CHAPTER II

LITERATURE REVIEW

1. Cholesterol and blood lipids

Blood lipid constituents include free fatty acid, cholesterol, triglyceride, and phospholipids. The two main lipids in blood are triglyceride and cholesterol. Triglyceride is important for transferring energy from foods into cells. Cholesterol is an essential element of all animal cell membranes and forms the backbone of steroid hormones, vitamin D and bile salts. High cholesterol levels in blood increases the risk of heart disease, including heart attack (Pace et al., 2001). About 75% of the daily cholesterol requirement is made in the liver and the remainder is obtained from diets. Cholesterol production in the liver normally responds to dietary cholesterol intake. If cholesterol intakc increases, internal cholesterol synthesis decreases (Mason, 2000).

Triglyceride and cholesterol are water insoluble and must be transported in plasma by combining with specific proteins. The resulting complexes are called lipoproteins which are usually classified by density (Browner, 1994; Mason, 2000; Thomas, 2001). Density is determined by the amounts of triglyceride (which make them less dense) and apoproteins (which have the opposite effect). The least dense particles, known as chylomicrons, are normally found in the blood only after fat-containing foods have been eaten. Chylomicrons carry dietary cholesterol and triglyceride to the peripheral tissues. The other lipoproteins are suspended in serum and must be separated using a centrifuge. The densest (and smallest) family of particles consists mainly of apoproteins and cholesterol are called high density lipoproteins (HDL). They carry excess cholesterol from the peripheral tissues to the liver for disposal. HDL cholesterol is sometimes referred to as a "good cholesterol". High concentrations of HDL cholesterol are beneficial and inversely related to CHD. In contrast, the low density lipoproteins (LDL) referred to as a "bad cholesterol". LDL are derived from very low density lipoproteins (VLDL) and carry cholesterol from the liver to the peripheral tissues. Excess LDL particles are taken up by the liver, and the cholesterol contained is then excreted into the bile. It has long been known as a cause of cholesterol building up in the wall of the arteries. VLDL are large lipoproteins, which consist mainly of triglyceride. VLDL maintain a supply of triglyceride for energy production to body tissues in the fasting state. High levels of VLDL are associated with a high risk of CHD. Intermediate density lipoproteins (IDL) which are transient particles derived from the breakdown of VLDL. They are short-lived intermediates. IDL are taken up by the liver and some are converted to LDL (Mason, 2000).

Hyperlipidemia defined as primary cause or secondary causes (Thornton and Holt, 2000, Mahley and Bersot, 2001). Primary cause is genetic predisposition. Secondary causes are diet, medications, lifestyle and underlying disease. Hyperlipidemia has been established as a pathogenic risk factor for development of CHD (Farmer and Gotto, 1992; Willerson and Cohn, 2000). The major type of hyperlipidemia in the affluent-urban Thais was hypercholesterolemia resulting from elevated serum LDL cholesterol (Leelahagul et al., 1996).

Hypercholesterolemia with high serum levels of LDL cholesterol accelerates coronary atherogenesis and predisposes to CHD. Lowering total cholesterol, particularly LDL cholesterol, decreases the incidence of CHD (Sellers and Brubaker, 1999; Lauer and Fontanarosa, 2001; Van Aalat-Cohen, 2004). Classifications of hypercholesterolemia are divided into mild, moderate and severe categories (Table 1).

Table 1 Classification of hypercholesterolemia (Grundy, 1999)

Degree of hypercholesterolemia	Total cholesterol mg/dl (mM/l)	LDL cholesterol mg/dl (mM/l)
Mild	200-239 (5.18-6.16)	130-159 (3.36-4.11)
Moderate	240-299 (6.21-7.76)	160-219 (4.14-5.67)
Severe	≥300 (≥7.76)	≥220 (≥5.67)

Analysis of the National Health and Nutrition Examination Survey, 1999 to 2000 data suggested that renewed efforts are necessary to lower total cholesterol concentrations in the United State population. Theses efforts should include aggressive promotion of heart-healthy lifestyles to prevent and control hypercholesterolemia and a sustained public health commitment at the national, state, and local levels toward screening, primary and secondary prevention, treatment, and control of hypercholesterolemia (Ford et al., 2003).

The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, ATP III) constitutes the National Cholesterol Education Program's (NCEP's) updated clinical guidelines for cholesterol testing and management (NCEP, 2001). ATP III continues to identify elevated LDL cholesterol as the primary target of cholesterol-lowering therapy. The classification of total, LDL, and HDL cholesterol levels adopted by ATP III are shown in Table 2.

The two major modalities of LDL-lowering therapy are *therapeutic lifestyle changes* (TLC) and *drug therapy.* LDL cholesterol goals and cutpoints for initiation of TLC and for drug consideration are shown in Table 3.

