HYPOCHOLESTEROLEMIC EFFECTS OF DRIED PLUMS IN POSTMENOPAUSAL WOMEN

By

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NOMENCLATURE

Apo A-1	apolipoprotein A-1
Apo B	apolipoprotein B
AHA	American Heart Association
BMI	body mass index
CAD	coronary artery disease
CHD	coronary heart disease
CRP	c-reactive protein
CVD	cardiovascular disease
E_2	estradiol
ERA	Estrogen Replacement and Atherosclerosis study
ERT	estrogen replacement therapy
HDL	high-density lipoproteins
HERS	Heart and Estrogen/progestin Replacement study
HMG-CoA	3-hydroxy-3-methylglutaryl coenzyme A
HRT	hormone replacement therapy
LDL	low-density lipoproteins
Lp (a)	lipoprotein a
MUFA	monounsaturated fatty acids
NCEP	National Cholesterol Education Program
NHLBI	National Heart, Lung and Blood Institute

NOMENCLATURE (continued)

ORAC	oxygen radical absorbance capacity
PUFA	polyunsaturated fatty acids
SERMs	selective estrogen receptor modulators
TC	total cholesterol
TG	triglycerides

CHAPTER I

INTRODUCTION

Cardiovascular disease (CVD) is the most common cause of death among men and women in the United States. Since 1900 it has been the number one killer in the country, with the exception of 1918 (AHA, 2001). CVD includes hypertension, coronary heart disease (myocardial infarction and angina pectoris), stroke, congenital cardiovascular defects, and congestive heart failure. On average, one death occurs every 33 seconds from CVD. This disease claims approximately 150,000 lives, under the age of 65, each year. Out of all the cardiovascular diseases, coronary heart disease (CHD) is the single largest killer of Americans (AHA, 2001).

It is estimated that CVD will cost $329.2 billion in the year 2002. This amount includes direct (i.e. health expenditures, medications, etc.) and indirect costs (i.e. lost productivity). CHD alone is predicted to cost the economy $111.8 billion in 2002 (AHA, 2001).

Risk factors for CVD are numerous and include smoking, elevated low-density lipoprotein (LDL), high triglycerides (TG), low high-density lipoprotein (HDL), elevated lipoprotein (a) (Lp(a)), oxidative stress, hypertension, high fat diet, physical inactivity, obesity, diabetes mellitus, and postmenopausal status without hormone replacement therapy (HRT) (Davidson & Maki, 1998). Between 1988-1994, 61% of American men and 51% of American women were found to be overweight [body mass index (BMI) $\geq$ 25.0], compared to 1960-1962 when only 49.1% and 40.2% respectively were found to be overweight (AHA, 2001).

Research has revealed that after the age of 50 more women have high cholesterol than men. Forty-eight percent of American men and 43.3% of American women age 20 years and older were found to have elevated LDL levels. In the same age group 39% of American men and 14.9% of American women were found to have HDL levels $\leq$ 40 mg/dl (AHA, 2001).

After the onset of menopause CHD risk appears to increase 2-3 times in women (AHA, 2001). Ovarian hormones including estradiol (E_2) and estrone (E_1) levels drastically decrease at the onset of menopause (Mosca, 2000; von Holst, 1994). Decreased E_2 production has been linked to an increase in total cholesterol, LDL-cholesterol, and TG (Schwab, 2000). However, the true relationship between estrogen production and CHD in postmenopausal women remains unclear. Studies have shown that estrogens decrease CHD risk by acting directly on the vascular wall and decreasing the rate of atherosclerotic progression (Tremollieres et al., 1999).

One of the most common methods used to treat symptoms of menopause is exogenous estrogen in the form of HRT. Research has shown HRT to be beneficial for postmenopausal women as far as improving lipid profiles and decreasing the risk of osteoporosis. However, certain risks have been associated with HRT. Some studies have shown that HRT might increase the risk of breast and/or endometrial cancer, and thrombosis (Greendale et al., 1999). As a result some women might not be willing or able to receive HRT.

