The Effects of Consumption of California Dried Mission Figs on Serum Lipid Concentrations in Hyperlipidemic Adults

Joycelyn M. Peterson

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THE EFFECTS OF CONSUMPTION OF CALIFORNIA DRIED MISSION FIGS ON SERUM LIPID CONCENTRATIONS IN HYPERLIPIDEMIC ADULTS

By

Joycelyn M. Peterson

A Dissertation in Partial Fulfillment of the Requirements for the Degree of Doctor of Public Health in Preventive Care

March 2011
Each person whose signature appears below certifies that this dissertation, in his/her opinion, is adequate in the scope and quality as a dissertation for the degree of Doctor of Public Health.

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ABSTRACT OF DISSERTATION

The Effects of Consumption of California Dried Mission Figs on Serum Lipid Concentrations in Hyperlipidemic Adults

by

Joycelyn M. Peterson

Doctor of Public Health in Preventive Care

Loma Linda University, Loma Linda, 2011

Serena Tonstad, Chair

Background: The National Cholesterol Education Program and American Heart Association have recommended the use of functional or cholesterol-reducing foods, some categories of which include viscous or soluble fibers, soy protein, plant sterols, and nuts, as aids to reduce serum cholesterol concentrations. Figs are a rich source of viscous fiber and antioxidants. Fig consumption has not been studied in regard to effects in reducing serum lipid concentrations. In previous pilot data, increasing fig consumption for six weeks among volunteers was found to be feasible.

Objective: To evaluate the effect of the consumption of California dried mission figs on serum lipid concentrations in hyperlipidemic adults.

Research Methods and Procedures: We conducted a randomized controlled crossover clinical trial on the effects of consumption of California dried mission figs in men and women aged 30 to 75 years with low-density lipoprotein (LDL) cholesterol concentrations in the above optimal (100-129 mg/dL), borderline (130-159 mg/dL), or high (160-189 mg/dL) - if cleared by their physician - range. Participants were recruited
from communities in or surrounding San Bernardino, California. The length of the study was 12 weeks and involved 8 visits: screening between weeks 0 to 2, randomization at week 2, follow-up at each of weeks 6 and 7 at the end of the first dietary period (after five weeks of consumption of usual diet or usual diet and figs) and at each of weeks 11 and 12 at the end of the second dietary period (after five weeks of consumption of usual diet or usual diet and figs) as well as at weeks 4 and 9 for fig pickup and/or a 24-hour dietary recall.

At screening 141 potentially eligible subjects were informed about the study and asked to sign informed consent forms. Inclusion and exclusion criteria were checked and fasting serum lipid concentrations measured. Subjects that met all inclusion criteria returned within two weeks for randomization. Participants were randomly assigned to consume their usual diet, or their usual diet plus 40 g of prepackaged and weighed California dried mission figs with meals three times daily (total of 120 g) for a period of five weeks, then switched to the other condition for the following five week period. Figs replaced some desserts and sweet snacks to maintain stable energy consumption. Participants were asked not to make other changes in their usual diet and physical activity level for the duration of the study, and consumption of figs outside those provided by the study or prunes were be allowed. Total and LDL cholesterol, vital signs and anthropometrics were measured at screening and follow-up visits. Mean serum lipid concentrations at the end of each dietary period (mean of weeks 5 and 6 and mean of weeks 11 and 12) were compared using paired t-test statistics. Given an estimated 5% reduction in LDL cholesterol concentration with a standard deviation of 8% we estimated that to achieve 80% power with \( \alpha \) of 0.05, 84 participants were required and 102 were
randomized. 41 subjects that started with the usual diet had complete blood tests and 43 subjects that started with the figs-added diet had complete blood tests.

**Results and Conclusions:** The results showed that LDL and HDL cholesterol and triglyceride concentrations did not differ between usual and figs-added diets (Bonferroni-corrected P-values >0.017) while total cholesterol tended to increase with fig consumption (P=0.02). Total cholesterol increased in participants (n=41) randomized to usual followed by figs-added diet (p=0.01), but remained unchanged in subjects (n=42) who started with figs-added followed by usual diet (p=0.4). During the figs-added diet, soluble fiber intake was 12.6±3.7 g/day versus 8.2±4.1 g/day in the usual diet (P<0.0001). Sugar intake increased from 23.4±6.5% of kcalories to 32.2±6.3% of kcalories in the figs-added diet (P<0.0001). Body weight did not change (P=0.08). Thus, daily consumption of figs did not reduce LDL cholesterol. Triglyceride concentrations were not significantly changed despite an increase in sugar intake.

**Significance to Preventive Care:** Interventions such as the inclusion of figs in the usual diet are feasible in a community setting. The judicious use of plant foods is recommended by Preventive Care Specialists as a simple measure to reduce elevated serum lipids.
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ACKNOWLEDGEMENTS

Much hard work, thought, planning and preparation was involved in this dissertation. I am deeply indebted to the many individuals who assisted me in reaching this milestone of my education and in completing this publication. I am deeply grateful to the California Fig Advisory Board, for the generous funding of this research and for Mr. Richard Matoian, former executive director, especially, who believed in the benefits this research might potentially have for the public at large.

I want to give special tribute to the members of my dissertation committee, Dr. Serena Tonstad, Chairman, whose medical experience, strong insight, knowledge and consistent guidance and diligence assisted me in writing this paper. A special thank you to Dr. Susanne Montgomery for her expertise in study design, who carefully contributed her skills in the writing of this paper. Also Dr. Ella Haddad, whose thoughtfulness and attention to details worked with me diligently in making the comparisons of the participant’s blood analysis.

Thanks to Dr. Naomi Modeste, Chair, of the Department of Health Promotion and Education, whose consistent review and interest made it possible for me to achieve my goal of completing this dissertation. I appreciate my numerous colleagues and friends in the department who are experiencing the same challenges as I have and want to encourage them to hold on till they accomplish their goal.

I am grateful to Drs. David and Maxine Taylor, Dr. and Mrs. Samuel De Shay, whose friendship, prayers, and encouragement through the difficult times has made it all worthwhile; I love them for that. I am deeply grateful to my beloved husband Ralph and daughter Karen, for staying by my side through the challenges of this research project.
and always encouraging and supporting me in all my daily activities and keeping me on track as I made the sacrifices to see this dream become a reality.

I want to thank Loma Linda University for the opportunity to study at this fine institution, and most of all, I give God all of the Praise and Honor for keeping me in good health throughout my period of study, and research and seeing me through the completion and writing of this publication. I can truly say To God be the Glory, Great things He has done.
CHAPTER 1
INTRODUCTION

A. Statement of the Problem

Cardiovascular disease (CVD) continues to be the major health problem and the leading cause of death in the United States and Canada, claiming one life every 37 seconds (National Center for Health Statistics, 2006). More than a million Americans experience myocardial infarctions each year, and about a half million people die from heart disease yearly (U.S. Department of Health and Human Services: U.S. Department of Agriculture, 2005). Lowering raised serum cholesterol levels is firmly established as an effective intervention for reducing the mortality and morbidity due to coronary heart disease (CHD).

Numerous experimental and epidemiological studies have revealed a relationship between elevated blood lipid values and the development of atherosclerosis (Ross, 1999). Elevated low density lipoprotein (LDL) cholesterol levels specifically are linked with atherogenesis and CHD (Behall, Schofield & Hallfrisch, 1997). According to the Expert Committee on CHD prevention of the World Health Organization, the relationship between diet, serum cholesterol and coronary disease is a causal one (WHO, 2003). More than 30% of Americans have undesirably high serum cholesterol concentrations e.g. greater than 240 mg/dL (Anderson, et al., 2000). Studies have noted that for every 1% drop in serum cholesterol, there is a decrease of 2% or more in risk of coronary disease (Key et al., 2003).
It has been known for decades that polyunsaturated fatty acids lower total and LDL cholesterol concentrations while saturated fatty acids elevate atherogenic lipids. Based on these observations, an increase in consumption of monounsaturated and polyunsaturated fatty acids and a decrease in saturated fats has become the standard approach of nutritionists and clinicians attempting to improve the blood lipid profile and decrease the risk of CHD (Ornish et al., 1998). Although these dietary guidelines in conjunction with various other preventive and intervention procedures have historically accompanied reduced CHD mortality in the United States, the details of the most suited dietary fat recommendations to reduce CHD continue to be debated in terms of which specific fatty acids are most efficacious (Turpeinen et al., 1995).

The American Heart Association (AHA) and the National Cholesterol Education Program (NCEP) have published recommendations incorporating the scientific rationale for lowering lipids including total and LDL cholesterol by reducing dietary fat to 30% of total dietary calories, saturated fat to 7-10% or less and dietary cholesterol to <200-300 mg/dl with carbohydrates making up 50-60% of total calories (Lichtenstein et al., 2006; Expert Panel, 2001). Plant-based diets are naturally low in saturated fat but rich in complex carbohydrates and may lower LDL cholesterol substantially (Gardner et al., 2005). Some researchers have advocated a stringent high carbohydrate, very low fat (less than 10% of dietary energy) regimen, which has been shown to drastically reduce blood lipids and promote dissolution of arterial cholesterol deposits and atherosclerotic plaques (Ornish et al., 1998). On the other hand, guidelines have suggested that up to 35% of total dietary calories may come from fat, if much of the fat is monounsaturated and polyunsaturated (U.S. Department of Health and Human Services: U.S. Department of
Agriculture, 2005). In this case even diets with less than 50% carbohydrates may induce positive effects on blood lipid concentrations (Poli et al., 2008).

For many individuals, drug therapy must be started for the achievement of optimal lipid levels. While drug therapy plays an established role in lowering blood lipids and inhibiting atherosclerosis, some people do not tolerate certain pharmacotherapies or may be at too low a risk to receive drug therapy (Jenkins, Kendall & Marchie, 2005a). Some people may prefer and may benefit more from a dietary approach and may prefer some foods over others, rather than the use of a pharmacological approach (Behall et al., 1997). As CHD management costs spiral upwards, prescribing lipid-lowering drugs for all indicated patients is not always feasible within current resources. Statin-related drugs may increase the risk for myalgia and liver disorders and some patients have contraindications to drugs (Larosa et al., 2005).

One of the dietary approaches that are recommended is the incorporation of novel dietary components shown to reduce blood lipid concentrations. In addition to modifying the fatty acid composition of the diet, other dietary changes, for example, the inclusion of certain foods, nutrients or food components may lower blood lipid concentrations. Plant sterols have been shown to inhibit bile acid and cholesterol absorption, thereby reducing blood lipid concentrations (Gylling & Miettinen, 1995). Including soy protein in the diet as a partial replacement of animal protein reduces blood cholesterol levels (Poli et al., 2008). Continued and high interest has been shown concerning the impact of enriching the diet with foods high in fiber from cereal, grains, vegetables, and fruits (Rimm et al., 1996).
Over three decades ago the fiber hypothesis was proposed to explain low rates of CVD in sub-Saharan Africa (Trowell, 1972). Greater whole grain intakes but not refined grain intakes are associated with about a one-fifth lower risk of CVD events (Mellen, Walsh & Herrington, 2008). Numerous studies have confirmed that soluble fiber plays a role in lowering serum cholesterol (Brown, Rosner Willett & Sacks, 1999). This effect is more pronounced for soluble or gel-forming fibers found in cereals, such as barley and oat, and legumes. Furthermore, the most recent guidelines on lowering blood cholesterol recommend an increased consumption of fiber-rich foods to achieve a total daily intake of 30 grams per day (Lichtenstein et al., 2006; Expert Panel, 2001). The physicochemical properties of soluble fiber result in important modifications in volume, bulk and viscosity in the intestinal lumen, which will alter metabolic pathways of hepatic cholesterol and lipoprotein metabolism, resulting in lowering of blood LDL cholesterol concentrations (Fernandez, 2001). β-glucan is the pre-dominant soluble fiber in oats, which has been shown in a number of studies to lower blood total and LDL cholesterol concentrations. The mechanism by which β-glucan lowers serum cholesterol levels may be related to its viscosity, bile salt binding capacity or ability to ferment (Bell et al., 1999). Soluble fiber including β-glucan does not affect blood concentrations of other lipid fractions including high density lipoprotein (HDL) cholesterol and triglycerides (Poli et al., 2008).

The Food and Drug Administration (FDA) has permitted health claims for various plant based foods or food constituents including viscous fiber (oat β-glucan and psyllium), as well as for soy protein, plant sterols, and most recently, nuts (Jenkins et al., 2003). The combination of these food ingredients is the dietary equivalent of combining several cholesterol-lowering drugs and has the potential of drastically lowering blood
lipid concentrations (Insel, Turner & Ross, 2007). It is important from a public health approach to document the cholesterol-lowering effect of a functional food ingredient, and its mechanism of action under various conditions, such as in combination with cholesterol-lowering diets (Anderson, Deakins, Floore, Smith & Whittis, 1990). Certain supplements and foods enriched with these components are on the market in many countries and may be the basis for new functional foods (Vinson, Zubik, Bose, Samman & Proch, 2005). Attention should be paid to the beneficial dietary effects and the potential health risks of such a food ingredient (Jenkins, Kendall & Marchie, 2005b).

The doctoral student has considered, based on her previous experience in clinical dietetics, that one of the foods that may be effective in lowering blood lipid concentrations is figs. Figs contain β-glucan in appreciable amounts in both the fresh and concentrated form (Rimm et al., 1996; Vinson et al., 2005). Dried fruits like California mission figs have a greater nutrient density, greater fiber content, increased shelf life and significantly higher phenol antioxidant content compared to fresh fruit (Vinson et al., 2005). When figs are diluted in water they become highly soluble, viscous or gummy, producing an increased intestinal transit time, delayed gastric emptying, and decreased glucose absorption. Such actions have the potential to lower postprandial blood glucose concentrations and decrease blood cholesterol (Vinson et al., 2005). It might be helpful in several ways, including patient preference, to expand the present list of dietary foods rich in soluble fibers already known to be effective in lowering atherogenic lipid fractions. Oats, barley and legumes require preparation. Foods that require no preparation like dried fruit may improve compliance with recommendations to increase soluble fiber in the diet.
Presently, a review of PUBMED found no published studies that focus on the possibility of fig consumption to reduce total or LDL cholesterol concentrations.

B. Purpose of the Study

The purpose of this study is to determine whether dietary consumption of figs is effective in lowering atherogenic lipid fractions including total and LDL cholesterol, thereby potentially expanding the list of functional foods that may have a positive effect on blood lipid concentrations.

C. Research Questions

The following questions will be addressed in this study:

- Among people with elevated lipid concentrations who are not on drug therapy for cholesterol, does the daily consumption of California dried mission figs lower serum total and LDL cholesterol after a period of five weeks?
- Is the daily consumption of California dried mission figs feasible and well tolerated in these individuals for the period of time required to lower lipid concentrations?
- What is the effect of daily fig consumption on other lipid fractions including HDL cholesterol and triglycerides?