Table 2 ATP III classification of total, LDL, and HDL Cholesterol (NCEP, 2001)

LDL Cholesterol (mg/dl)	
< 100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥ 190	Very high
Total Cholesterol (mg/dl)	
< 200	Desirable
200-239	Borderline high
≥ 240	High
HDL Cholesterol (mg/dl)	
< 40	Low
≥ 60	High

Table 3 LDL cholesterol goals and cutpoints for therapeutics lifestyle changes (TLC) and drug therapy in different risk categories (NCEP, 2001).

Risk category	LDL goal	LDL level at which to initiate TLC	LDL level at which to consider drug therapy
CHD or CHD Risk Equivalents (10-year risk > 20%)	< 100 mg/dl	≥ 100 mg/dl	≥ 130 mg/dl (100-129 mg/dl: drug optional)
2+ Risk Factors (10-year risk ≤ 20%)	< 130 mg/dl	≥ 130 mg/dl	10-year risk 10-20%: ≥ 130 mg/dl 10-year risk < 10%: ≥ 160 mg/dl
0-1 Risk Factor	< 160 mg/dl	≥ 160 mg/dl	≥ 190 mg/dl (160-189 mg/dl: LDL-lowering drug optional)

ATP III recommends a multifaceted lifestyle approach to reduce risk for CHD. This approach is designated TLC. Its essential features are reducing intakes of saturated fats and cholesterol, increasing viscous fiber (10-25 g/day) or plant stanols/sterols (2 g/day), increasing physical activity and weight reduction.

The American Heart Association (AHA) no longer uses the terms "Step I" and "Step II" in reference to Heart-healthy diets. These terms, however, still appear in some old materials and journal articles. For people at high risk or who have knows cardiovascular disease, the TLC Diets have been adopted. This is the "next generation" of the Step II diet recommended in May 2001 when the NCEP released new guidelines for cholesterol management in ATP III. For people at higher risk, the new (TLC) dietary goals offer dietary therapy for subgroups of people with specific medical conditions and risk factors such as high LDL cholesterol or other lipid disorders, coronary heart disease or other cardiovascular disease, and diabetes mellitus, insulin resistance or metabolic syndrome (AHA, 2005). Table 4 shows overall composition of the TLC Diet.

To initiate TLC, intakes of saturated fats and cholesterol are reduced first to lower LDL cholesterol. To improve overall health, ATP III's TLC Diet generally contains the recommendations embodied in the Dietary guidelines for Americans 2000. One exception is that total fat is allowed to range from 25-35 % of total calories, and saturated fats and *trans* fatty acids are kept low. A higher intake of total fat, mostly in the form of unsaturated fat, can help to reduce triglyceride and raise HDL cholesterol in persons with the metabolic syndrome. In accordance with the dietary guidelines, moderate physical activity is encouraged.

Table 4 Nutrient composition of TLC diet recommended by ATP III (NCEP, 2001).

Nutrients	Recommended Intake
Saturated fatty acids (SFAs)	Less than 7 % of total calories
Polyunsaturated fatty acids (PUFAs)	Up to 10 % of total calories
Monounsaturated fatty acids (MUFAs)	Up to 20 % of total calories
Total fat	25-35 % of total calories
Carbohydrate	50-60 % of total calories
Fiber	20-30 g/day
Protein	Approximately 15 % of total calories
Cholesterol	Less than 200 mg/day
Total calories (energy)	Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain

After 6 weeks, the LDL response is determined; if the LDL cholesterol goal has not been achieved, other therapeutic options for LDL lowering such as plant stanol/sterols and viscous fiber can be added. After maximum reduction of LDL cholesterol with dietary therapy, emphasis is shifted to management of the metabolic syndrome and associated lipid risk factors. The majority of persons with these latter abnormalities are overweight or obese and sedentary. Weight reduction therapy for overweight or obese patients will promote LDL reduction and provide other health benefits including modifying other lipid and nonlipid risk factors. At all stages of dietary therapy, physicians are encouraged to refer patients to registered dietitians or other qualified nutritionists for medical nutrition therapy, which is the term for the nutritional intervention and guidance provided by a nutrition professionals (NCEP, 2001).

Lipid lowering therapy has been determined to be safe and beneficial to a large number of individuals at risk for coronary artery disease; cost-effective therapy is needed to extend treatment to all of those who may have benefit. Nutrition counseling should receive high priority, both in medical training and in patient care: In addition, referral to registered dietitians may save billions of healthcare dollars annually (Escott-Stump, 2002).

