ligand for LDL receptor.
B-48	260,000	Synthesized in intestine.
C-I	7,600	Possible activator of LCAT.
C-II	8,916	Activator of extrahepatic lipoprotein lipase.
C-III	8,750	Several polymorphic forms depending on content of Sialic acids.
D	19,300	Possibly identical to the cholesteryl ester transfer protein.
E (arginine-rich	34,000	Present in excess in the beta -VLDL of patients with type III hyperlipoproteinemia. It is the sole apoprotein found in HDL of diet-induced hypercholesterolemic animals. Ligand for chylomicron remnant receptor in liver and LDL receptor.

3. CHOLESTEROL EXCRETION

Cholesterol is excreted as cholesterol, bile acids or bile salts into the intestine, and excreted the body together with feces. Cholesterol 7-alpha hydroxylase is a catalyzing enzyme in the first step of the process, which converts cholesterol into bile acid (Mayes, 1993b). Kubo and Nanba (1997, cit Fukushima *et al.*, 2000) report that the antihyperlipemic influence of the maitake fruit is caused by an acceleration of cholesterol and bile acids excretion and cholesterol transformation into bile acids. Buhman *et al.* (1999) cit Fukushima *et al.*, (2000) found that feeding rats psyllium increases their fecal bile acids and steroid excretion as well as cholesterol 7-alpha hydroxylase activity.

4. The role of fiber in the regulation of the biosynthesis of lipoproteins that contain Apo B and mRNA receptors in hepatic LDL.

Fernandez *et al.*, (1997) injected rats with Triton W.R.- 1339 to stop the metabolism of VLDL. A difference was discovered in the rate of Apo B secretion, which was lower if pectin, guar gum and psyllium were fed to the eats. Pectin, guar gum and psyllium significantly changed the composition of the newly excreted VLDL, specifically with higher totals of triacylglycerol and phospholipids. The sise of secreted VLDL was larger and the composition of VLDL was also changed a larger-sized VLDL. These results indicate that changes in the rate of Apo B_{100} secretion in lipoprotein, the changes lipoprotein composition occur in the intravascular compartment and an increase in LDL receptor is a secondary metabolic response induced by dietary fiber, which supports the lowering of plasma cholesterol concentration.

This would seem to agree with the findings of Fukushima *et al.*, (2000) who found that cholesterol concentration in lipoproteins containing Apo B (total cholesterol, VLDL cholesterol, IDL cholesterol, LDL cholesterol) were lowered when mushroom fiber and beet fiber were given as compared to the control group (given cellulose powder). Hepatic LDL receptor mRNA content was higher for those given mushroom fiber and beet fiber compared with controle group. The results of Fukushima's research indicate that mushroom fiber and beet fiber lower cholesterol concentration by increasing hepatic LDL receptor mRNA. This indicates that the metabolism or introduction of LDL into the target cell is necessary for the synthesis of bile acid from cholesterol, to replace the bile acid that excreted together with feces. So the LDL cholesterol concentration will be lowered.

CONCLUSION

Various types of soluble fiber sources contain fibers, which have different structures and chemical compositions. These differences cause differences in biochemical induction with a hypocholesterolemic effect with regard to the cholesterol found in certain lipoprotein fraction. Thus we can determine the most appropriate fiber source, to be consumed for consumption by sufferers of certain types of hypercholesterolemia.

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