An alternative to HRT, still undergoing research, is selective estrogen receptor modulators (SERMs), e.g. raloxifene and tamoxifen. SERMs appear to have cardiovascular benefits for postmenopausal women with less risk of developing

hormone sensitive cancers as seen with HRT. However, SERMs appear to be less effective in treating some symptoms of menopause, such as hot flashes (Anthony et al., 2001). SERMs continue to remain controversial as far as benefiting the cardiovascular system (Roe et al., 2000; Valk-de Roo et al., 1999). As a result, postmenopausal women continue to seek alternative and more natural ways to decrease CHD risk associated with menopause. Animal and human research has shown that bioactive constituents of certain foods such as polyphenolic compounds and fiber are beneficial in decreasing CHD (Arjmandi et al., 1992; Lucas et al., 2000; Tinker et al., 1991; Wolk et al., 1999). Among fruits, dried plums are an excellent source of fiber and polyphenolic compounds (Donovan et al., 1998; Stacewicz-Sapuntzakis et al., 2001); however, the cholesterol-lowering properties of dried plum in postmenopausal women have not been investigated.

Dried plums, also known as prunes, (*Prunus domestica L.)* continue to show promising effects in decreasing some of the risks associated with heart disease. Dried plums are a good source of fiber, flavonoids, and phenols, which research has shown to possibly have a cardioprotective effect (Donovan et al., 1998; Lucas et al., 2000; Stacewicz-Sapuntzakis et al., 2001; Tinker et al., 1991). The purpose of this study is to determine if a relationship exists between dried plum intake and blood lipid levels in postmenopausal women.

The **hypothesis** of this study is that regular consumption of dried plums by postmenopausal women improves their blood lipid profiles including cholesterol and triglycerides.

The **objectives** of this study are:

1. To determine if consumption of 100 grams of dried plums versus 75 grams of dried apples daily will decrease total- and low density lipoprotein (LDL)-cholesterol, TG, Lp(a), apolipoprotein B (Apo B) and c-reactive protein (CRP).
2. To identify if daily intake of dried plums or dried apples increases HDL-cholesterol and apolipoprotein A (Apo A-1).

CHAPTER II

REVIEW OF LITERATURE

IMPACT OF CORONARY HEART DISEASE IN THE UNITED STATES

Coronary heart disease (CHD), also known as coronary artery disease, is a condition that decreases blood flow through the coronary arteries to the heart muscle. Sclerosis and thrombosis are conditions that can result in CHD. Atherosclerosis occurs by forming fatty streaks, which progress to advanced lesions possibly causing acute coronary events, such as myocardial infarction or angina pectoris (Davidson & Maki, 1998).

CHD is the most prevalent killer among American men and women. Approximately every minute an American's life is taken by CHD. CHD not only affects people, but also negatively impacts the economy. The Social Security Administration spends about 19% of disability allowances on CHD. Medicare beneficiaries were paid $10.6 billion in 1998 for CHD alone. More than 12 million people today have had a heart attack and/or a chest pain episode. On average a woman or man's first heart attack will occur at 70.4 years old and 65.8 years old respectively (AHA, 2002).

The National Heart, Lung, and Blood Institute's (NHLBI) Framingham Heart Study is one of the leading cardiovascular disease studies. Part of the Framingham Heart Study found that in a study group less than 75 years old, more than half of the cardiovascular events that occurred were caused by CHD. At the age of 40, men have a 49% lifetime risk of developing CHD and women have a 32% risk (AHA, 2002). A cohort of 2,873 women who took part in the Framingham study were followed up 24

years after the initiation of the study. Postmenopausal women experienced significantly more coronary events than premenopausal women. The same study also observed that after the onset of menopause a woman is 2-3 times more likely to develop CHD compared to premenopausal women in the same age group (Gordon et al., 1978). This study demonstrated that menopause is a risk factor for CHD. This research has raised many questions on the relationship between menopause and CHD leaving researchers seeking ways to find the exact mechanisms menopause has on CHD and ways to decrease CHD risk factors associated with menopause.

Risk Factors Related to Coronary Heart Disease in Postmenopausal Women

Common risk factors associated with CHD include: elevated TC (>200 mg/dL), decreased HDL (<35 mg/dL), increased TG, obesity, high fat/cholesterol diet, cigarette smoking, hypertension, diabetes mellitus, physical inactivity, age (male >45 years old and women >55) and gender (Davidson & Maki, 1998). Women increase their risk for CHD after menopause when HRT is not initiated (Dallongeville et al., 1995; Tremollieres et al., 1999).