2. Effects of dietary cholesterol and fat on serum lipids

Dietary cholesterol is now recognized as one of nutritional factors that plays a role in the etiology of heart disease. Dietary modification can be used as a strategy to reduce risk of CVD (Tanpahichitr et al., 1996; Supujchara Nopchinda, 1997; Bergland et al., 1999). The dietary effect is due to influence on blood cholesterol levels (Piper, 1996; Smolin and Grosvenor, 1997). "Choose a diet that is low in saturated fat and cholesterol and moderate in total fat" issued in *Nutrition and Your Health: Dietary Guidelines for American* in the year 2000, has an interesting and lengthy history. The lower intakes of saturated fat and cholesterol are consistent with decrease in blood cholesterol level and lower rate of coronary mortality over the past 30 years. Strategies are needed and some are suggested, to further encourage the population to achieve a dietary pattern that is low in saturated fat and cholesterol and moderate in total fat (Dixon and Ernst, 2001).

Comprehending the difference between dietary cholesterol and dietary fat about their relation to plasma cholesterol regulation is often conceptually difficult for the average consumer. One of the reasons is that the relative importance of dietary fat is thought to be greater than that of dietary cholesterol (Hayes, 2002). Plasma fatty acid composition reflects dietary fatty acids. Total fat content of the diet alters the fatty acid composition of plasma phospholipids, cholesteryl ester, triacylglycerol and free fatty acid. But the mechanism is unknown (Raatz et al., 2001). Raeini-Sarjaz et al.

(2001) found that LDL cholesterol was significantly lower after consuming both low fat diet with adequate energy and low fat diet with low energy. Reductions in both dietary fat and energy may modify LDL cholesterol by lowering cholesterol biosynthesis.

Liu et al. (1994) studied the relationship between dietary factors and serum lipids in southern Chinese population. Analyses of correlation showed that the keys "dietary lipid score" was positively associated with total cholesterol, LDL cholesterol, and HDL cholesterol and specifically dietary cholesterol was positively associated with total cholesterol. SFA and MUFA in diet were positively correlated with HDL cholesterol.

Leung and Lam (1994) studied serum cholesterol and dietary fat of two groups of Southern Chinese. The association between affluence and coronary risk was investigated by comparing the serum cholesterol and dietary fat intake of children in Hong Kong and Jiangmen. The mean cholesterol levels of Hong Kong children were significantly higher than Jiangmen children. The daily fat intake by the Hong Kong children was higher than those of Jiangmen children. In order to lower the total serum cholesterol of Hong Kong children, dietary intervention to lessen total fat, particularly milk and animal fat, was seemed to be appropriate.

Millen et al. (1996) examined relationship between diet and plasma total and LDL cholesterol levels in 695 premenopausal and 727 postmenopausal women participating in the Framingham Offspring/Spouse Study. Regression analyses controlled for age, caloric intake, apolipoprotein E isoform type, estrogen use, and important CVD risk factors indicated that plasma total and LDL-cholesterol levels were directly associated with consumption of saturated fat and inversely associated with total calorie intake. However, dietary cholesterol was not a predictor of plasma total or LDL cholesterol levels. Total cholesterol levels were also directly associated with total fat, oleic acid, and animal fat, and inversely associated with carbohydrate intake. Stepwise regressions with key nutrients indicated that saturated fat was consistently associated with total and LDL cholesterol levels in Framingham women.

Tanphaichitr et al. (1996) found that appropriate dietary intake played an important role in regulating serum lipoprotein levels. High intakes of saturated fatty acids, dietary cholesterol, and total energy raised the serum total cholesterol levels. The study showed that total fat intakes of 30% of total calories can lower serum total cholesterol and LDL cholesterol levels, but this effect depends on the amount of cholesterol intake.

The intake of fat from animal products, fish and vegetable oils, depending on fatty acid patterns and, possibly other constituents, are candidate contributors to the different atherogenic and thrombotic effects. Countries with a higher mortality from CHD tend to have a higher intake of energy from fat and proportion of fat from animal products. These fat intakes may lead to increase hypercholesterolemia and overweight in various countries (Khor, 1997). In addition a meta-analysis showed that dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans (Weggemans et al., 2001).

Beauchesne-Rondeau et al. (2003) investigated the effects of the incorporation of lean beef, lean fish, and poultry (without skin) diets into an AHA diet that has high polyunsaturated-to-saturated fatty acid ratio on lipoprotein profiles in hypercholesterolemic men. The study showed reduced plasma total and LDL cholesterol by 5-9%, LDL apolipoprotein B by 16-19%, VLDL triacylglycerols by 22-31%, and the ratio of total cholesterol to HDL cholesterol by 6-11% with the lean beef, lean fish, and poultry (without skin) diets. These results indicated that an AHA diet with a high polyunsaturated-to-saturated fatty acid ratio induced numerous favorable changes in coronary artery disease risk factors in hypercholesterolemic men.