D. Significance to Preventive Care

Diet plays a major role in reducing the risk of CHD. This has sparked intensive research to unravel the role of specific nutrients and foods, to identify dietary patterns that affect individual risk factors. Over past decades the information obtained has led to a search for specific foods and food components that may help improve the serum
lipoprotein profile. It is important to monitor not only the effects of food components on the lipoprotein profile but also on other aspects of health. Some people may prefer to choose a dietary approach rather than a pharmacological one to lowering serum cholesterol and may benefit more from dietary changes with fewer side effects.

Non-pharmacological dietary interventions such as the inclusion of figs in the normal diet are feasible in a community setting. If shown to have significant lipid-lowering benefits, such natural dietary products can make an impact on overall health status and reduce the cost and need for pharmacological treatment (Fernandez, 2001). The judicious use of dietary foods is recommended by Preventive Care Specialists as a simple measure to reduce the problem of elevated serum cholesterol. This study might demonstrate the potential impact that the use of a dietary intervention can have on lowering serum cholesterol levels and provide a basis for recommendations to the general population at large if confirmed in future studies.
A. Lipids: Physiology and Risk

The purpose of this review is to provide an overview of research evaluating dietary patterns and their effect on blood lipid concentrations, and to review evidence for specific foods that have demonstrated cardio-protective effects. Collectively, emerging food-based research in conjunction with our present knowledge of healthful dietary patterns will provide an impetus for future, well-controlled, clinical trials to evaluate whether inclusion in dietary patterns of specific foods that have been shown to reduce risk of CVD can be of further benefit.

Lipids refer to substances known as fats and oils, but also to fatlike substances in foods, such as cholesterol and phospholipids. Dietary sources of lipids include the fats and oils used in cooking or added to foods, the natural occurring fats in meats and dairy products, and plant sources such as coconut, olives and avocado. Fat is an essential nutrient and the body produces and stores fat in the form of triglycerides, however, the body cannot make some types of fatty acids (a component of triglycerides), so these compounds must come from the diet. Triglycerides are fats we associate with fried foods, cream cheese, baked goods, and salad dressing. In the body triglycerides are stored in fatty tissue. Cholesterol is a waxy substance that is part of all cellular membranes, the precursor of hormones and involved in triglyceride and fatty soluble vitamin transport in the blood. Sufficient cholesterol for all needs is produced in the liver, the primary cholesterol-manufacturing site. The liver produces about 1,000 milligrams per day, and
far more than is found in the average diet. Cholesterol is not needed in the diet and only occurs in foods of animal origin. Its distribution is based on its biological roles: it is highest in brain, liver, and other organ meats, and moderate in muscle tissue. Since it is fat soluble, cholesterol is found in the butterfat portion of dairy products. Egg yolks are high in cholesterol containing about 212 milligrams per large egg (Insel et al., 2007).

When dietary fat is eaten it appears in the bloodstream about one to two hours later. Digestion breaks down triglycerides into glycerol, free fatty acids, and monoglycerides. Lipids need special handling to be transported around the body in the bloodstream. They are packaged into lipoprotein carriers, which have a lipid core of triglycerides and cholesterol esters surrounded by a shell of phospholipids with embedded proteins and cholesterol. Carriers from the intestine to the blood are named chylomicrons. These are rapidly cleared and the triglycerides hydrolyzed. Chylomicron remnants are what is left, and are taken up by the liver after about 20 minutes of a meal. The liver assembles very low density lipoproteins (VLDL). VLDL is then transported in the blood, the triglyceride fraction is hydrolyzed and the cholesterol core that remains is called LDL. LDL may be taken up by LDL receptors in the liver. A lack of LDL receptors for example in people with familial hypercholesterolemia reduces the uptake of cholesterol, forcing it to remain in circulation at dangerously high levels.

Elevated levels of LDL in the blood increase the risk of atherosclerosis and coronary heart disease, earning LDL cholesterol the nickname "bad cholesterol" (Dietschy, Turkey & Spady, 1993). Dietary saturated fats block LDL receptors, limiting their clearance of cholesterol from the blood. The receptors also are weakened with age, and postmenopausally in women. Consumption of trans fats may also lead to elevated
LDL cholesterol levels in the blood (Wijendran & Hayes, 2004). Over decades, LDL may transverse the endothelium lining arteries leading to an accumulation of cholesterol in macrophages and the development of plaque that thickens and narrows the artery, a condition known as atherosclerosis (Insel et al., 2007).

High-density lipoprotein (HDL) is referred to as the “good” cholesterol, because it carries cholesterol away from arteries and back to the liver where it is then removed from the body. Levels of HDL cholesterol are inversely associated with CHD (Insel et al., 2007).

B. Measurement of Lipoproteins and Lipids

Carriers of lipid in the blood including chylomicrons, VLDL, LDL and HDL all include one or more proteins, called apolipoproteins. Thus the complete lipid and protein particles are called lipoproteins. Proteins are present in order to solubulize cholesterol in the blood. Apolipoproteins have a number of enzymatic functions thus modifying and controlling the metabolism of lipids. Apolipoprotein B is the only protein found in LDL. VLDL encompasses a number of apolipoproteins, including apolipoproteins B, E and C. HDL particles are characterized by apolipoprotein A. Apolipoproteins will not be further discussed in this proposal, but blood will be frozen for the quantification of apolipoprotein B at a future date.

In clinical and epidemiological research, the entire lipoprotein particle is not quantified in the laboratory. Total and HDL cholesterol fractions of the particles are measured, and LDL cholesterol may be measured directly or estimated using a standard formula. Total cholesterol designates the entire amount of cholesterol in the blood. LDL cholesterol designates that part of total cholesterol that is carried in the LDL particle and
constitutes two thirds or more of total cholesterol. HDL cholesterol designates that part of total cholesterol that is carried in the HDL particle and constitutes about a fourth of total cholesterol. Cholesterol in VLDL accounts for the remaining cholesterol (but is not measured). Triglycerides are found in all particles, but mostly in VLDL. Measured triglycerides thus include triglycerides found in all particles, VLDL primarily but also HDL and LDL.

Blood lipids are measured in the fasting condition for the purpose of standardization. Concentrations of triglycerides are elevated after eating, depending on the type and amount of food consumed, as well as other factors including genetic ones. Chylomicrons disappear within a few minutes of eating and are normally not found in the blood in fasting conditions. Nonfasting conditions influence total and HDL cholesterol concentrations minimally. Non-HDL cholesterol may be used as a measure of risk, and includes cholesterol from LDL and VLDL. Non-HDL cholesterol may be measured in blood samples from nonfasting individuals but is not further discussed here.

C. Modification of Risk Associated with Elevated Blood Lipids

The appearance of these guidelines signified a new approach to risk modification. The remarkable progress made in recent years has shown that overall CVD risk is, in large part, the result of the interplay of multiple risk factors. Not only is the level of total and LDL cholesterol important, but the presence of other risk factors modifies risk substantially. Thus, some people with relatively low lipid concentrations may be at substantially high risk due to the presence of risk factors. When more risk factors that are present (other than LDL cholesterol), the probability of development of atherosclerosis in coronary arteries and cardiovascular events increase accordingly. A proportion of the population are at high risk because of already established CHD or other atherosclerotic CVD or multiple risk factors that increase the risk to 20% or more over the next 10 years. Diabetes is also associated with markedly elevated risk. The major risk factors that affect the level of risk and LDL cholesterol goals of treatment include:

- Cigarette smoking
- High blood pressure (140/90 mmHg or higher or taking blood pressure medication)
- Low HDL cholesterol (less than 40 mg/dL)
- Family history of early CHD (CHD in father or brother before age 55 years; CHD in mother or sister before age 65 years)
- Age (men 45 years or older; women 55 years or older)

Risk due to these factors is calculated according to Framingham scores. For educational purposes the various levels of risk may be summarized in Table 2.1.
Table 2.1 Levels of Risk

<table>
<thead>
<tr>
<th>If a Person Has</th>
<th>He or She is in Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease, diabetes, or risk score more than 20%*</td>
<td>I. High Risk</td>
</tr>
<tr>
<td>2 or more risk factors and risk score 10-20%</td>
<td>II. Next Highest Risk</td>
</tr>
<tr>
<td>2 or more risk factors and risk score less than 10%</td>
<td>III. Moderate Risk</td>
</tr>
<tr>
<td>0 or 1 risk factor</td>
<td>IV. Low-to-Moderate Risk</td>
</tr>
</tbody>
</table>

D. Guidelines for Cholesterol Reduction and Management

The NCEP updated clinical guidelines for cholesterol testing and management for the treatment of high blood cholesterol in adults is an evidence-based extensively referenced report that provides the scientific rational for the recommendations to cholesterol-lowering therapy in clinical practice. These guidelines are intended to inform, not replace the physician’s clinical judgment, which must ultimately determine the appropriate treatment for each individual (Expert Panel, 2001).

The first step in selection of LDL lowering therapy is to assess a person’s risk status as noted above. Risk assessment requires measurement of LDL cholesterol and other lipids and identification of accompanying risk determinants including cigarette smoking, hypertension, low HDL cholesterol, family history of premature CHD and age. Levels of blood lipids are characterized in Table 2.2.

The main goal of cholesterol-lowering treatment is to lower LDL cholesterol concentration sufficiently to reduce risk. This is accomplished by therapeutic lifestyle changes (TLC) in all cases and medication in some cases. TLC is for anyone whose LDL cholesterol level is above goal. Drug treatment is instituted if level of risk is high and TLC is always recommended together with drug therapy. TLC includes a cholesterol-lowering diet (called the TLC diet), physical activity, and weight management.
Table 2.2 Levels of Blood Lipids

<table>
<thead>
<tr>
<th><strong>Total cholesterol</strong></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Less than 200 mg/dL</td>
<td>Desirable</td>
</tr>
<tr>
<td>200 to 239 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>240 mg/dL and up</td>
<td>High</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>HDL cholesterol</strong></th>
<th></th>
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<tbody>
<tr>
<td>Less than 40 mg/dL (men)</td>
<td>Low</td>
</tr>
<tr>
<td>Less than 50 mg/dL (women)</td>
<td>Low</td>
</tr>
<tr>
<td>60 mg/dL and up</td>
<td>High (protective against heart disease)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>LDL cholesterol</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 100 mg/dL</td>
<td>Optimal</td>
</tr>
<tr>
<td>100 to 129 mg/dL</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td>130 to 159 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160 to 189 mg/dL</td>
<td>High</td>
</tr>
<tr>
<td>190 mg/dL and up</td>
<td>Very high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Triglycerides</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 150 mg/dL</td>
<td>Normal</td>
</tr>
<tr>
<td>150 to 199 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>200 to 499 mg/dL</td>
<td>High</td>
</tr>
<tr>
<td>500 mg/dL and up</td>
<td>Very high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Cholesterol ratio (total cholesterol divided by HDL)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 5.0 to 1</td>
</tr>
<tr>
<td>3.5 to 1</td>
</tr>
</tbody>
</table>

TLC diet includes the following principles:

- Reduced saturated fat to <7% of calories, cholesterol <200 mg/day,
  increased viscous fiber (10-24 g/day) and plant stanols/sterols (2g/day)
  to enhance LDL cholesterol lowering
- Increased physical activity
- Weight management

As an example of the amount of lipid reduction that may be achieved with the dietary recommendations, the be-FIT study in 2000 tested implementing the NCEP diet
(Walden, Retzlaff, Buck, McCann & Knopp, 2000). This study found that the diet was an effective therapy in hypercholesterolemic women and men with or without elevated triglycerides. Subjects were randomized to receive dietary intervention immediately or 6 months later. After 6 months, LDL cholesterol was significantly reduced in women by 7.7% and 8.1%, respectively and in men by 8.8% and 8.1%, respectively (Walden et al., 2000). No studies have examined the effect of the TLC diet on morbidity and mortality in randomized controlled clinical trials.

After a collaborated review of recent clinical evidence, the ATP III update that appeared in 2005 recommended that physicians set a LDL cholesterol goal of less than 1.8 mmol/L (<70 mg/dL) for high risk patients, based on studies such as the Heart Protection Study. The goals of 130 mg/dL and 160 mg/dL for LDL cholesterol in moderate and to low-risk individuals remained unchanged (Jenkins et al., 2005b). In the 2005 Guidelines for Americans a maximum fat intake of 35% of total calories is recommended (U.S. Department of Health and Human Services: U.S. Department of Agriculture, 2005). These guidelines also stated that:

- Saturated fat should supply no more than 10% of total calories
- Cholesterol intake should be limited to less than 300 milligrams per day.
- Trans fat intake is to be kept as low as possible.
- Fiber-rich fruits, vegetables, and whole grains should be chosen often.

In 2006, the AHA released revised diet and lifestyle recommendations (Lichtenstein et al. 2006; Mozaffarian, Katan, Ascherio, Stampfer & Willett, 2006). One of the most significant changes from prior guidelines was a recommendation to consume
at least two weekly servings of oily fish, such as tuna or salmon. The other recommendations were:

- Balance calorie intake and physical activity to achieve or maintain a healthy weight.
- Consume a diet rich in vegetables and fruit.
- Choose whole grain, high-fiber foods.
- Limit the intake of saturated fat to <7% of energy, \textit{trans} fat to <1% of energy and cholesterol to <300 mg per day.
- Minimize the intake of beverages and foods with added sugar.
- Choose and prepare foods with little or no salt.
- If you consume alcohol, do so in moderation.
- When you eat food that is prepared outside the home, follow the American Dietetic Association diet and lifestyle recommendations.

In addition to guidelines in the United States, European and British guidelines for the management of hypercholesterolemia recommend dietary modification as first-line therapy and emphasize that soluble fiber lowers serum cholesterol and could therefore potentially reduce the risk of CHD. It is suggested that treatment guidelines be revised to include a soluble fiber product as an adjunct to diet for patients where diet alone has failed and where lifelong therapy with lipid-lowering drugs is inappropriate (MacMahon, 1999).
E. Soluble Fiber and Lowering of CVD Risk

1. Epidemiological Studies

The association between elevated LDL cholesterol concentrations and increased risk for CHD has made the scientific community aware of dietary sources that might effectively reduce blood cholesterol concentrations. Much attention has been given to the role of dietary fiber intake in the control of lipid and lipoprotein metabolism (Anderson et al., 1990). Epidemiological studies have suggested that a diet high in water-soluble fiber is inversely associated with the risk of CVD. Observational studies show a 20 to 40% difference in CHD risk between the highest and lowest fiber intake groups (Institute of Medicine: Food and Nutrition board, 2005). Observational data from 10 cohort studies suggested that a 10 gram per day increase in dietary fiber was associated with a 14% lower risk of all coronary events (Pereira et al., 2004). These findings underlie current dietary recommendations to increase water-soluble fiber intake (Elke et al., 2008).

In a meta-analysis of observational data from 10 cohort studies on fiber and CVD risk, Pereira et al. (2004) reported that a diet containing 10 grams per day of dietary fiber was associated with a 14% lower risk for all coronary risk disorders. Fiber derived from cereal and fruit sources, and not vegetables, was inversely associated with coronary risk. Although both insoluble and soluble fiber have been associated with lower risk of CHD (Pereira et al., 2004), evidence for the association of fiber in reducing coronary risks appears to be much stronger for soluble than insoluble fiber (Bazzano et al., 2003).