A reduction in SFA and TFA intakes and an increase in PUFA intake are favorable to lipoprotein status. A reduction in total fat intake by decrease in dietary SFAs would be a favorable effect on CVD events and mortality (Hodgson et al., 1995). Current dietary guidance for desirable blood cholesterol profile recommend that general population (2 years of age and older) should limit foods high in saturated fat and cholesterol and substitute with unsaturated fat from vegetables, fish, legumes and nuts (Wardlaw et al., 2004). Current recommendations are to keep saturated fatty acid, *trans* fatty acid, and cholesterol intakes as low as possible while consuming a nutritionally adequate diet. To date, no safe limit of specific saturated fatty acid intakes has been identified. Whether a finite quantity of specific dietary fatty acids actually benefits health is not yet known (German and Dillard, 2004).

Diets enriched in saturated fat and cholesterol contributes to the elevated lipid levels. Increasing consumption of dietary cholesterol and fat leads to increased blood cholesterol levels. A reduction in high fat and cholesterol containing food has favorable effects on total and LDL cholesterol. Then, patients with hypercholesterolemia are advised to reduce their intake of high fat and cholesterol foods.

3. Nutrition counseling

Nutrition counseling or dietary therapy plays an important role in the treatment of hypercholesterolemia. It is defined as the process of guiding a client toward a healthy nutrition lifestyle to meet normal nutrition needs and solve problems that are barriers to change. Medical nutrition therapy (MNT) and nutrition counseling are essentially interchangeable. In general, the term medical nutrition therapy is used when medical treatment of disease is involved. The term nutrition counseling is used when counseling is an approach to disease prevention and general good health (Curry and Jaffe, 1998; Bauer and Sokolik, 2002). To be fully effective, a medical nutrition therapist must not only instruct clients on the principles of basic nutrition and nutrition therapy but also build a relationship that will facilitate changes in behavior and enhance problem-solving skills. The concept of nutrition counseling encompasses facilitative techniques, interpersonal skills, expertise in nutrition in health and disease, and the ability to guide clients in solving nutrition-related problems.

The clinical and cost outcomes of nutrition counseling for patients with hypercholesterolemia are good. Schiller et al. (1998) assessed outcomes of patient nutrition counseling. They found that most of the patients (83%) gave a partial or full description of their diet modifications and 79% had a moderate or good understanding of their diet. Nutrition counseling has positive outcomes for hypercholesterolemic patients.

Nutrition counseling is a reasonable investment of resources because it results in significantly better lipid, diet, activity, and weight (Hebert et al., 1999; Delahanty et al., 2001). Not only is MNT effective in lowering LDL-C concentrations but also cost-effective when compared with initial treatment with pharmacotherapy. Increased knowledge, benefits, and efficacy and lower-fat eating behaviors associated with additional nutrition therapy may have significant complications on the ability of persons to follow long term low-fat eating plans, which could reduce the need for costly medication intervention (Rhodes et al., 1996). When pharmacotherapy is necessary, concurrent MNT can lower the required medication dose resulting cost reduction. MNT resulted in 6% decrease in total and LDL-cholesterol concentrations after three months with one-third of the group showing at least 10% decrease in total cholesterol concentrations (Hager and Hutchins, 2003). The effectiveness of nutrition counseling in changing dietary habits is well documented. Most studies did not use primary care physicians as the source of the nutrition counseling but rather used a combination of health educators, nurses or dieticians and self-help materials and an office-based organized approach to nutrition counseling (Eaton et al., 2003).

Thidarat Wisetjindavat (1996) studied the effect of fat limitation by self control in hypercholesterolemic persons. Thirty subjects with hypercholesterolemia were assigned to either the control group or the experimental group (low-fat diet). Dietary counseling was provided for 3 months. The results showed that all subjects on experimental group tolerated the low-fat diet well, and average dietary adherence was good. Serum total cholesterol and LDL cholesterol were significantly reduced while serum HDL cholesterol and triglyceride did not change. The study confirms the beneficial role of dietary intervention for reducing atherogenic serum lipid levels.

Sikand et al. (1998) found that medical nutrition therapy lowered serum total cholesterol levels (13%), LDL (15%), triglyceride (11%), and HDL cholesterol (4%). Lipid drug eligibility was obviated in 34 of 67 (51%) subjects per the National Cholesterol Treatment Program guidelines algorithm. The estimated annualized cost savings from the avoidance of lipid medications was $60,561.68.

Acharaya Samphao-ngern (1999) studied outcome of the provision of pharmaceutical care service to hypercholesterolemia outpatients. Forty-two patients who were not able to control LDL cholesterol level according to NCEP ATP II guideline were participated in the study. In the first three months, patients in the study group were received pharmaceutical care services provided by pharmacists, including education of hypercholesterolemia, counseling on dietary control, exercises as well as medication use. Results from the study showed that LDL cholesterol level of the study group significantly decreased, compared with baseline level and control group. Significant improvement of LDL cholesterol concentrations was found in dietary control in the first three months. Provision of pharmaceutical care can significantly improve patient's knowledge at 3- and 6-month services.

Bluml et al. (2000) studied outcome of Pharmaceutical Care Services. The objective of this study was to demonstrate that pharmacists promote patient persistence and compliance with prescribed dyslipidemic therapy and enable patients to achieve their NCEP goals. The results showed that in a population of 397 patients over and average period of 24.6 months, the observed rates for persistence and compliance with medication therapy were 93.6% and 90.1% respectively. At the end of the study, 62.5% of patients had reached the NCEP lipid goal.

Cheng et al. (2004) assessed the effectiveness of the patient nutrition tool, suggested by Food for Heart Program, in hypercholesterolemic outpatients. The intervention involved four monthly dietary counseling visits, using the Food for Heart Program. The results showed that total and LDL cholesterol decreased 0.40 ± 0.65 mM/l and 0.32 ± 0.58 mM/l respectively in the intervention group compared with 0.06 ± 0.57 mM/l and 0.0088 ± 0.56 mM/l in the control group. There was no significant change in HDL cholesterol.

4. Dietary Fibers (Jalili et al., 2000; Thomas, 2001; Wardlaw et al., 2004)

The term "dietary fiber" is still controversial. In the report of the UK COMA Panel (DH 1991) on dietary reference values (DRVs) considered that it should become obsolete, and the term "non-starch polysaccharide" should be used in preference. Dietary fibers are composed primarily of the non-starch polysaccharides including cellulose, hemicelluloses, pectin, gums, and mucilage. The only noncarbohydrate component of dietary fibers is lignin. Almost all forms of fiber come from plants and none is digested in the human stomach or small intestine. Two general classes of fiber are shown in table 5. Undigestible dietary fibers generally do not dissolve in water and thus are called insoluble fibers. More formally called poorly fermented fibers. Pectin, gums, and mucilage are found inside and around plant cells. They glue plant cells together. These dietary fibers can dissolve or swell when put into water and thus are called soluble fibers, more formally called viscous fibers. It seems that pectic substances, mucilages, and hemicelluloses have the greatest water-holding capacity. The terms soluble and insoluble fiber were not retained in the DRI document. The term viscous fiber was defined despite good reasons including the use of the term by ATP III with cholesterol reduction (Jenkins et al., 2004)

Table 5 Classification of dietary fibers (Wardlaw et al., 2004)

Type	Component	Physiological effects	Major Food Sources
Insoluble (Poorly Fermented)			
Noncarbohydrate	Lignin	Increases fecal bulk	Whole grains
Carbohydrate	Cellulose	Increases fecal bulk	All plants
	Hemicelluloses	Decreases intestinal transit time	Wheat, rye, rice, vegetables
Soluble (Viscous)			
Carbohydrate	Pectin, gums, mucilage	Delays gastric emptying; slows glucose absorption; reduces blood cholesterol	Citrus fruits, oat products, beans, apples, bananas

5. Effect of viscous fiber on serum lipid levels

Viscous fibers have been recognized since the 1960s as having cholesterol-lowering properties (Jenkins, Kendall and Vuksun, 2000). High intake of fibers resulted in decreased serum cholesterol levels both total and LDL cholesterol without significant change in serum triglyceride. Non-viscous particulate or insoluble fibers had no metabolic effect on blood lipids (Glore et al., 1994; Jenkins et al., 1998; Anderson and Hanna, 1999; Jenkins et al., 2004).

The AHA Dietary Guidelines Revision 2000 (Krauss et al., 2000) and NCEP ATP III recommendations are to increase fiber intake in the diet. This goal can be achieved through the guidelines for food consumption, for example, emphasis on vegetables, cereals, grains, and fruits. Fiber is also implicated in the reduction of cholesterol. Soluble fiber has been found modestly effective in decreasing cholesterol. NCEP dietary advice focuses on dietary fat and cholesterol which may reduce LDL cholesterol by as much as 18%. Nevertheless, other modifications including increased intake of soluble fiber, vegetable protein and plant sterols may reduce serum cholesterol by an additional 5% to 10% or more (Jenkin, Kendall, Vidgen, et al., 2000).