In 2002 the National Academy of Science summarized the results of large, prospective, epidemiologic studies having a protective effect of dietary fiber against CHD
and formed the basis for new recommendations for fiber intake. Thus, 38 and 25 grams per day is recommended for men and women, respectively, for all ages beginning in youth, based on an intake of 14 g of fiber per 1000 kilocalories (Institute of Medicine 2002).

Data has also appeared indicating that dietary fiber may reduce the risk of stroke. The Nurses’ Health study showed that women with a high ingestion of whole grains, fruit, and vegetables had a slightly reduced risk of stroke (Liu et al., 2003). However, the data from the Atherosclerosis Risk in Communities study were not in line with these findings (Steffen et al., 2003). Two other studies, the National Health and Nutrition Examination Survey (NHANES) study, and a Danish study, showed a weak inverse association between fruit and vegetable fiber ingestion and stroke incidence (Bazzano et al., 2002; Johnsen et al., 2003).

2. Clinical Studies

Dietary fiber is a collective term which includes a variety of plant substances, mainly non-starch polysaccharides and lignins, which are resistant to digestion by digestive enzymes. These can be classified into two groups based on water solubility. In humans, the structural or matrix fibers (lignins, cellulose, and some hemicelluloses) are insoluble, and the natural gel-forming fibers (pectins, gums, mucilages, and the remainder of the hemicelluloses) are soluble (Truswell, 1995). In contrast to water-insoluble fibers, clinical studies have focused on soluble fibers like oats and psyllium, pectin and guar gum that may lower blood total and LDL cholesterol (Glore, Van Treek, Knehans & Guild, 1994).
More than four decades ago De Groot, Luyken & Pikaar (1963) were the first to demonstrate that a daily consumption of 300 grams of bread containing 140 grams of rolled oats, a rich source of soluble fiber, for three weeks resulted in an 11% decrease in serum total cholesterol concentration in men. Many trials using oat products were done thereafter. In a meta-analysis of 12 such trials, Ripsin, Keenan & Jacobs (1992) found that a daily intake of ~3 grams of soluble fiber from oat products for 18 days to three months resulted in a modest reduction of total cholesterol concentrations of ~0.13 mmol/l. This reduction of total serum cholesterol was seen in both men and women. Subsequently, Braaten et al. (1994) demonstrated that the cholesterol lowering effect of oat products can be attributed to their main soluble fiber component, β-glucan. On January 21, 1997, the FDA approved a health claim on food products which stated, that “a diet high in soluble fiber from whole oats (oat bran, oatmeal and oat flour) and low in saturated fat and cholesterol may reduce the risk of heart disease” (FDA, 1997). The approved amount for health claims was 3 grams of soluble fiber a day. To qualify for the health claim, the whole oat-containing food must provide at least 0.75 grams of soluble fiber per serving. The FDA later updated health claims to support barley as a source of soluble fiber on May 19, 2006. On May 12, 2008 an amendment stated that foods that could claim to be sources of soluble fiber did not have to be low fat foods.

A meta-analysis subsequent to the FDA health claim (Brown et al., 1999) included 67 controlled trials. The 67 trials included 25 trials of oat products, 17 of psyllium, 7 of pectin, and 18 of guar gum. The meta-analysis included 2990 subjects (1733 men, 1011 women) with an average age of 50 years. The average dose of soluble fiber was 9.5 grams daily administered over a mean treatment period of 49 days. Fifty-
seven of 67 studies (85%) in the meta-analysis used a control fiber low in soluble fiber, as wheat bran, cellulose-based placebo, or corn flakes.

The effect of soluble fiber in the full dose response range showed that 2-10 grams per day of soluble fiber significantly reduced total cholesterol by 1.7 mg/dL and LDL cholesterol by 2.2 mg/dL. Soluble fiber consumption did not significantly affect triglyceride or HDL cholesterol concentrations (Brown et al., 1999). The various sources of soluble fiber including oats, psyllium, pectin and guar gum each significantly lowered total cholesterol and LDL cholesterol respectively as shown in Table 2.3.

**Table 2.3** One Gram of Various Sources of Soluble Fiber and Their Effects on Total and LDL Cholesterol.

<table>
<thead>
<tr>
<th>Lipid Fraction</th>
<th>1 gram oats</th>
<th>1 gram psyllium</th>
<th>1 gram pectin</th>
<th>1 gram guar gum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>-0.037 mmol/L</td>
<td>-0.028 mmol/L</td>
<td>-0.070 mmol/L</td>
<td>-0.026 mmol/L</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>(-1.42 mg/dL)</td>
<td>(-1.10 mg/dL)</td>
<td>(-2.69 mg/dL)</td>
<td>(-1.13 mg/dL)</td>
</tr>
<tr>
<td>LDL</td>
<td>-0.032 mmol/L</td>
<td>-0.029 mmol/L</td>
<td>-0.055 mmol/L</td>
<td>-0.033 mmol/L</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>(-1.23 mg/dL)</td>
<td>(-1.11 mg/dL)</td>
<td>(-1.96 mg/dL)</td>
<td>(-1.20 mg/dL)</td>
</tr>
</tbody>
</table>

One gram of soluble fiber from oats, psyllium, pectin or guar gum resulted in decreased total cholesterol and LDL cholesterol as shown in the table above. When the meta-analysis was repeated for the practical dose range (≤10 g/d) it was found that the overall effects of fiber were greater compared with the results for the total dose range: 1 g soluble fiber/d produced a change in total and LDL cholesterol of -0.045 and -0.057 mmol/L (-1.73 and -2.21 mg/dL, respectively). There was no significant dose-response relation between soluble fiber and changes in HDL-cholesterol or triglyceride.
concentrations. The type of soluble fiber used was not a significant predictor of lipid changes after the initial lipid concentration was controlled by linear regression. Ripsin et al. (1992) had reported a more pronounced decrease in serum concentrations of total cholesterol when baseline concentrations were increased. On the other hand, Brown et al. (1999) found no evidence that initial serum concentrations of total cholesterol were related to changes in total cholesterol. However, LDL cholesterol concentrations decreased significantly more at higher baseline concentrations of LDL cholesterol.

A number of studies that succeeded the 1999 meta-analysis will be reviewed to illustrate some of the supporting data for this research project. Kris-Etherton et al. (2002) evaluated 150 moderately hypercholesterolemic men and women 25 to 70 years of age to understand whether an intervention of foods high in soluble fiber from psyllium and/or oats (four servings of high fiber foods daily) plus a telephone-based, personalized behavior change support service of improved serum lipids and elicited cholesterol-managing lifestyle changes vs. usual care. This 7-week study showed that total cholesterol decreased 5.6%, LDL cholesterol decreased 7.1% and triglycerides 14.2% in the intervention group (significantly different from the usual care group).

Two studies measured the progression of atherosclerosis in relation to fiber intake and revealed that viscous fiber showed an inverse relationship to the progression of carotid atherosclerosis in 40 to 60 year aged men and women without heart disease (Wu et al., 2003), with higher ingestion of whole-grain foods and cereal fiber associated with lower progression of coronary atherosclerosis (Erkkila, Herrington, Mozaffarian & Lichtenstein, 2005).
Gardner and colleagues performed a four week study in which a complete plant-based diet was provided for participants in the study. This achieved an additional reduction in the LDL cholesterol level of 4% over the 4.6% reduction in the control group giving a reduction of nearly 9% in LDL cholesterol from baseline in participants on a plant-based diet. The greater reduction in serum LDL cholesterol was attributed to the inclusion of foods with more viscous fiber (41g/2000 kcal vs. 22g/2000 kcal) (Gardner et al., 2005).

A recent summary of the literature by Elke & Mensink (2008) emphasizes that the importance of increasing the dietary intake of water-soluble dietary fibers is increasingly recognized. Well-controlled intervention studies have now shown that four major water-soluble fiber types—β-glucan, psyllium, pectin and guar gum—effectively lower serum LDL cholesterol concentrations, without affecting HDL cholesterol or triglyceride concentrations. It is estimated that for each additional gram of water-soluble fiber in the diet serum total and LDL cholesterol concentrations decrease by −0.028 mmol/L (-1.08 mg/dL) and −0.029 mmol/L (-1.122 mg/dL), respectively. This would be equivalent to a 5% reduction in total cholesterol from a baseline of 200 mg/dL with the consumption of 10 grams of soluble fiber a day. Despite large differences in molecular structure, no major differences existed between the different types of water-soluble fiber, suggesting a common underlying mechanism. It is most likely that water-soluble fibers lower the (re)absorption of bile acids in particular. As a result hepatic conversion of cholesterol into bile acids increases, which will ultimately lead to increased LDL uptake by the liver.

The most recent systematic consideration of the relationship between oat consumption and cholesterol reduction was published in the form of a review by the
Cochrane Collaboration (Kelly, Summerbell, Brynes & Whittaker, 2007). Three of the eight oat-based studies selected in the Cochrane review were included in the FDA’s evaluation of the oat-soluble fiber health claim, and the remaining five studies were published after 1997. When all eight oat studies were pooled in a meta-analysis, a significant effect of oat consumption to lower total and LDL cholesterol concentrations was observed. The reduction in LDL cholesterol from baseline was -4.9% (95% confidence interval of -7.6% to -2.4%) (Kelly et al., 2007). The review concluded that “there is surprisingly little evidence available from controlled trials about the effects of wholegrain foods and diets other than oats and there is a need for studies in this area.”

3. Recommendations

Given this background it is not surprising that both the NCEP and AHA guidelines recommend an increased consumption of fiber-rich foods to achieve a total daily intake of 30 grams per day (Lichtenstein et al., 2006; Expert Panel, 2001). The consumption of 5-10 grams per day of soluble fiber such as β glucans, guar and psyllium reduces blood LDL cholesterol levels by about 5% (Expert Panel, 2001). While fiber supplements are often touted as a convenient way of achieving this intake, there is no evidence that supplements achieve the same effects as whole foods (Poli et al., 2008). A diet rich in vegetables, fruit, whole grains and legumes is supported by a wealth of evidence, and may work via diverse biological mechanisms to prevent CVD.

F. The β-Glucan Component of Dietary Fiber

All types of plant foods including fruits, vegetables, legumes and whole grains contain fiber. Many types of dietary fiber resemble starches, they are polysaccharides, but
are not digested in the human gastro-intestinal tract. Examples of these nonstarch polysaccharides include cellulose, hemicellulose, pectins, gums and β-glucan. β-glucans are polysaccharides of branched glucose units which are found in large amounts in oats and barley (Insel et al., 2007). While oats contain around 4% β-glucan, 5-10% β-glucan is present in barley. Despite its naturally high β-glucan content, barley fiber has been investigated in fewer trials since barley is less palatable than oats and a less common dietary component. Nevertheless, the FDA concluded, based on the totality of available scientific evidence that, whole grain barley and dry milled barley products, such as flakes, grits, flour, and pearled barley, are appropriate sources of β-glucan water-soluble fiber to claim that they reduce the risk of CVD (US FDA 2001, 2004).

It has been suggested, however, that the cholesterol-lowering effect of β-glucan depends on the food matrix or the method of processing of the oat products. For example, incorporation of β-glucan into oat milk lowered serum concentrations of LDL cholesterol by 0.063 mmol/L for each gram of β-glucan (Onning et al., 1999). These results suggested the efficacy of β-glucan preparations increased when they were incorporated into liquid products.

Brown et al., in their meta-analysis in 1999 found serum concentrations of total cholesterol decreased significantly by 0.060 mmol/L and those of LDL cholesterol by 0.062 mmol/L, when expressed per gram of β-glucan intake. These decreases were approximately twice those of 0.037 and 0.032 mmol/L, respectively, for each gram of soluble fiber intake from oats. This is equal to decreases of about 2 mg/dL and 2.5 mg/dl, respectively. Subsequently, Naumann et al. (2006) examined the effects of β-glucan-
enriched fruit juice on serum lipids and lipoproteins and on markers of cholesterol absorption (serum concentrations of plant sterols) and synthesis (serum concentrations of lathosterol). In addition, they measured effects on lipid-soluble antioxidants. Healthy subjects consumed daily a fruit drink providing 5 g rice starch (control group) or β-glucan from oats for five weeks (parallel design). Results showed the differences between the control and β-glucan groups in the change in serum concentrations of total and LDL cholesterol, respectively, were -4.8% (P = 0.012) and -7.7% (P = 0.005). The differences between the groups in the change in serum concentrations of lathosterol and sitosterol were -13% (P = 0.023) and -11% (P = 0.030), respectively. No significant effects were found on fat-soluble antioxidants. β-glucan lowers serum concentrations of total and LDL cholesterol when incorporated into a fruit drink. The study concluded that reduced cholesterol absorption contributes to the cholesterol-lowering effect of β-glucan without affecting plasma concentrations of lipid-soluble antioxidants (Naumann et al., 2006).

**G. Mechanisms of Lipid Lowering by Soluble Fiber**

Several mechanisms of action for the hypocholesterolemic effect of soluble fibers have been suggested. Soluble fiber may increase the binding of the acids in the intestinal lumen leading to a decreased enterohepatic circulation of bile acids and a subsequent increase in the hepatic conversion of cholesterol to bile acids (Bell et al., 1999). This has been demonstrated for psyllium, but not other fiber types (Poli et al., 2008). Soluble fiber binds bile acids in the gastrointestinal tract, and excretes them in the feces rather than recycling and reusing them. Additional bile acids must be made from cholesterol, thus lowering the total amount in the body. In the large intestine, intestinal bacteria partially
digest fiber and then produce short-chain fatty acids, which are linked to reduced cholesterol synthesis (Institute of Medicine: Food and Nutrition Board 2005).

Another suggested mechanism of action is that the increased viscosity of the food mass in the small intestine because of soluble fiber leads to the formation of a thick unstirred water layer, adjacent to the mucosa, which may act as a physical barrier to reduce the absorption of nutrients and bile acids (Beer, Arrigoni & Amad’O, 1995). Furthermore, soluble fiber may reduce the rate of glucose absorption, yielding a lower glycemic response and lower insulin concentrations, which may later result in a reduced hepatic cholesterol synthesis (Glore et al., 1994).

High intakes of oat bran was shown to be associated with increased bile acid synthesis, which increased cholesterol uptake from the circulation and decreased plasma cholesterol concentrations (Andersson, Ellegard & Andersson, 2002). Oat products have been reported to decrease the concentrations of small, dense LDL particles which are considered to be more atherogenic than larger, less dense LDL particles (Lamarche et al., 1997).