Fiber-rich foods in combination with diets low in fat and cholesterol provide additional benefits in cholesterol-lowering effects (Anderson, Smith, and Gustafson, 1994; Hunninghake et al., 1994; Whitney et al., 2001). Data from studies in 2002 support to the US Food and Drug Administration (FDA) approved health claim that in the context of a low-fat, low cholesterol-diet, 4 servings/day of foods containing the viscous fibers "psyllium" and oat β-glucan can be expected to reduce serum lipids and the risk of cardiovascular disease (Jenkin et al., 2002). Soluble fibers, including those from psyllium husk, have been shown to augment the cholesterol-lowering effect of a low-fat diet in persons with hypercholesterolemia. Psyllium supplementation significantly lowered serum total and LDL-cholesterol concentrations in subjects consuming a low-fat diet. Psyllium is well tolerated and safe when used adjunctive to a low-fat diet in individuals with mild-to-moderate hypercholesterolemia (Wolever et al., 1994; Anderson, Allgood, et al., 2000).

Miettinen and Tarpila (1989) studied the effects of viscous and nonviscous fiber on serum lipids, cholesterol absorption and cholesterol synthesis. This study found that short-term viscous dietary fibers (*Plantago ovata* and guar gum) preparations decreased serum LDL cholesterol, as compared to low fiber or nonviscous high fiber period.

Putadechakum (1996) studied the effects of dietary changes on serum lipoprotein levels in US peace crops volunteers working in Thailand with the age ranging from 21-35 years. Dietary, anthropometric, and biochemical assessments were performed 3 days after their arrival and during working in Thailand at weeks 12 and 36. The subjects decreased their dietary fiber intakes at weeks 12 and 36. The negative correlations between dietary fiber intakes and serum total cholesterol or serum LDL cholesterol levels were found.

Jensen et al. (1997) studied long term effects of water-soluble dietary fiber in the management of hypercholesterolemia in healthy men and women. Fifty-one healthy, moderately hypercholesterolemic men and women consuming their usual fat-modified diets completed a 6-month, randomized, double-blind, placebo-controlled, parallel comparison of 15 g/day supplemental water-soluble dietary fiber and an inactive water-soluble dietary fiber control. Before the study, all subjects were stabilized on self-selected, low-fat and low-cholesterol diets comparable to the NCEP step I diet and were not taking any dietary fiber supplements. This study found that the water-soluble dietary fiber supplementation for 8 weeks reduced plasma total and LDL cholesterol concentrations by 6.4% and 10.5% respectively and the results were sustained at 16 and 24 weeks. Mean plasma HDL cholesterol and triglyceride concentrations were unchanged. No significant changes in mean plasma lipid or lipoprotein concentrations were observed in the control group.

Olson et al. (1997) conducted a meta-analysis to determine the effect of consumption of psyllium-enriched cereal products on blood total cholesterol, LDL cholesterol and HDL cholesterol levels, and to estimate the magnitude of the effect among 404 adults with mild to moderate hypercholesterolemia (TC of 5.17–7.8 mM/l) who consumed a low fat diet. The meta-analysis showed that subjects who consumed a psyllium cereal had lower TC and LDL-C concentrations than subjects who ate a control cereal. HDL-C concentrations were unaffected in subjects eating psyllium cereal. The results indicated that consumption of a psyllium-enriched cereal as part of a low fat diet improved the blood lipid profile of hypercholesterolemic adults over that which could be achieved with a low fat diet alone.

Anderson, Allgood, et al. (1999) evaluated the safety and effectiveness of psyllium husk fiber used adjunctively to a traditional diet for diabetes in the treatment of men with type 2 diabetes and mild-to-moderate hypercholesterolemia. After a 2-week dietary stabilization phase, 34 subjects were randomly assigned to receive 5.1 g psyllium or cellulose placebo twice daily for 8 weeks. Serum lipid and glycemic indexes were evaluated every 2 weeks. After treatment, the psyllium group showed significant improvements in glucose and lipid values compared with the placebo group. Serum total and LDL-cholesterol concentrations were 8.9% and 13.0% lower, respectively, in the psyllium group than those in the placebo group. The addition of psyllium to a traditional diet for persons with diabetes is safe, well tolerated, and improves glycemic and lipid control in men with type 2 diabetes and hypercholesterolemia.

Brown et al. (1999) studied cholesterol-lowering effect of dietary fiber. This meta-analysis of 67 controlled trials was performed to quantify the cholesterol-lowering effect of major dietary fibers. The results showed that soluble fiber, 2-10 g/day, was associated with small but significant decreases in total cholesterol and LDL cholesterol. The effects on plasma lipids of soluble fiber from oat, psyllium, or pectin were not significantly different. Triglyceride and HDL cholesterol were not significantly influenced by soluble fiber. Lipid changes were independent of study design, treatment length, and background dietary fat content.

Knopp et al. (1999) evaluated long term blood cholesterol-lowering effects of a dietary supplement of water-soluble fibers and mostly non-water-soluble fibers in subjects with mild to moderate hypercholesterolemia. After stabilization for 9 weeks on a NCEP step I diet, subjects were randomly assigned to receive 20 g/day of the fiber supplement or matching placebo for 15 weeks and then receive the fiber supplement for 36 weeks. The efficacy analyses included the 125 subjects (58 fiber; 67 placebo). One hundred and two subjects (52 fiber; 50 placebo) completed the 15-week comparative phase. Eighty five of these subjects (45 fiber; 40 placebo) elected to continue in the 36-week noncomparative extension phase. Results from this study showed that the mean decreases during the 15-week period for LDL cholesterol, total cholesterol, and LDL/HDL cholesterol ratio were greater in the fiber group. Fiber supplementation had no significant effects on HDL cholesterol and triglyceride. Similar effects were seen over the subsequent 36-weeks noncomparative part of the study.

Aller et al. (2004) studied effects of soluble fiber intake in lipid and glucose levels in healthy subjects. Fifty-three subjects were prospectively randomized to two groups. One group received a diet with 10.40 g of fiber (1.97 g soluble fiber and 8.13 g of insoluble fiber), and the other group received a diet with 30.50 g of fiber (4.11 g soluble fiber and 25.08 g insoluble fiber). In the both groups, dietary advice was given by a registered dietitian using a dietary counseling program based on standard nutrition principles. Prospective serial assessments of weight and nutrition intake were made. These determinations were performed at baseline and at 3 months. This study was found that during treatment, a significant change in LDL cholesterol and fasting glucose levels from baseline was detected in the group that received more of fiber. No statistical difference was detected among triglyceride, HDL cholesterol, and insulin levels.

Behall et al. (2004) investigated whether consumption of barley would reduce cardiovascular disease risk factors comparably with that of other sources of soluble fiber. Mildly hypercholesterolemic subjects consumed controlled American Heart Association Step I diets for 17 week. After a 2-week adaptation period, whole-grain foods containing 0, 3, or 6 g β-glucan/d from barley were included in the Step I diet menus. Diets were consumed for 5 week each and were fed in a Latin-square design. This study found that total cholesterol significantly lower when the diet contained 3 or 6 g β-glucan/d from barley than that contained no β-glucan. HDL and triacylglycerol concentrations did not differ with the 3 amounts of dietary β-glucan. Large LDL and small VLDL fractions and mean LDL particle size significantly decreased when whole grains were incorporated into the 3 diets.

High intake of fiber-riched diets resulted in decreased serum cholesterol levels both total and LDL cholesterol without significant change in serum triglyceride. Hypercholesterolemic patients are recommended to increase dietary fiber intakes.

6. *Ocimum canum* seeds

Ocimum canum is one of the common plants and well known in Thailand. Other scientific names are *O. basilicum* Linn. var. *citratum* and *O. americanum* Linn. Common names are Hairy basil, Mang lak and Komko khaao (Northern). Its leaves and seeds are used for cooking in various menus and not expensive. *O. canum* seeds are usually used in the form of raw whole seeds (Farnsworth and Bunyapraphatsara, 1992). It has been widely used to make desserts (ก่องกานดา ชยามฤต, 2540; พรทิพย์ สุประดิฐ์, 2541).

The analysis of *O. canum* seeds shows that the seed is composed of D-arabinose, L-arabinose, D-galactose, D-glucose, D-mannose, L-rhamnose, D-xylose, D- galacturonic acid, D-mannuronic acid, pentosans, polysaccharide, camphene, camphor, myrcene, oil and mucilage (นันทวัน บุณยะประภัศร, 2530). Seed has mucilage that forms a gel in water with a high viscosity (นันทวัน บุณยะประภัศร, 2530; คณะเภสัชศาสตร์ มหาวิทยาลัยมหิดล, 2535; สุนทรี สิงหบุตรา, 2540). When 1 g of the seeds is soaked in water it becomes swollen to 45 ml. The seed is composed of 55.70% carbohydrate, 19.60% fat, 17.87% protein, and 6.87 % minerals (Muangman et al., 1985). Fatty acid composition of basil seed oil is presented in Table 6.