H. Time Course and Choice of Dose

Lifestyle change takes about 3-6 weeks to result in a drop in serum cholesterol (Brown et al., 1999). Changes in blood lipid concentrations are evident within 3-5 weeks of TLC (Expert Panel, 2001). The half-life of LDL is 3-4 days, meaning that most LDL in the blood is gone and replaced by new LDL by about two weeks. So any changes in diet require at least 2-3 weeks to be reflected in serum lipid levels. In a previous unpublished pilot study conducted by the doctoral student, the length of time chosen to see the effect of increased fig consumption on blood lipid concentrations was 6 weeks;
however, a shorter period of 3-5 weeks is adequate based on lipid physiology. Most studies have chosen time periods of 4-8 weeks (Brown et al., 1999; Gardner et al., 2005; Naumann et al., 2006). After eight weeks, LDL cholesterol concentrations remained the same (FDA, 1997).

The rationale of choice of dose is based on studies in the literature along with the FDA advisory board which indicated that 3 grams of ß-glucan may lead to a drop in cholesterol by about 6% after 4 weeks of intervention (FDA, 1997). This study design provides three servings of figs daily (3-6 grams of soluble fiber/ß-glucan). Each serving of figs (40 grams) provides about 1-2 grams of ß-glucan, yielding a total of 3 grams at the minimum, if three servings (120 grams) are eaten per day (California Fig Advisory Board, 2003). Given an expected decrease of about 2 mg/dL and 2.5 mg/dl respectively, in total and LDL cholesterol per gram of ß-glucan (total decreases of 6 mg/dL and 7.5 mg/dL, respectively) as cited by Brown et al. (1999) and an estimated average serum LDL cholesterol at baseline of about 130 mg/dL, corresponding to a serum total cholesterol of about 220 mg/dL, the absolute reduction of total and LDL cholesterol would be about 3% and 6%, respectively.

I. **Preparation and Composition of California Mission Figs**

Dried fruit are simple and easy to administer. There is no preparation time needed. The fruit should be served as part of a meal, so that the liquidity of other food increases the desired effects. A recent study found that figs have the best nutrient score among the dried fruits when examining calcium, iron, potassium and fiber (Vinson et al., 2005). California black mission figs (40 grams) provide five grams of fiber which is 20% of the recommended daily fiber intake, more fiber than two slices of whole grain bread,
an ounce of almonds, a medium orange, or one half cup of broccoli. As Table 2.4 shows, of all dried fruits, figs contain the largest amount of dietary fiber.

**Table 2.4 Nutritional Information for Raisins, Dates, Dried Figs and Prunes/Plums**

<table>
<thead>
<tr>
<th>Nutrition facts</th>
<th>Raisins</th>
<th>Dates</th>
<th>Dried Figs</th>
<th>Prunes/Plums</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serving Size:</td>
<td>⅛ cup (40g)</td>
<td>⅛ cup (40g)</td>
<td>⅛ cup (40g)</td>
<td>⅛ cup (40g)</td>
</tr>
<tr>
<td>Calories</td>
<td>130</td>
<td>120</td>
<td>113</td>
<td>110</td>
</tr>
<tr>
<td>Calories from Fat</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>% Daily Value</td>
<td>% Daily Value</td>
<td>% Daily Value</td>
<td>% Daily Value</td>
<td>% Daily Value</td>
</tr>
<tr>
<td>Total Fat</td>
<td>Total Fat 0g 0%</td>
<td>Total Fat 0g 0%</td>
<td>Total Fat 0g 0%</td>
<td>Total Fat 0g 0%</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>Saturated Fat 0g 0%</td>
<td>Saturated Fat 0g 0%</td>
<td>Saturated Fat 0g 0%</td>
<td>Saturated Fat 0g 0%</td>
</tr>
<tr>
<td>Trans Fat</td>
<td>Trans Fat 0g 0%</td>
<td>Trans Fat 0g 0%</td>
<td>Trans Fat 0g 0%</td>
<td>Trans Fat 0g 0%</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Cholesterol 0mg 0%</td>
<td>Cholesterol 0mg 0%</td>
<td>Cholesterol 0mg 0%</td>
<td>Cholesterol 0mg 0%</td>
</tr>
<tr>
<td>Sodium</td>
<td>Sodium 10mg 0%</td>
<td>Sodium 0mg 0%</td>
<td>Sodium 5mg 0%</td>
<td>Sodium 5mg 0%</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>Total Carbohydrate</td>
<td>31g 10%</td>
<td>Total Carbohydrate</td>
<td>26g 9%</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>2g 8%</td>
<td>2g 14%</td>
<td>3g 20%</td>
<td>5g 10%</td>
</tr>
<tr>
<td>Sugars</td>
<td>Sugars 29g</td>
<td>Sugars 29g</td>
<td>Sugars 29g</td>
<td>Sugars 29g</td>
</tr>
<tr>
<td>Protein</td>
<td>Protein 1g</td>
<td>Protein 1g</td>
<td>Protein 1g</td>
<td>Protein 1g</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Vitamin A &lt;2%</td>
<td>Vitamin A 0%</td>
<td>Vitamin A &lt;2%</td>
<td>Vitamin A &lt;5%</td>
</tr>
<tr>
<td>Calcium</td>
<td>2%</td>
<td>2%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Vitamin C &lt;2%</td>
<td>Vitamin C &lt;2%</td>
<td>Vitamin C &lt;2%</td>
<td>Vitamin C 4%</td>
</tr>
<tr>
<td>Iron</td>
<td>6%</td>
<td>2%</td>
<td>6%</td>
<td>6%</td>
</tr>
</tbody>
</table>

J. Other Potential Health Benefits

For many years, the concept of the ingestion of high fiber meals has been offered as an effective manner to reduce the risk of obesity, promote low glycemic food intake and feelings of satiety (Ball et al., 2003; Liu et al., 2003). This aspect of is beyond the proportions of this proposal.

Saltzman et al. (2001) reported that regardless of whether or not weight is lost, diets that are high in fiber contribute to a modest decrease in blood pressure. Though this proposal does not focus on blood pressure, blood pressure will be considered. Lower C-reactive protein values have also been reported in conjunction with the consumption of high fiber diets (King, Egan & Geesey, 2003; Ajani, Ford & Mokdad, 2004). A viscous fiber intake of 9.8g/1,000 kcalories lowered C-reactive protein concentrations (Jenkins et al., 2003) in one study, suggesting that dietary fiber may have anti-inflammatory properties. However, additional data is needed to provide a clearer understanding of the potential effect of fiber on C-reactive protein. If financially possible, blood samples may be frozen for analyses of markers of inflammation in this study.

In a randomized crossover study, 10 non-smoking individuals were assigned to consume 40 grams of dried mission figs. The control group ingested 240 ml of the soft drink, Sprite. Blood samples were taken at 0,1,2,4 and 6 hours after consumption. Lunch was eaten after the 4 hour blood sample. Consumption of mission figs produced a significant increase in plasma antioxidant capacity for four hours after consumption compared to the control group (Vinson et al., 2005). If financially possible, blood samples may be frozen for analyses of antioxidant capacity in this study.
K. Conclusions

Diet plays a major role in reducing the risk of CHD. This has led to a search for specific foods and food components that may help improve the blood lipid profile. Nutrition research is transitioning an era that began with the study of macronutrients and micronutrients and now focuses on evaluating food-based approaches, specifically on identifying foods that maximally reduce risk for CVD. Novel foods that are rich in soluble fiber may be potentially useful for the purpose of modifying atherogenic blood lipid concentrations.
CHAPTER 3

METHODS

A. Overview

Approximately one-half of the adults in the United States have elevated cholesterol levels (Expert Panel, 2001). The hypothesis of the study is that consumption of California mission figs may lower serum lipid concentrations. California mission figs have been reported to contain appreciable amounts of antioxidants plus high levels of soluble fiber (Vinson et al., 2005; California Fig Advisory Board, 2003). To date, to our knowledge, no studies have been conducted to study the effect of fig consumption in lowering serum lipid concentrations. If the consumption of California mission figs is proven to lower total and LDL cholesterol concentrations, this can make an impact in the public setting by adding to the list of functional foods that lower serum lipids. Since studies (Rispin et al., 1992) indicate that 3 grams of soluble fiber have shown to lower total cholesterol and LDL cholesterol, it would be beneficial to use the same amount or a similar dosage in this study.

B. Study Design

The California Mission Figs Feeding Trial was a 12 week randomized, crossover intervention study, which consisted of two phases, intervention and control. Following screening procedures lasting two weeks, one hundred adult men and women were randomly assigned to either the intervention or control study phase for the first five weeks of the trial and then switched to the other phase for the second five weeks of the trial. During the intervention phase, participants were asked to incorporate a prepackaged,
pre-weighed 40 gram serving of California mission figs (3-5 figs) at each meal for a total of three meals a day in their habitual diet for five weeks. Consumption of figs outside of the packages provided by the study and prune (dried plum) consumption were not allowed, as prunes are dried fruits that are also rich in soluble fiber. During the control study phase, participants followed their habitual diet without the consumption of figs or prunes. Each study participant received a $25.00 honorarium for participating in the study.

<table>
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<tr>
<th>Weeks 2 to 7</th>
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<td>Group 1: Habitual diet</td>
<td>6 and 7</td>
<td>Mission fig</td>
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<td>supplemented diet</td>
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<td>Group 2: Mission fig</td>
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<td>Blood draws</td>
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**Figure 3.1** The Study Design

The Gantt chart and the budget for the study are shown in appendices B and C.

**C. Study Participants and Recruitment**

141 potential subjects were recruited and screened. Eligible participants were men and women aged 30 to 75 years with LDL cholesterol concentrations in the following ranges: above optimal (100-129 mg/dL), borderline (130-159 mg/dL) or high (160-189 mg/dL) – only if given clearance by their physician. Additional inclusion criteria were
body mass index of 18.5-35 kg/m², no cigarette smoking within the past 1 year, and written, informed consent. Exclusion criteria were any secondary cause of hyperlipidemia (kidney or liver disease, untreated hypothyroidism), current or previous (within the past two months) use of any lipid-lowering drug, type 1 diabetes or uncontrolled type 2 diabetes (HbA1c > 7%), triglyceride concentrations >300 mg/dL, current or previous (within the past three months) treatment with estrogen or steroid therapy, stated dislike of figs, use of certain dietary supplements e.g. Metamucil, sterol/stanol margarine and others that may have influenced lipid concentrations, chronic disease that may have affected concentrations of lipids or markers of inflammation (e.g. cancer other than skin cancer within the last 5 years, chronic rheumatological disease, chronic severe depression) and any condition deemed by the study investigators to limit compliance with the protocol (e.g. drug abuse).

Participants were recruited from churches and businesses in communities surrounding San Bernardino, California. Presentations and flyers about the California mission fig study were presented at churches and business establishments as well as at the Drayson Center (gym) at Loma Linda University. Potential subjects were recruited by flyers approved by the Institutional Review Board. Individuals who filled out the flyer with their name and phone number were called for an appointment for the screening visit. Upon arrival at their screening appointment they were provide with explanations of all study procedures in detail and given the informed consent form (Appendix C). Only subjects that signed the consent form were allowed to continue with the following procedures.
D. Procedures

1. **Weeks 0 to 2 Screening (fasting, if not fasting, one extra visit will be required within this period)**

   At the screening visit potential subjects were individually given a detailed explanation about the purpose of the study and the procedures to be followed during the course of the 12-week study as described above. The subjects were informed that the only change required in their regular diet was to be the inclusion of 3-5 dried mission figs (serving size of 40 grams) to be eaten at each meal three times daily (totaling 120 grams) seven days a week for a period of five weeks during the intervention phase of the trial. Consumption of figs outside of this limit or of prunes was not allowed throughout the study. Informed, written consent was obtained. The study subjects completed a brief health and physical activity questionnaire (appendix D). Baseline blood samples were drawn after a 12 hour fasting period at the screening visit, or within 10 days. Vital signs and anthropometrics were measured and recorded.

   Potential participants who met the study criteria in regard to the fasting serum concentrations were contacted by telephone and given an appointment for the week 2 randomization visits which were scheduled within 2 weeks of the screening visit.

2. **Week 2 Randomization (fasting not required)**

   Vital signs and anthropometrics were measured and recorded. The study procedures were reiterated and subjects were asked to complete a short health questionnaire (appendix E), to check whether any changes had occurred in their health status or use of medications since the screening visit.
a. Procedure for Randomization. A random numbers table was used to generate a list of randomized numbers. Even numbers were designated randomization to the intervention phase followed by the control phase. Odd numbers were designated randomization to the control phase followed by the intervention phase. Intervention or control was written on slips of paper, and these slips were placed in consecutively numbered opaque envelopes. Subjects were consecutively given a randomization number corresponding to the numbered envelopes. After assignment of the number, the envelope was opened, the group assignment noted, and the subject informed.

Subjects randomized to the fig consumption phase (intervention) first received enough prepackaged fig portions for three weeks of consumption (1 extra week in case the follow-up visit was delayed). They were instructed not to make any changes in their habitual diet (with the exception of not eating additional figs or prunes) except as noted below. They were asked to consume (40 g) of figs three times a day totaling 120 grams, with meals. Subjects concerned about weight gain were permitted to substitute the figs for their usual desserts or sweet snacks. If the fig portions were forgotten (e.g. not taken to work) they could be consumed at a later time in the day with meals or as a snack. Daily compliance with the assigned portions of figs was recorded on a compliance form provided (see appendix E).

Subjects randomized to the usual diet phase (control) first were asked to follow their usual diet (with the exception of not eating figs or prunes).

A telephone interview to obtain a 24-hour dietary recall was performed on a day chosen randomly between weeks 2 and 4.
3. **Week 4 Follow-up Visit- Fig Pickup for Intervention Group (nonfasting)**

Participants who were consuming figs were assigned to attend the study center to receive the remaining portion of the prepackaged figs for the last three weeks (4 week supply). They were reminded to follow the study protocol and encouraged to ask any questions and explain any changes that may have affected them while on the study. Compliance sheets were gathered and new ones were delivered. Those consuming their usual diet were reminded not to consume any figs or prunes for the remaining next three weeks.

Subjects were interviewed in person to obtain a 24 hour diet recall. A telephone interview to obtain a 24-hour dietary recall was performed on a day chosen randomly between weeks 4 and 6.

4. **Week 6 Follow-up Visit (fasting)**

Vital signs and anthropometrics were measured and recorded. All the participants in the study had blood samples drawn after a 12 hour fast. Compliance sheets were gathered from participants consuming figs and new ones were delivered.

5. **Week 7 Follow-up Visit (fasting)**

Vital signs and anthropometrics were measured and recorded. All the participants in the study had blood samples drawn after a 12 hour fast. Compliance sheets were gathered from participants consuming figs.

**This visit is the crossover visit.** Participants who were not eating figs began to consume 40 g prepackaged figs at each meal three times daily totaling 120 grams, were given compliance sheets and a three week supply of figs (1 extra week in case of delay of follow-up appointment). Instructions were given to participants not to consume any other
dried fruit other than the prepackaged figs or prunes during the subsequent five weeks. Those concerned about weight gain from the additional 330 kcalories/day from figs, were advised to substitute the figs for their usual desserts.

Those persons crossing over from figs to their usual diet were reminded not to consume any figs or prunes for the next five weeks. All subjects completed a brief health questionnaire (appendix E) that also included fig attitude questions for those just completing fig consumption.

A telephone interview to obtain a 24-hour dietary recall was performed on a day chosen randomly between weeks 7 and 9.

6. **Week 9 Follow-up Visit- Fig Pick-up for the Intervention Group**

*(nonfasting)*

Participants were assigned to attend the study center to receive the remaining portion of the prepackaged figs for the last three weeks (4 week supply). They were reminded to follow the study protocol and encouraged to ask any questions and explain any changes that affected them while on the study. Compliance sheets were gathered and new ones delivered.

Those consuming their usual diet were reminded not to consume any figs or prunes for the remaining next three weeks.

All subjects were interviewed in person to obtain a 24 hour diet recall. A telephone interview to obtain a 24-hour dietary recall was performed on a day chosen randomly between weeks 9 and 11.
7. **Week 11 Follow-up Visit (fasting)**

Vital signs and anthropometrics were measured and recorded. All the participants in the study had blood samples drawn after a 12 hour fast. Compliance sheets were gathered from participants consuming figs and new ones were delivered.

8. **Week 12 Follow-up Visit (fasting)**

Vital signs and anthropometrics will be measured and recorded. All the participants in the study had blood samples drawn after a 12 hour fast. Compliance sheets were gathered from participants consuming figs. All subjects completed a brief health questionnaire (appendix E) that also included fig attitude questions for those just completing fig consumption.

A thank you letter was given to each participant who completed the 12 week fig research study. Participants were asked to leave their current address (if it was changed after joining the study) so that the $25.00 check could mailed to them.

**E. Procedures for Blood Draws**

At each visit involving blood sampling (screening, week 6, week 7, week 11, week 12), subjects were asked to fast overnight. Water and standard allowed medication was permitted to be taken on the morning prior to the visit. Blood samples were drawn between 7:00 to 10:00 AM. At screening one 10 ml red top tube was drawn and centrifuged. Samples were sent to the Loma Linda University Medical Center Clinical Laboratory for analysis of total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride levels as well as ALT, creatinine and glucose. At follow-up visits 6, 7, 11 and 12, one red top tube of 10 ml and one 4 ml purple top tube for plasma were drawn. The blood was allowed to cool for about 10-15 minutes at room temperature before being put
on ice. Then samples were placed in a cooler and transported to Nichol Hall Room 1112. There samples were separated in a refrigerated centrifuge at 1800 x g and 4 degrees centigrade. Serum/plasma was then drawn by aliquot and placed into vials kept in the -70 freezer in Nichol Hall Room 1112A. Frozen samples for the analysis of lipids were sent all together at the end of the trial for analysis at the Research Laboratory, University of California at Davis. The rest of the samples may be used when financing is available for analysis of apolipoprotein B, C-reactive protein (CRP), markers of endothelial activation and oxidized LDL (all hypotheses related to lipids and atherosclerosis). Experienced certified venipuncturists were hired to perform the blood sampling.

F. Measurement of Blood Pressure and Pulse (Vital Signs)

The measurements were taken after the blood tests were completed and considered part of usual clinical study practice. The following procedure was followed when taking blood pressure and pulse measurements on all participants.

- Subjects were seated with back supported and arm bared and supported
- Subjects refrained from ingesting caffeine for 30 minutes before measurement were taken.
- Measurements were begun after at least 5 minutes of rest
- Appropriate cuff size and calibrated equipment was used
- Two readings were averaged
- Pulse was measured for 60 seconds before blood pressure measurement

G. Measurement and Justification of Anthropometrics

Moderate weight loss and increased physical activity are important components of blood lipid control (Poli et al., 2008). These interventions may have lead to declines in
triacylglycerols and increased HDL cholesterol concentrations. As this study is attempting to isolate the effect of a single factor, increased soluble fiber consumption, on blood lipid concentrations, participants were encouraged to maintain a stable weight and not change physical activity habits. Body weight was monitored.

1. Height and Weight

Subjects’ height was measured (without shoes) using a standard and calibrated wall stadiometer only at the screening visit. Subjects were weighed using the Scale-Tronix 5005 stand-on digital scale at screening and visits at weeks 6, 7, 11 and 12. This scale is designed for patients up to 600 pounds and was last calibrated November 2007.

2. Weighing-In Procedure

- Remove shoes
- Remove jacket and other outer garments
- Empty pockets
- Stand on scale and wait for digital reading and
- Record results in the chart

3. Waist Circumference

Waist circumference was measured to the nearest 0.1 cm at the narrowest level over light clothing, with the use of an unstretched tape measure and without any pressure to the body surface. Waist was measured at screening and at weeks 7 and 12.

H. Dietary Assessment and Tracking Procedures

Dietary assessment was needed to monitor other changes in the diet than increased consumption of figs during the intervention phase compared to the control.
phase. This was documented by two phone interviews and 1 in person interview to obtain dietary information (24 hour diet recall as described in appendix H) on all randomized participants in each study phase for a total of 6 recalls. The phone interview was completed on a random day between weeks 2 and 4, 4 and 6, 7 and 9 and 9 and 11. The day was be chosen by pulling a weekday or weekend day from a box containing Sundays through Fridays designed on folded papers. The day was returned to the box after being drawn. If the interview was not possible to have been drawn on the day, it was conducted as soon as possible thereafter. The in-person interviews were completed on the week 4 and week 9 visits.

The Nutrition Data System for Research (NDSR) which is maintained by the Nutrition Coordinating Center at the University of Minnesota was the software used to acquire the 24 hour dietary recall. The recall was performed by registered dietitians who were blinded to the subject’s group assignment.

Appendix I is a list for the information of the dietitian and study investigators indicating portions of sweet snacks and desserts that could be substituted by figs. Appendix J show the dietary recommendations distributed at the beginning of the study to all participants regarding the NCEP recommended diet for elevated blood cholesterol.

I. Tracking Procedures

On the evening before appointments, participants were called to be reminded about their appointment and for fasting visits, to be fasting on the morning of the visit. Text messages were permitted to be used instead of a phone call for appropriate participants. Participants who missed their scheduled appointments were contacted for a new appointment if they wished to continue in the study.

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J. Nutritional Analysis of California Mission Figs

California mission figs were obtained from the California Fig Board. An analysis was performed on California mission figs to determine the amount of soluble and total fiber present in a serving (40 grams) of figs. The California Fig Advisory Board has comparison data showing the β-glucan content of mission figs.

K. Data Analysis

Data analysis was conducted by the doctoral student. All data was entered into the SPSS version 16 database and rechecked. Variables were checked for skewedness and log transformation was done on skewed variables prior to analysis (e.g. triglyceride was likely to be skewed).

Data were analyzed by means of comparative tests. Descriptive statistics were expressed as means and standard deviations for normally distributed variables, and medians and percentiles for skewed variables. Dietary treatments effects on blood cholesterol variables were estimated by using mixed linear models, which included a random factor for the subjects. Statistical analyses were performed with SPSS software for windows (version 13, Chicago, IL) which assumed the variances and sample sizes were equal.

The gender distribution of participants and mean values of BMI, waist circumference, blood pressure, pulse, and lipid concentrations at screening were presented for each group. Compliance with fig consumption were estimated from the compliance sheets and subjects that consumed <75% of the assigned figs were designated as non-compliers, and analysis were performed with and without these participants. Lipid concentrations at weeks 6 and 7 and at weeks 11 and 12 were averaged to minimize day
to day variability. The averaged values were presented and analyzed. The percentage difference for each lipid variable between the intervention and control phases was calculated.

Dietary data were analyzed and presented. Mean blood pressure, pulse and body weight measurements at the end of the intervention and control phases were calculated and presented.

All results were considered significant if the two-tailed P values is <0.05. Statistical analysis will be performed using SPSS for WINDOWS (SPSS, Chicago, IL).

L. Power Analysis

Since the population parameter \( s \) is not known then \( s_1 \) and \( s_2 \) can be used to calculate a weighted average that estimates \( s \)

\[
 s^2 = \frac{n_1 - 1}{s_1^2} \frac{n_2 - 1}{s_2^2} \frac{n_1 + n_2 - 2}{n_1 + n_2 - 2}
\]

The sample size was given a mean expected 5-6% reduction in LDL cholesterol with an SD of the change of 5-6%. For a mean difference of 5 and SD of 8 using the equation shown resulted in a sample size of \((1.96+0.84)^2*2*64/25=40.1 \sim 41\) giving a total sample size of 82. From SPSS output the total sample size requirement for the study is 84. The power is 80%. If we allow for a dropout rate of up to 20% the final number for the study was to be \( 84 + 16 = 100 \) participants.

M. Strengths and Limitations

The main strength of the study was the randomized, crossover design with subjects serving as their own controls and the adequate, calculated power. The theoretical
underpinnings were excellent. As the doctoral students have previously performed a preliminary study, feasibility seems likely. She had a wide network of potential participants from the nearby San Bernardino areas. The intervention was simple to administer to participants. It was simple to administer the intervention phase of the study, with the inclusion of pre-packaged figs in the habitual diet.

There were also several limitations. Subjects were free living and there was no control over other food intake. Subjects concerned about weight gain were allowed to substitute figs for desserts and sweet snacks, which may have lowered lipid concentrations due to the substitution. The dietary recalls provided data to show whether the composition of the diet changed between the two periods, other than in regard to soluble fiber.

Compliance to the study may have been reduced, if the participants’ got tired of eating figs, though this is unlikely for a period of five weeks. The main limitation was the lack of dietary counsel to follow AHA and NCEP recommendations for individuals with elevated cholesterol concentrations. Ideally, subjects would be given dietary instruction to follow these recommendations prior to inclusion in the study. However, it is feared that lengthening the study by another 4 weeks would have limited compliance and the number of blood tests would have been increased. A list of patient recommendations for elevated cholesterol was given at the initial visit.

N. Research Ethics

Respect was maintained by keeping the information of participants confidential, not allowing anyone else beside the research group to have access to the personal information. Data were kept in a database with a password known only to researchers.
Data were assigned linking codes. All data were stored separately from identifying information. Only the primary investigator was permitted to have linking access. All data analyses were conducted on de-identified data. Only trained IRB certified health professionals were in contact with participants.

Providing participants with the informed consent explaining all the test procedures and possible side effects or risks, if applicable, was used to maximize benefits and minimize possible harms. Harms in this study are limited to hematoma, lightheadedness or other complications of venipuncture.
Effect of Consumption of Dried California Mission Figs on Lipid Concentrations

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Key words: figs, dietary fiber, hypercholesterolemia, dietary intake, lipids

For Submission to: Annals of Nutrition and Metabolism

Referencing style is in accordance with journal guidelines and is not in accordance with dissertation formatting guidelines.
Abstract

Background: Figs are a rich source of soluble fiber. We evaluated the effect of consuming dried California Mission figs on serum lipids in hyperlipidemic adults.

Methods: In a crossover trial men and women aged 30-75 years with elevated LDL cholesterol (100-189 mg/dL) were randomized to add dried California Mission figs (120 grams/day) to their usual diet for 5 weeks, or eat their usual diet for 5 weeks, then crossed over to the other condition for another 5 weeks. Six 24-hour dietary recalls were obtained.

Results: LDL and HDL cholesterol and triglyceride concentrations did not differ between usual and figs-added diets (Bonferroni-corrected P-values >0.017) while total cholesterol tended to increase with fig consumption (P=0.02). Total cholesterol increased in participants (n=41) randomized to usual followed by figs-added diet (p=0.01), but remained unchanged in subjects (n=42) who started with figs-added followed by usual diet (p=0.4). During the figs-added diet, soluble fiber intake was 12.6±3.7 g/day versus 8.2±4.1 g/day in the usual diet (P<0.0001). Sugar intake increased from 23.4±6.5% of kcaldies to 32.2±6.3% of kcalories in the figs-added diet (P<0.0001). Body weight did not change (P=0.08).

Conclusions: Daily consumption of figs did not reduce LDL cholesterol. Triglyceride concentrations were not significantly changed despite an increase in sugar intake.
Introduction

Elevated low density lipoprotein (LDL) cholesterol concentrations are causally linked with atherogenesis and coronary heart disease (1,2). One of the dietary approaches to lower LDL cholesterol is the incorporation of foods with hypocholesterolemic effects into the daily diet, including fiber, plant sterols, soy protein, and isoflavones. Numerous studies have established that soluble fiber plays a role in lowering serum cholesterol [3]. This effect is more pronounced for soluble or gel-forming fibers found in cereals, such as barley and oat, and legumes. Recent guidelines on lowering blood cholesterol recommend increased consumption of fiber-rich foods to achieve a total daily intake of 30 grams/day [4-5].

One of the foods that may be effective in lowering blood lipid concentrations is figs. Figs in both the fresh and dried forms contain soluble fiber in appreciable amounts [6-7]. Each 100 grams of dried figs provides about 1g of soluble fiber according to a 1999 database [8] but about four times that amount according to Vinson [9]. Dried fruits like California Mission figs have a greater nutrient density, greater fiber content, increased shelf life, and significantly higher phenol antioxidant content compared to fresh fruit [7]. When figs are diluted in water their viscosity increases, and intestinal transit time may be lengthened, gastric emptying delayed, and glucose absorption decreased. Such actions have the potential to lower postprandial blood glucose concentrations and decrease blood cholesterol [7].

Presently, a review of PUBMED found no published studies studying the effect of fig consumption on reducing serum cholesterol concentrations. In order to evaluate the effect of the consumption of dried California Mission figs (Ficus carica ‘Mission’) on
serum lipid concentrations, we conducted a randomized controlled clinical trial in men and women with LDL cholesterol concentrations in the above optimal to high ranges.

**Methods**

This was a randomized controlled 2 week screening and 10 week intervention crossover study conducted at Loma Linda University School of Public Health. The study was conducted from September through December 2008. The protocol was approved by the Loma Linda University Institutional Review Board. All subjects provided informed written consent. Participants were recruited from communities in and surrounding San Bernardino, California. Information and flyers were presented at churches and business establishments as well as at the fitness center at Loma Linda University. All subjects provided background health history information in the form of a brief health questionnaire.

Participants were women and men ages 30-75 years with LDL cholesterol concentrations in the above optimal (100-129 mg/dL), borderline (130-159 mg/dL) or high (160-189 mg/dL) ranges, the latter after clearance by their physician. Additional inclusion criteria were a body mass index of 18.5-35 kg/m², and no cigarette smoking within the past year. Exclusion criteria were any secondary cause of hyperlipidemia (kidney or liver disease, untreated hypothyroidism); current or previous use (within the past 2 months) of any lipid-lowering drug; type 1 diabetes or uncontrolled type 2 diabetes (HbA1c >7%); triglyceride concentrations >300 mg/dL; current or previous treatment (within the past 3 months) with estrogen or steroid therapy; stated dislike of figs; use of certain dietary supplements, e.g. Metamucil, sterol/stanol margarine, and others that may influence lipid concentrations; chronic disease that may affect concentrations of lipids or
markers of inflammation (e.g. cancer other than skin cancer within the last 5 years, chronic rheumatological disease, chronic severe depression), and any condition that would limit compliance with the protocol (e.g. drug abuse).