Table 6 Fatty acid composition of basil seed oil (Anger et al., 1995)

Variable	% w/w
Oil content (% w/w)*	18
Palmitic (16:0)	6.1
Stearic (18:0)	2.3
Palmitoletic (16:1)	0.2
Oleic (18:1)	8.5
Linoleic (18:2)	17.8
Alpha-linolenic (alpha-18:3)	64.8
Gamma-linolenic (gamma-18:3)	0.3
Arachidic (20:0)	0.2
Eicosenoic (20:1)	< 0.1%

* Based on dry weight

The physical properties of the mucilage isolated from seeds in a dry powder form show a high moisture content and moisture adsorption with poor flow ability and good compressibility (Leelahagul et al., 1992). The seeds contain mucilage 23.00 g/100g of dry weight (Lakana Mohmai, 2002).

Acute toxicity test of the seeds, orally administered at a dose of 0.25-5 g/kg in male and female rats, showed no toxic effect within 7 days of observation. Subchronic toxicity test, orally administered at a dose of 1 g/kg continuously for 10 days, exhibited no effects in rabbits, rats or cats (อโนชา อุทัยพัฒน์และคณะ, 2539: 17-20). For chronic toxicity test, the seeds were orally administered at doses of 0.25, 0.5,1 and 2 g in each group of rats continuously for 12 weeks. No change in the histopathological characters of the livers, small and large intestines was observed (อโนชา อุทัยพัฒน์และคณะ, 2539: 19-20). Being used as foods, precaution should be noted that the seeds should be prepared with sufficient water for completely swelling before taking to prevent dehydration, flatulence, constipation or intestinal obstruction (นันทวัน บุณยะประภัสศร, 2530; คณะเภสัชศาสตร์ มหาวิทยาลัยมหิดล, 2535; Farnsworth and Bunyapraphatsara, 1992).

Premwatana et al. (1985) determined the dietary fiber content by the neutral detergent fiber method in 29 commonly eaten Thai plants. The results revealed that *O. canum* seeds contained the highest dietary fiber with low sugar content (80 g of dietary fiber and 0.55 g of sugar/100 g dry weight). Thus, *O. canum* seeds are a good source of viscous fiber which has physiological effects on the gastrointestinal tract and systemic effects. In 1985, Muangman et al. reported a beneficial effect of *O. canum* seeds intake in reducing the incidence of constipation in 53 elderly postoperative patients. Sriratanaban et al (1992) studied effect of *O. canum* seeds on bowel movement of healthy volunteers in comparison with a psyllium seed product, oranged-flavored Metamucil® (Psyllium seed), in order to assess its potential use as a bulk laxative. There was statistically significant increase in stool weight during *O. canum* seed period when compared with control period, and during the psyllium seed period when compared with control period. However, the significant difference was not found between the *O. canum* seed period and the psyllium seed period.

Viseshakul et al. (1985) evaluated the effect of *O. canum* seed intake on oral glucose tolerance tests in 14 patients with non insulin dependent diabetes mellitus and 2 patients with insulin dependent diabetes mellitus. They were instructed to continue usual dietary habits and medication during one-month study. They received a daily intake of 30 g of *O. canum* seeds (10 g after each meal) for one month. Oral glucose tolerance tests were undertaken before and after the experimental period, the results showed a significant improvement.

In Thailand, *O. canum* seeds were used to substitute psyllium seeds that were necessary imported from another country (วันดี กฤษณพันธ์, 2537). *O. canum* seeds can form gel in water as same as psyllium seeds. Psyllium is classified as a mucilaginous fiber due to its powerful ability to form gel in water (*Plantago ovata* (Psyllium), 2002) and has hypocholesterolemic effect (Chan and Schroeder, 1995; Davidson, Maki, et al., 1998; Anderson, Davidson, et al., 2000; *Plantago ovata* (Psyllium), 2002).

Chularojanamontri, Kewsiri, and Chuprasert (1987) studied the effect of dietary fiber (*O. canum* seeds or hairy basil seeds) on serum lipoprotein. This study was carried out on 20 hyperlipoproteinaemia patients, 24 g of *O. canum* seeds were daily given for 30 days. The results showed that HDL cholesterol was significantly increased. Cholesterol, chylomicron, pre-beta lipoprotein, and beta lipoprotein were significantly decreased. No significant change was found in serum triglyceride, blood sugar, and body weight and body mass index (BMI) during treatment.

Montana Theerajantranon (1996) studied the clinical outcome of nutrition therapy and *O. canum* seeds in 36 outpatients at public health center 47 Klongkwang by educating the patients about dietary therapy, cause and complication of diabetes mellitus, and blood glucose and lipid level control. The energy requirement for each patient was calculated and menus were set up. After the intake of *O. canum* seeds (10 gram per time), the fasting blood glucose and cholesterol were significantly decreased.

O. canum seeds are good source of dietary fiber. They have a variety of beneficial physiological effects. Cholesterol-lowering effect is one of beneficial effects. An increase in dietary fiber intake by supplementation of *O. canum* seeds may promote the reduction of serum cholesterol levels.