Following screening procedures, 102 adult men and women were randomly assigned to either figs-added or their usual diet for the first 5 weeks after randomization and then switched to the other phase for the second 5 weeks. For randomization the study coordinator opened opaque pre-numbered envelopes that revealed assignment. During the figs-added diet, participants were asked to consume a prepackaged, pre-weighed 120 gram serving of dried California Mission figs (12-15 figs) as part of their 3 daily meals for 5 weeks. Consumption of figs other than those provided by the study and prune (dried plum) consumption was not allowed. During the usual diet participants followed their habitual diet but without the consumption of figs or prunes. All participants were given a list of desserts and sweets to replace with figs in order to maintain stable caloric intake. Dried California Mission figs were provided by the California Fig Advisory Board.

Study visits were scheduled at weeks 2, 4, 5, 7, 9, and 10 after randomization. Week 5 was the crossover visit. At each study visit vital signs and anthropometrics were measured. The study procedures were reiterated and subjects completed a short health questionnaire to check whether any changes had occurred in their health status or use of medications since the screening visit. If the fig portions were forgotten (e.g. not taken to work) they were consumed at a later time in the day with meals or as a snack. Daily compliance with the assigned portions of figs was recorded on a compliance form. A $25 gift certificate was given to each participant who completed the 12 week study.
Dietary Analyses

Six interviews to obtain 24-hour dietary recalls were performed at week 2 and onwards; three of these recalls were obtained during the figs-added period and three were obtained during the usual diet period. The recalls were performed by registered dietitians and a trained graduate student via two phone interviews and one in-person interview in each study phase. Two randomly chosen weekdays and one weekend day were targeted in each period. To select the day the dietitian or student pulled a selection from a box containing folded papers with the day (Sunday through Friday) for each participant. If the interview was not possible on the drawn day, it was conducted as soon as possible thereafter. The Nutrition Data System for Research (NDSR [10]), which is maintained by the Nutrition Coordinating Center at the University of Minnesota, was the software used to acquire the 24 hour dietary recall. We also analyzed changes in fiber intake during the usual diet and fig phases using the Vinson data [9] on the fiber content of dried figs.

Laboratory Methods

All the participants had blood samples drawn after a 12 hour fast at screening, and at weeks 4, 5, 9 and 10 after randomization. Water and usual medications were allowed on the morning prior to the visit. Blood samples were drawn early in the morning between 6:30 am and 9 am. Samples obtained at screening were sent to the Loma Linda University Medical Center Clinical Laboratory for analysis of total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels as well as alanine aminotransferase (ALT), creatinine, and glucose.
Blood samples were separated in a refrigerated centrifuge at 1800 x g and 4 degrees centigrade. Serum/plasma was then aliquoted into vials kept in a -70 degree freezer. Frozen samples were analyzed batchwise at the Research Laboratory at the University of California at Davis using a Poly-Chem system. Total cholesterol and triglycerides were measured enzymatically by automated procedures. Two distinct reaction steps for direct measurements of LDL and HDL cholesterol were conducted: 1. Elimination of chylomicron, VLDL-cholesterol, and LDL-cholesterol (for HDL cholesterol) or HDL-cholesterol (for LDL cholesterol) by cholesterol esterase, oxidase, and catalase; 2. Specific measurement of lipids was done after the release of other lipids by detergents.

**Statistical Analyses**

Previous literature indicated a decrease of 0.028 mmol/L (1.1 mg/dL) and 0.029 mml/L (1.1 mg/dL) in total and LDL cholesterol, respectively, for each additional g of water soluble fiber in the diet. For a daily intake of 120 g of dried figs, the additional amount of soluble fiber was predicted to be ~4 g/day [9] resulting in about a 4.6 mg/dL reduction in total and LDL cholesterol. Given the estimated average serum LDL cholesterol at baseline of about 130 mg/dL, the reduction of LDL cholesterol would be about 3.5%. With a standard deviation of 8% we estimated that to achieve 80% power with $\alpha$ of 0.05, 84 participants were required. To allow for an attrition rate of up to 20%, 100 participants were planned.

Following data entry a random sample of 10% was re-entered. A student’s t test or chi-square analysis, as appropriate, was used to compare participant characteristics. Lipids at weeks 5 and 10 after randomization were compared by a paired t-test, which
was also used to compare changes in body weight and diet within each period. Analyses using the means of weeks 4 and 5 and 9 and 10 did not differ substantially. Comparisons were also made across groups at the end of each period (Student’s t-test). A general linear model of repeated measures analysis was done to determine if there were period treatment interactions (none were found). Because 3 p-values were calculated for each lipid, the Bonferroni adjustment was used to determine statistical significance. Thus, only p-values <0.017 were considered statistically significant. Software utilized for analyses was SPSS version 15.0 (SPSS Inc., Chicago, IL, USA; [11].

Results

Figure 1 shows the flow chart (n=141). Ineligibility for the study was due to too low LDL cholesterol (n=15); too high LDL cholesterol levels (n=4); too high triglycerides (n=6); BMI above the cut-off (n=4); BMI below the cut-off (n=1); and lack of interest in the study (n=9). Thus the total number randomized was 102, of which 51 subjects began with the figs-added diet, and 51 subjects began with the usual diet. There were 8 participants who dropped out among those initially randomized to the figs-added diet (3 were lost to follow-up, 1 developed persistent diarrhea, 1 disliked figs, 1 had a family emergency, 1 was diagnosed with cancer, and 1 started cholesterol-lowering medication). Among those that started with the usual diet, 6 dropped out (3 were lost to follow-up, 1 had a family emergency, 1 developed diarrhea, and 1 disliked figs). Of 88 completing subjects, 83 had final blood tests drawn, but 1-3 were missing a specific lipid value.

Table 4.1 lists the characteristics of participants randomized to usual or to added-figs diet at screening. They were evenly distributed in relation to demographic,
anthropometric, and laboratory values. Table 4.2 shows that body weight increased slightly at the end of the added-figs diet compared to the usual diet with a mean difference of 0.4 kg, however, this difference did not achieve statistical significance. Table 4.3 shows the dietary data. There was an increase in energy intake (187±44 kcalories) during the figs-added compared to the usual diet. The percentage of energy from fat and protein was reduced while the percentage of energy from carbohydrates and sugar was increased. When examined according to the Vinson (1999) data, there was an increase in soluble fiber intake in the figs-added diet.

Total cholesterol was 224±45 mg/dL with the usual diet versus 230±41 mg/dL with the figs-added diet (P=0.021); LDL cholesterol was 127±31 mg/dL with the usual diet versus 130±27 mg/dL with the figs-added diet (P=0.111); HDL cholesterol was 53±15 mg/dL in both dietary phases (P=1.0); triglycerides were 132±91 mg/dL with the usual diet versus 135±109 mg/dL with the figs-added diet (P=0.06). However, inspection of data indicated that the two groups’ lipid concentrations differed. Thus, analyses of subjects starting with figs-added and switching to usual diet are shown separately from analyses of subjects starting with usual diet and crossing over to the figs-added diet. Table 4.4 shows that for subjects who started with figs-added diet, there was no change in lipid concentrations. However, for subjects that started with the usual and crossed over to the figs-added diet, there was an increase in total cholesterol and a similar trend in LDL cholesterol, though not with the Bonferroni correction. Triglyceride and HDL cholesterol concentrations were unchanged within both groups.
Discussion

We found no changes in LDL cholesterol concentrations in hyperlipidemic subjects who added figs to their usual diet, compared to their usual diet alone. HDL cholesterol levels were also unchanged. The study population was a hyperlipidemic one, in which any effects of fiber in lower LDL cholesterol would be expected to be manifest. Foods from sources like oats and barley that are high in soluble fiber significantly lower LDL cholesterol and thereby total cholesterol [4]. However, oats and barley do not contain the large amounts of sugar per gram as figs (Table 4.5); despite the increase in sugar intake triglyceride concentrations did not change significantly.

We are not aware of previous studies examining the effects of dried fruit, specifically dried California Mission figs, as a source of soluble fiber to lower LDL cholesterol in hyperlipidemic adults. Our study was planned to expect an approximately 3-4% reduction in LDL cholesterol based on the amount of soluble fiber in dried California mission figs reported by Vinson in 1999. Though the study power was adequate, no effect was seen. A number of explanations may be relevant. While consuming their usual diet, subjects reported that ~59% of energy was from carbohydrates including almost one-fourth from sugar while <30% of energy was from fat. Compared to the general population [5], fat intake was lower and carbohydrate intake was higher, probably reflecting the subjects’ awareness of hypercholesterolemia and attempts to limit dietary fat. Furthermore, subjects’ intake of dietary fiber was exceptionally high (mean of 29 grams/day), about double of what is reported by the general population. Thus, the baseline fiber intake may have been too high for the effects of moderate amounts of added fiber to be revealed.
Serum total cholesterol levels increased in the group that began with their usual diet and crossed over to the figs-added diet, a finding that is not explained by the dietary changes observed. It is possible that the ~38% increase in sugar intake in the figs-added diet stimulated very low density lipoprotein (VLDL) synthesis [12]. It is well established that dietary carbohydrates stimulate hepatic VLDL, and simple carbohydrates have a great stimulatory effect than complex ones [13]. Increased VLDL may lead to increased LDL formation and thus, increased total cholesterol levels.

There was no change in HDL cholesterol with fig consumption. Some data have indicated an effect of dietary fiber on increasing HDL cholesterol, but most studies indicate that HDL cholesterol concentrations are unchanged [12]. Increased dietary carbohydrates are associated with decreased HDL cholesterol [12]. Furthermore the decrease in fat intake, particularly saturated fat intake, with the figs-added diet would be expected to lower HDL cholesterol. In general, study subjects reported high levels of physical activity (data not shown) and a number were recruited from the local fitness center. High levels of physical activity may counteract dietary effects on HDL cholesterol [14].

The supplemented figs provided about 330 kcalories/day, while the reported diet showed an increase of 187 kcalories/day, indicating compensatory restriction of other foods. Over the course of 5 weeks, an increase of 6500 kcalories would be expected to be associated with a weight increase of about 0.9 kg. The observed weight change was somewhat smaller and unlikely to cause significant lipid changes.

The strengths of the study include the randomized controlled design, adequately powered number of participants, and length of follow-up which was sufficient to show
the tolerability of fig consumption and lipid changes. As LDL cholesterol was measured directly, we avoided the typical artefactual reduction in LDL cholesterol that is seen when the Friedewald formula is used to calculate LDL cholesterol in the presence of an increase in triglycerides. A limitation is that we were unable to obtain adequate blood samples from all subjects that completed the study. Furthermore, the subjects were free living, and assessing dietary intake in free living subjects is fraught with threats to validity, which include underreporting and biased reporting of dietary intakes [15]. The use of repeated 24-hour recalls is increasingly recommended to avoid limitations on other methods requiring more effort on the part of the subject [16]. Though the study was conducted within a short time period to avoid seasonal changes, such effects may have been present.

In conclusion, consumption of dried figs, despite the high content of soluble fiber, did not lower serum LDL or total cholesterol concentrations. Paradoxically, an increase in total cholesterol was observed in the group randomized to usual followed by figs-added diet. No increase in triglyceride concentrations or lowering of HDL cholesterol was seen despite the increase in dietary sugar.
Acknowledgements

The study was funded in its entirety by the California Fig Advisory Board.

None of the authors have conflicts of interest related to this work. We thank the participants and research assistants that made the study possible.
141 Screened

- 14 Low overall lipid values
- 6 Triglycerides >300 mg/dL
- 4 LDL cholesterol too high
- 8 No longer interested
- 4 BMI too high
- 1 BMI too low
  - 1 Family emergency
  - 1 Started hormone therapy

102 Randomized

- 51 Randomized to usual diet first
  - 5 Lost to follow-up
  - 1 Family emergency
  - 1 Diarrhea
  - 1 Disliked figs

- 51 Randomized to added figs first
  - 1 Diarrhea
  - 1 Started cholesterol-lowering medication
  - 1 Cancer
  - 1 Family emergency
  - 1 Disliked figs
  - 1 Lost to follow-up

43 completed (41 with complete final blood tests)

45 completed (42 with complete final blood tests)

Figure 4.1 Participant Flowchart
**Table 4.1** Study Participant Characteristics (mean±SD) at Screening for Subjects that were Randomized to Start with Usual Diet (n=51) versus Subjects that Started with Figs Added Diet (n=51).

<table>
<thead>
<tr>
<th></th>
<th>Usual diet</th>
<th>Figs-added</th>
<th><strong>P-value</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>54.8±11</td>
<td>56.2±10</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>Gender- n (%)</strong></td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>Female</td>
<td>34 (66.7)</td>
<td>36 (70.6)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (33.3)</td>
<td>15 (29.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity- n (%)</strong></td>
<td></td>
<td></td>
<td>0.49</td>
</tr>
<tr>
<td>White</td>
<td>17 (33.3)</td>
<td>19 (37.3)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>13 (25.5)</td>
<td>10 (19.6)</td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>3 (5.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Black/Hispanic</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>8 (15.7)</td>
<td>6 (11.8)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>7 (13.7)</td>
<td>10 (19.6)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (5.9)</td>
<td>5 (9.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Lipid values</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>205±32</td>
<td>203±27</td>
<td>0.77</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>128±60</td>
<td>113±59</td>
<td>0.20</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>55±15</td>
<td>56±13</td>
<td>0.78</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>136±23</td>
<td>135±22</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>25±4</td>
<td>26±3</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>TSH (mIU/mL)</strong></td>
<td>2.4±1.3</td>
<td>2.5±1.4</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>Glucose (mg/dL)</strong></td>
<td>93±11</td>
<td>93±13</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Creatinine (mg/dL)</strong></td>
<td>0.9±0.2</td>
<td>0.9±0.3</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>ALT (U/L)</strong></td>
<td>21±11</td>
<td>28±15</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Systolic blood pressure (mmHg)</strong></td>
<td>125±19</td>
<td>125±22</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure (mmHg)</strong></td>
<td>79±9</td>
<td>80±10</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Table 4.2 Anthropometric Data of Participants that Completed the Study at Screening and at the End of the Figs-Added and Usual Diet Phases. Mean±SD values are shown.

<table>
<thead>
<tr>
<th></th>
<th>Screening (n=88)</th>
<th>Usual diet (n=85)</th>
<th>Figs-added (n=88)</th>
<th>Mean Difference</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>26.4±4.0</td>
<td>26.4±4.0</td>
<td>26.6±4.0</td>
<td>-0.2</td>
<td>.06</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>71.0±13.4</td>
<td>71.0±13.5</td>
<td>71.4±14.0</td>
<td>-0.4</td>
<td>.08</td>
</tr>
</tbody>
</table>

*P values indicate significance level for paired t-tests comparing the end of the figs-added versus usual diet. Body weight was missing for 3 subjects at the end of the usual.
Table 4.3 Nutrient Intake of Study Participants During the Usual Versus Figs-Added Diets (n=84; data missing for 4 subjects).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Usual diet</th>
<th>Figs-added</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Energy (kcalories)</td>
<td>1646</td>
<td>621</td>
<td>1854</td>
</tr>
<tr>
<td>% Energy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>29.1</td>
<td>7.6</td>
<td>25.0</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>8.1</td>
<td>3.0</td>
<td>6.6</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>7.8</td>
<td>3.1</td>
<td>6.5</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>10.9</td>
<td>3.6</td>
<td>9.6</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>58.5</td>
<td>8.7</td>
<td>64.9</td>
</tr>
<tr>
<td>Sugar</td>
<td>23.4</td>
<td>6.5</td>
<td>32.2</td>
</tr>
<tr>
<td>Protein</td>
<td>15.6</td>
<td>4.7</td>
<td>14.4</td>
</tr>
<tr>
<td>Fiber, total (grams)</td>
<td>29.0</td>
<td>13.5</td>
<td>37.7</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>137</td>
<td>114</td>
<td>138</td>
</tr>
<tr>
<td>Soluble fiber (grams)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Database</td>
<td>8.2</td>
<td>4.1</td>
<td>8.5</td>
</tr>
<tr>
<td>Measured (Vinson 1999)</td>
<td>8.2</td>
<td>4.1</td>
<td>12.6</td>
</tr>
</tbody>
</table>
Table 4.4 Serum Lipid Concentrations in Participants Randomized to Figs-Added versus Usual Diet for 5 Weeks (results of final blood tests shown). Mean±SD values are shown.*

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (5 weeks)**</th>
<th>Period 2 (5 weeks)***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Figs-added</td>
<td>Usual diet</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>231±46</td>
<td>227±34</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>53±17</td>
<td>54±14</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>141±132</td>
<td>139±78</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>134±32</td>
<td>127±22</td>
</tr>
</tbody>
</table>

|                                | Usual diet          | Figs+usual diet      | P value (N=41) |
| Total cholesterol, mg/dL       | 215±41              | 235±48               | 0.01          |
| HDL cholesterol, mg/dL         | 52±14               | 55±17                | 0.1           |
| Triglycerides, mg/dL           | 131±82              | 141±131              | 0.1           |
| LDL cholesterol, mg/dL         | 119±27              | 135±32               | 0.02          |

*5 participants did not have final blood tests.
**At the end of period 1, lipid values did not differ between the two groups (p=0.1 for total cholesterol; p=0.9 for HDL cholesterol; p=0.7 for triglycerides; and p=0.02 for LDL cholesterol).
***At the end of period 2, lipid values did not differ between the two groups (p=0.4 for total cholesterol; p=0.7 for HDL cholesterol; p=0.9 for triglycerides; and p=0.2 for LDL cholesterol).
### Table 4.5 Comparison of Food Sources Rich in Soluble Fiber (per 100 gram)

<table>
<thead>
<tr>
<th></th>
<th>Energy (kcal)</th>
<th>Carbohydrate (g)</th>
<th>Sugar (g)</th>
<th>Fiber (g)</th>
<th>Pectin (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figs, dried, uncooked</td>
<td>249</td>
<td>63.9</td>
<td>47.9</td>
<td>9.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Corn flakes</td>
<td>361</td>
<td>87.1</td>
<td>10.5</td>
<td>.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Carrots, raw</td>
<td>52</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>0.8</td>
</tr>
<tr>
<td>Apple, fresh</td>
<td>49</td>
<td>16</td>
<td>3.3</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>Apricots, dried</td>
<td>55</td>
<td>62</td>
<td>41.7</td>
<td>7</td>
<td>0.7</td>
</tr>
<tr>
<td>Lentils</td>
<td>116</td>
<td>20.1</td>
<td>1.8</td>
<td>7.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Peaches, fresh</td>
<td>50</td>
<td>9</td>
<td>9</td>
<td>1.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Prunes, dried</td>
<td>339</td>
<td>62.7</td>
<td>25</td>
<td>7</td>
<td>1.8</td>
</tr>
<tr>
<td>Orange, fresh</td>
<td>64</td>
<td>16</td>
<td>13</td>
<td>3</td>
<td>2.6</td>
</tr>
</tbody>
</table>
REFERENCES


10. Nutrition Data System for Research (NDSR), Nutrition Coordinating Center at the University of Minnesota, Table 1. J Am Diet Assoc 1997; v97:1139-1151.

11. SPSS, Version 15.0, Chicago: SPSS, Inc.


CHAPTER 5
OTHER FINDINGS

Table 5.1 shows the mean age, gender, lipid values, BMI height and weight of the participants excluding the dropouts (completers only). The groups are evenly distributed, except that body weight was slightly higher in the group randomly assigned to consume figs compared to the than the usual diet group and triglycerides were higher in the usual diet group than the fig consumption group.

Table 5.1 Descriptives at Baseline Comparing Participants Randomized to Fig versus Usual Diet Consumption.

<table>
<thead>
<tr>
<th></th>
<th>Figs (n=45)</th>
<th>Usual diet (n=43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.1 (11)</td>
<td>55.2 (12)</td>
<td>.71</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>.94</td>
</tr>
<tr>
<td>Female</td>
<td>30 (67)</td>
<td>29 (67)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 (33)</td>
<td>14 (33)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>.40</td>
</tr>
<tr>
<td>White</td>
<td>16 (37)</td>
<td>14 (31)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>7 (16)</td>
<td>12 (26)</td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>0 (.0)</td>
<td>3 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Black/Hispanic</td>
<td>1 (2.3)</td>
<td>0 (.0)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>6 (14.0)</td>
<td>7 (16)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>9 (21)</td>
<td>6 (13)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (9.3)</td>
<td>3 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Lipids at screening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>204 (30)</td>
<td>202 (27)</td>
<td>.77</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>107 (59)</td>
<td>131 (63)</td>
<td>.08</td>
</tr>
</tbody>
</table>
Table 5.1 (Continued) Descriptives at Baseline Comparing Participants Randomized to Fig versus Usual Diet Consumption

<table>
<thead>
<tr>
<th>Lipids at screening (continued)</th>
<th>Figs (n=45)</th>
<th>Usual diet (n=43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>57 (13)</td>
<td>55 (14)</td>
<td>.51</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>133 (22)</td>
<td>135 (23)</td>
<td>.67</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.3 (9.5)</td>
<td>161.0 (9.3)</td>
<td>.88</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.4 (14.0)</td>
<td>71.0 (13.5)</td>
<td>.08</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.0 (3.3)</td>
<td>25.7 (4.0)</td>
<td>.11</td>
</tr>
</tbody>
</table>

Table 5.2 shows that of the 235 diet recalls obtained in 80 participants during the fig consumption phase, the mean amount of figs consumed was 126 grams per dietary recall, which is just above the target of 120 grams/day. For the 243 diet recalls obtained in 81 participants during the usual diet phase, the mean amount of figs consumed was 0.19 per diet recall. This indicates excellent compliance with the randomized assignment.

Table 5.2 Average Amount of Figs Consumed per Dietary Recall

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of dietary recalls</th>
<th>Mean amount of figs consumed (grams/day)</th>
<th>SD</th>
<th>Median (grams/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fig consumption group</td>
<td>235</td>
<td>126</td>
<td>41</td>
<td>134</td>
</tr>
<tr>
<td>Usual diet group</td>
<td>243</td>
<td>0.19</td>
<td>2.17</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 5.3 shows mean lipid values when the mean of the two final weeks of each dietary phase is used, rather than the final blood value only, as shown in the publishable article. The results were very similar to those obtained when only the final values were used.
Table 5.3 Serum Lipid Concentrations in Participants Randomized to Fig versus Usual Diet Consumption for Five Weeks (mean of last two blood tests taken after 4 and 5 weeks after start of the study phase).

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (5 weeks)*</th>
<th>Period 2 (5 weeks)**</th>
<th>P value (N=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cholesterol, mg/dL</strong></td>
<td>231 (44)</td>
<td>230 (48)</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>HDL cholesterol, mg/dL</strong></td>
<td>53 (16)</td>
<td>54 (16)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Triglycerides, mg/dL</strong></td>
<td>140 (114)</td>
<td>135 (109)</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>LDL cholesterol, mg/dL</strong></td>
<td>134 (30)</td>
<td>132 (33)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Usual diet</th>
<th>Figs+usual diet</th>
<th>P value (N=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cholesterol, mg/dL</strong></td>
<td>216 (35)</td>
<td>228 (31)</td>
<td>&lt;0.0001***</td>
</tr>
<tr>
<td><strong>HDL cholesterol, mg/dL</strong></td>
<td>52 (13)</td>
<td>54 (12)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Triglycerides, mg/dL</strong></td>
<td>128 (69)</td>
<td>143 (84)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>LDL cholesterol, mg/dL</strong></td>
<td>120 (23)</td>
<td>127 (22)</td>
<td>0.001***</td>
</tr>
</tbody>
</table>

Mean (standard deviation) values are shown.

*At the end of period 1, lipid values did not differ between the two groups (p=0.08 for total cholesterol; p=0.8 for HDL cholesterol; p=0.6 for triglycerides; and p=0.02 for LDL cholesterol).

**At the end of period 2, lipid values did not differ between the two groups (p=0.8 for total cholesterol; p=0.9 for HDL cholesterol; p=0.7 for triglycerides; and p=0.4 for LDL cholesterol).

***Using the Bonferroni correction, only p values <0.017 were considered statistically significant.
A. Summary of Findings

Recent research has shown a relationship between high fiber diets and its affect on body chemistry. A recent report on dietary fiber by the Institute of Medicine (IOM) suggests that there is a distinction between different types of dietary fiber. For example functional fiber is soluble, highly viscous, and demonstrates physiological responses to, but is not limited to maintaining healthy total cholesterol and LDL cholesterol (Carabin et al, 2009).

Lifestyle changes take about 3-6 weeks to result in a reduction in serum cholesterol (Brown et al., 1999). Changes in blood lipid concentrations are evident within 3-5 weeks of change of diet. The half-life of LDL is 3-4 days, which suggests that most LDL in the blood is gone and replaced by new LDL within a two-week period. Dietary changes require at least 2-3 weeks for changes to be reflected in serum lipid levels (Expert Panel, 2001). Among the hyperlipidemic adults in this crossover study consuming California Mission figs for 5 weeks, the mean LDL cholesterol was unchanged.

Based on the overall findings in the study it appears that the consumption of 40 or more grams of California mission figs at each meal was not effective at reducing LDL cholesterol and coronary heart disease risk.
B. Implications for Preventive Care Practice

The aim of preventive care is to address today’s most pressing health concerns in public health and promote healthy lifestyles to prevent chronic diseases such as cardiovascular disease as well as provide effective and cost-saving interventions for clients and health care providers. Diet and lifestyle are modifiable factors in the development and prevention of a number of non-communicable diseases, including cardiovascular disease. It is important from a public health approach to document the cholesterol-lowering effect of a functional food, whose mechanism of action under various conditions might provide both effective intervention and cost-savings, as it works in combination with cholesterol-lowering diets (Anderson, Deakins, Floore, Smith & Whittis, 1990).

The judicious use of plant foods is recommended by Preventive Care Specialists as a simple measure to effectively lower elevated serum lipids at a reasonable cost. This study may provide a basis for recommendations to the general population at large, if confirmed in future studies. California mission figs are natural dietary products that can potentially reduce the need for pharmacological treatment, and easily incorporated into the diet as a functional food because of the potential benefits. The increase of dietary fiber in the diet also has potentially positive effects on overall health. Dried fruits like California mission figs have a greater nutrient density, greater fiber content, increased shelf life and significantly higher phenol antioxidant content compared to fresh fruit (Vinson et al., 2005). Some people may prefer to choose a dietary approach rather than a pharmacological one to lowering serum cholesterol and may benefit more from dietary changes with fewer side effects.
C. Limitations

Participants were free living without controls over their other food intake. Those concerned about weight gain may have substituted figs for desserts and sweet snacks, which may have increased lipid concentrations due to the substitution. The dietary recalls only gave data showing whether the composition of the diet changed between the two periods other than in regard to soluble fiber. The primary tools used in the study, were six 24 hour dietary food records, which are less sensitive when compared with more reliable methods, such as having assigned dietary meals with the figs prepared in a metabolic kitchen.

D. Recommendations for Future Study

It is well established that poor dietary practices are linked with major causes of morbidity and mortality, including cardiovascular disease, hypertension, type 2 diabetes, overweight and obesity (Dietary Guidelines for Americans 2005). The health and nutrition paradigm have also changed significantly during the past two decades. Today, food is not merely viewed as a vehicle for essential nutrients for proper growth and development, but as a route to optimal wellness (IFIC, 2009). This paradigm of food as medicine will continue to be driven by several factors including, increased consumer interest in controlling their health; escalating health care costs advances in biotechnology and medical technology; nutrigenomics—the study of molecular relationships between nutrition and the response of genes, with the aim of extrapolating how such subtle changes can affect human health; and changes in food regulations, which will increase the need for future evidence-based scientific research linking diet to chronic disease risk reduction (J Am Diet Assoc. 2009).
E. Conclusions

Daily consumption of California dried mission figs did not have a significant effect on lowering serum total and LDL cholesterol after a period of five weeks among people with elevated lipid concentrations who made no alterations in their regular diet and are not on drug therapy for lowering cholesterol. Daily consumption of California dried mission figs was feasible and well tolerated in these individuals for the 5 week period of time required to lower lipid concentrations. There were no significant changes in HDL cholesterol. The findings support additional study is warranted on the long-term use of California mission figs for the lowering of serum cholesterol and the maintenance of low serum cholesterol levels in the general population.
REFERENCES


California Fig Advisory Board, personal communication, 2003.


FDA Talk Paper. FDA allows whole oat foods to make health claim on reducing the risk of heart disease. 21 January 1997.


*Arteriosclerosis. Thrombosis and Vascular Biology, 20,* 1580-1587.


APPENDIX A: IRB APPROVAL

INSTITUTIONAL REVIEW BOARD
Initial Approval Notice - Expedited Review
OFFICE OF SPONSORED RESEARCH • 11188 Anderson Street • Loma Linda, CA 92501
(909) 558-4531 (vocal) • (909) 558-0131 (fax)

<table>
<thead>
<tr>
<th>To:</th>
<th>Tonstad, Serena</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department:</td>
<td>Health Promotion &amp; Education</td>
</tr>
<tr>
<td>Protocol:</td>
<td>The effects of consumption of California dried mission figs on serum lipid concentrations in hyperlipidemic adults</td>
</tr>
</tbody>
</table>

This study was reviewed and approved administratively on behalf of the IRB. This decision includes the following determinations:

- **Risk to research subjects:** Minimal
- **Approval period begins:** 20-Aug-2008 and ends 19-Aug-2009
- **Stipulations of approval:**

**Consent Form**
Unless IRB has given a specific waiver of informed consent (as documented in the approval stipulations above) the IRB-approved and stamped consent form accompanies this letter. This now becomes the official master consent form for making copies to provide to study participants.

**Adverse Events / Protocol Changes**
The IRB should be notified in writing of any modifications to the approved research protocol. Adverse effects must be reported to the IRB in accordance with institutional policy. If sponsor or contractual adverse event reporting requirements differ from requirements for reporting to IRB, all reporting requirements must still be met.

**Protocol Review**
Your protocol is tentatively scheduled for review and renewal at least two weeks prior to the approval end-date indicated above. To assure uninterrupted approval of this project, you will be sent a report form to request renewal by completing and timely returning to Office of Sponsored Research. Anticipate the approval expiration, so your study does not lapse; contact IRB for assistance if necessary. In addition to reporting the requested renewal status information, you may also use the form to close the study at that time, if applicable.

**Records**
All records relating to this project, including signed consent forms, must be kept on file for three years following completion of the study. Please note the PI's name and the IRB number assigned to this IRB protocol (as indicated above) on any future communications with the IRB. Direct all communications to the IRB c/o the Office of Sponsored Research. Thank you for your cooperation in LLU's shared responsibility for the ethical use of human subjects in research.

Signature of IRB Chair/Designee: [Signature]

---

Loma Linda University Adventist Health Sciences Center holds Federalwide Assurance (FWA) No. 9447 with the U.S. Office for Human Research Protections, and this IRB registration no. 1033228. This Assurance applies to the following institutions: Loma Linda University, Loma Linda University Medical Center (including Loma Linda University Children's Hospital; LLU Community Medical Center), Loma Linda University Behavioral Medicine, and affiliated medical practice groups.

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APPENDIX B: INFORMED CONSENT

The Effects of Consumption of California Dried Mission Figs on Serum Lipid Concentrations in Hyperlipidemic Adults

Purpose and Procedures
You are invited to participate in a research study because your blood cholesterol is not optimal. The purpose of this study is to identify whether eating California dried mission figs three times daily with meals for five weeks lowers total cholesterol and low density lipoprotein (LDL) cholesterol in adults with above optimal, borderline or high cholesterol levels.

At the first visit you need to be fasting. You will be asked questions about your health history and your blood lipids, glucose and liver function will be measured. We will check if you meet the requirements for participation. If you do, we will call you up to arrange the next visit. At this visit you will be assigned through chance to start eating 1 portion (1/4 cup) of prepackaged California dried mission figs with your meals three times daily for 5 weeks OR to continue your usual diet. If you start with the figs, after five weeks you will return to your usual diet. If you start with your usual diet, after five weeks you will start eating figs as described above. Figs will be provided at no charge.

The study involves 8 visits in the course of the 12 weeks. The purpose of the visits is to deliver the figs and take blood tests. All the study visits are required. There will be blood drawings after 4 and 5 weeks and again after 11 and 12 weeks of the study. This adds up to a total of 5 blood drawings. At each blood drawing two tubes of blood totaling 5 tablespoons will be obtained. The results of the blood tests after the first one will not be available until after the end of the study.

We will measure your body weight, waistline and blood pressure at 6 of the 7 study visits. You will be asked to report your food intake during the last 24 hours on 6 occasions. On 4 of these occasions you will be called up at home by a dietitian for a telephone report. The other two reports will be done during site visits.

Who can take part
Men and women aged 25 to 75 years with LDL cholesterol that are in the above optimal (100-129 mg/dL), borderline (130-159 mg/dL) or high (160-189 mg/dL) range can take part. If your cholesterol is treated with medications you cannot take part. If your cholesterol is in the high range, we need the permission of your physician. If you have other diseases that are the cause of your high cholesterol you cannot take part. If you have type 1 diabetes, type 2 diabetes that is not well controlled or use certain medications you cannot take part.
**Risk**

Pain and minor bruising at the site of the needle insertion and possible lightheadedness upon arising after the blood is drawn are possible complications of blood drawing. The committee at Loma Linda University that reviews human studies (Institutional Review Board) has determined that participating in this study exposes you to minimal risk.

**Benefits**

You may not receive any direct benefit from participating in this study. You will be told your cholesterol levels and receive dietary advice about lowering blood cholesterol. The dietary changes including figs may lead to lower blood cholesterol. The benefit to humanity is an understanding of whether a simple dietary change (eating dried figs) can lower blood cholesterol.

**Participants' Rights**

Your participation in this study is voluntary. Your decision whether or not to participate or terminate at any time will not affect your present or future medical care. If you decide to stop, please inform the study investigator.

**Confidentiality**

All of the information that is collected in this study will be kept strictly confidential. Information that we collect will be assigned linking codes. All this information will be stored separately from your name and other personal data. Only the primary investigator will have linking access. Any publication resulting from this study will refer to the participants as a group.

**Additional Costs/Reimbursement**

You will be given free figs for the duration of the study. There is no cost to you for participating in this study. The blood tests will be performed at no cost. There is a modest monetary compensation of $25.00 for your effort upon completion of the study.

**Impartial Third Party Contact**

If you wish to contact an impartial third party not associated with this study regarding any question or complaint you may have about the study, you may contact the Office of Patient Relations, Loma Linda University Medical Center, Loma Linda, CA 92354, or call the Office of Patient Relations at (909) 559-4647 for information and assistance.
Informed Consent Statement

I have read the contents of this consent form, and have listened to the verbal explanation given by the investigator. My questions concerning this study have been answered to my satisfaction. I hereby give voluntary consent to participate in this study. This consent does not waive my rights, nor does it release the investigators, institution, or sponsors from their responsibilities. I may call the graduate student investigator, Joycelyn M. Peterson or the faculty advisor, Serena Tonstad, MD PhD at Loma Linda University, Department of Health Education & Promotion during routine office hours at (909) 558-4741 if I have additional questions or concerns. I have been given a copy of this letter for future reference.

Initials and date: ________________

Subject name (print)  Signature subject  Date

Witness name (print)  Signature witness  Date

I have reviewed the contents of the consent form with the person signing above. I have explained potential study risks and benefits.

Joycelyn M., Peterson MPH, RD
Department of Health
Education & Promotion
Loma Linda University
(909) 558-8577

Serena Tonstad, MD PhD
Department of Health
Education & Promotion
Loma Linda University
(909) 558-4575
APPENDIX C: PARTICIPANT QUESTIONNAIRE (BASELINE)

LOMA LINDA UNIVERSITY
FIG RESEARCH STUDY

Welcome to the fig research study! Please take a few minutes to complete the following questionnaire. It will be used to facilitate information only and does not represent a diagnostic evaluation. If you are uncomfortable answering any of these questions, leave them blank. Thank you for taking the time to fill out this questionnaire.

Name: ___________________________ Date of Birth: ___________________

Gender (please circle): Male or Female

Ethnicity (please circle): Asian, Black (African American or Caribbean), Hispanic, White

Telephone number:

(Home): ____________ (Cell): ____________ (Work): ____________

Mailing Address: _______________________________________________________

_____________________________________________________________________

Email address and fax: _________________________________________________

I. Are you under medical care for any of the following conditions or diseases? If yes, please circle

High blood pressure arteries) ___________________________ Angina pectoris (chest pain due to blocked

Stroke ___________________________ Blocked arteries in legs

Diabetes type 2 arteries) ___________________________ Heart attack or surgery for blocked coronary

Gallbladder disease ___________________________ Diverticulosis

Irritable bowel syndrome ___________________________ Heartburn or esophageal reflux

Cancer (write in what type ________) ___________________________ Thyroid disease
Family history of high cholesterol
High blood cholesterol
Food allergies or intolerances (please write in)

Other:

B. Please list all current medications, pain meds, vitamin or other supplements, and over the counter meds that you are taking at present

C. What has been your highest cholesterol reading? ________________
   Approximate date: ________________________
   What was your most recent cholesterol reading? ________________
   Approximate date: ________________________
   Are you taking medication to lower cholesterol (within the last two months) Circle Yes or No

D. Do you engage in any regular physical activity? Circle Yes or No
   What type and how often? ________________________

E. Do you smoke? Circle Yes or No
   If yes, for how long and how much ________________________
   If you quit smoking within the past year, please write the date: ________________________
   Signature ________________________
APPENDIX D: SHORT HEALTH HISTORY QUESTIONNAIRE
(RANDOMIZATION, CROSSOVER AND FINAL VISIT)

Have there been any changes in your medical condition since the start of the study?

____ No
____ Yes

If yes, describe.

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Have there been changes in your use of medication since the start of the study?

____ No
____ Yes

If yes, describe.

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

At crossover or final visit:

On a scale of 1 to 10, with 1 indicating not at all, and 10 indicating very much, how well
do you like eating the provided figs three times a day?

Not at all  1 2 3 4 5 6 7 8 9 10      Very much

Have you noticed any effects of figs on your overall health?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
APPENDIX E: COMPLIANCE SHEET

LOMA LINDA UNIVERSITY SCHOOL OF PUBLIC HEALTH

FIG COMPLIANCE SHEET

Dear Participant,
Please take the time at the end of each day to circle Yes or No for each meal in the boxes provided below, to indicate whether or not you ate the required amount of figs. Begin at the first week (one) to the fifth week (five)
Thank you for taking the time to fill out the compliance sheet.

Any questions please call your research interventionist Joy Peterson at 909-261-0359, or email to joysfigresearch@yahoo.com

Circle in the box at the end of each day: (Yes) or (No)

<table>
<thead>
<tr>
<th>Week</th>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breakfast</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Lunch</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Dinner</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
</tbody>
</table>

| Two   |         |        |         |           |          |        |          |
| Breakfast | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Lunch  | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Dinner | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |

| Three  |         |        |         |           |          |        |          |
| Breakfast | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Lunch  | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Dinner | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |

| Four   |         |        |         |           |          |        |          |
| Breakfast | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Lunch  | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Dinner | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |

| Five   |         |        |         |           |          |        |          |
| Breakfast | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Lunch  | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
| Dinner | Yes/No  | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No | Yes/No |
APPENDIX F: 24 HOUR DIETARY RECALL

24-Hour Dietary Recall Collection

The NCC Service Center has extensive expertise and experience in conducting 24-hour dietary recall interviews via telephone with a variety of populations, including children. Trained and certified NCC staff will train the study dietitian to conduct the 24-hour dietary recall interviews. Interviews take place over the telephone using NDSR, and are conducted by Joycelyn Peterson. Because dietary practices have been found to vary by time of week, interviews are scheduled to capture both weekend and weekday intakes. The NDSR multiple-pass interview methodology allows the respondent repeated opportunities to recall their intake within the past 24 hours and to provide detailed food descriptions. Food portion estimation visual aids are provided to respondents to assist in portion size estimation.

Contact person is Mary Stevens at 612.626.9428 or steve004@umn.edu for more information.
APPENDIX G: COMMON SWEET SNACKS AND DESSERTS CONTAINING ≈ 330 KCALORIES

Three servings of figs = 330 kcalories

<table>
<thead>
<tr>
<th>Type</th>
<th>Serving size</th>
<th>Kcalories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chocolate chip</td>
<td>4 oz</td>
<td>350</td>
</tr>
<tr>
<td>Oatmeal</td>
<td>4 oz</td>
<td>360</td>
</tr>
<tr>
<td>Oreo</td>
<td>4 oz</td>
<td>320</td>
</tr>
<tr>
<td>Pound cake</td>
<td>3 oz</td>
<td>330</td>
</tr>
<tr>
<td>Brownie</td>
<td>3 oz</td>
<td>350</td>
</tr>
<tr>
<td>Two fig bars</td>
<td>4 oz</td>
<td>320</td>
</tr>
<tr>
<td>Apple pie</td>
<td>4 oz</td>
<td>340</td>
</tr>
<tr>
<td>Carrot cake</td>
<td>3 oz</td>
<td>350</td>
</tr>
<tr>
<td>Granola bar</td>
<td>6 oz</td>
<td>360</td>
</tr>
<tr>
<td>Three Musketeers candy bar</td>
<td>3 oz</td>
<td>360</td>
</tr>
<tr>
<td>Ice cream</td>
<td>4 oz</td>
<td>420</td>
</tr>
</tbody>
</table>
APPENDIX I: NCEP DIETARY RECOMMENDATIONS

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 these:

- high LDL cholesterol or other lipid disorders
- coronary heart disease or other cardiovascular disease
- diabetes mellitus, insulin resistance or metabolic syndrome

What does the TLC diet recommend?

In May 2001 the NCEP released new guidelines for cholesterol management. These new guidelines are in the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]). The American Heart Association accepted and endorsed this report and began incorporating these recommendations into its materials on dietary and lifestyle change for people with high blood cholesterol.

ATP III recommends that therapy for elevated cholesterol begin with more intensive life-habit intervention to lower cholesterol and reduce the risk for developing heart disease and having a heart attack. This approach is referred to as the "Therapeutic Lifestyle Changes (TLC)" diet. It’s targeted to people whose LDL cholesterol is above the goal level for their category of risk for heart disease. These are the essential components of TLC:

<table>
<thead>
<tr>
<th>Component</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-raising nutrients</td>
<td></td>
</tr>
<tr>
<td>Saturated fats*</td>
<td>Less than 7% of total calories</td>
</tr>
<tr>
<td>Dietary cholesterol</td>
<td>Less than 200 mg/day</td>
</tr>
</tbody>
</table>

Therapeutic options for LDL-lowering:

- Plant stanols/sterols: 2 grams per day
- Increased viscous (soluble) fiber: 10–25 grams per day

Total calories (energy): Adjust total caloric intake to maintain desirable body weight/prevent weight gain

Physical activity: Include enough moderate exercise to expend at least 200 kcal per day

* Trans fatty acids also raise LDL and should be kept at a low intake.
TLC Diet in ATP III

Nutrient          Recommended Intake as Percent of Total Calories

Total Fat\(^1\)  25–35%
Saturated         Less than 7%
Polyunsaturated   Up to 10%
Monounsaturated   Up to 20%
Carbohydrate\(^2\) 50–60% of total calories
Protein           Approximately 15%
Cholesterol       Less than 200 mg per day
Total Calories\(^3\) Balance energy intake and expenditure to maintain desirable body weight and prevent weight gain

1. The 25–35% fat recommendation allows for increased intake of unsaturated fat in place of carbohydrates in people with the metabolic syndrome or diabetes.
2. Carbohydrate should come mainly from foods rich in complex carbohydrates. These include grains (especially whole grains), fruits and vegetables.
3. Daily energy expenditure should include at least moderate physical activity (contributing about 200 Kcal a day).
4. Options include adding 10–25 grams of viscous (soluble) fiber; 2 g/day of plant-derived sterols or stanols. Soy protein may be used as a replacement for some animal products.

Related AHA publications:

- Easy Food Tips for Heart-Healthy Eating (also in Spanish)
- "How Can I Cook Healthfully?", "How Do I Follow a Low-Fat Diet?" and "How Can I Manage My Weight?" in Answers By Heart kit (also in Spanish kit)
- "What About Eating Out?", "How Do I Read Food Labels?", "How Do I Change Recipes?" and "Why Should I Lose Weight?" in Answers By Heart kit

Related AHA Scientific Statements
Diet/Nutrition