Menopause occurs when ovarian follicular activity ceases along with menstruation; therefore, decreasing endogenous estrogen levels (Burger et al., 2002). An increase in CHD risk has been associated with both, natural and surgical menopause (Hjortland et al., 1976; Kannel W, 1987). After the onset of menopause the decrease in estrogen production is believed to directly impact CHD risk. One proposed mechanism of how estrogen is cardioprotective is by directly affecting the vascular wall (Mendelsohn & Karas, 1994). Another study found that menopause decreases the activity of

antioxidant enzymes, which increases CAD risk (Krstevska et al., 2001). Menopause and its effect on CHD risk continues to remain a controversial issue (Do et al., 2000; Rossouw, 2000).

Over 100,000,000 Americans, 20 years or older, are considered overweight and the number continues to increase worldwide (AHA, 2002). Obesity is linked to other CHD risk factors, such as diabetes, physical inactivity, elevated TG and hypertension (Campos et al., 1991; Cordero-MacIntyre et al., 2000; Schulte et al., 1999).

Hypertension also increases endothelial cell damage, further increasing a person's risk for CHD (Davidson & Maki, 1998). When comparing postmenopausal women to men and premenopausal women in the same age group, postmenopausal women showed a greater increase in blood pressure (Bulliyya, 2001). Studies have shown mixed results on systolic and diastolic blood pressure among postmenopausal women (Bonithon-Kopp, 1990; Dallongeville et al., 1995). Controversy still remains if blood pressure is affected by menopause or if it is age related (Franklin et al., 2001; Rossouw, 2000).

A French study including 1,684 women not on HRT, found that menopause increased blood pressure, TC, LDL-cholesterol, TG, apo B, and decreased HDL-cholesterol. This study also reevaluated the data by restricting the data to women age 45-55 years old to see if age unfavorably influenced CHD risk over menopause, menopause continued to have a greater impact on CHD than age (Tremollieres et al., 1999).

Other CHD risk factors to consider are apo A-1, apo B and Lp(a). Apo A-1 is the major apolipoprotein of HDL-cholesterol and apo B is the major apolipoprotein of LDL-cholesterol (Gardner et al., 2000). Menopause was found to significantly increase apo A-1 and apo B; however, after age, BMI, and smoking status were controlled for, apo B

remained significantly higher when comparing premenopausal to postmenopausal women (Bonithon-Kopp et al., 1990; Dallongeville et al., 1995). Tremollieres et al. (1999), also demonstrated that apo B increased with menopause; however, apo A-1 levels did not significantly change. Dallongeville et al. (1995), also found menopause negatively influenced total cholesterol, triglycerides, apo B, apo A-1, and diastolic blood pressure independent of age, BMI, glycemia, smoking, alcohol intake, exercise and parity. The Framingham offspring study found a direct relationship between age and LDL-cholesterol and apo B, after adjusting for age and BMI. LDL-cholesterol and apo B remained higher in postmenopausal women when compared to premenopausal women, thus proposing a hormonal effect (Schaefer et al., 1994).

It is beneficial to evaluate the entire lipoprotein profile instead of just the TC level, which can incorrectly categorize a person's CHD risk (Branchi et al., 1994). It is still unclear if menopause directly alters HDL-cholesterol. One study comparing pre-, peri-, and postmenopausal women found postmenopausal women had higher HDL-cholesterol levels than premenopausal women. TC, LDL-cholesterol and Lp(a) were higher in postmenopausal women compared to premenopausal women; therefore, the authors concluded that HDL-cholesterol levels might be affected more by age than menopause (Kim et al., 2000). Do et al. (2000) followed women three years before and after their final menstrual period. HDL-cholesterol significantly decreased after the onset of menopause. In fact, a slight increase in HDL-cholesterol was observed about one year before menopause, then the greatest decrease in HDL-cholesterol was observed about one year after menopause. Age was found to significantly increase TG, diastolic blood pressure, BMI, and LDL cholesterol.

The impact of menopause on lipoproteins like HDL-cholesterol remains unanswered. Some studies have concluded that menopause has a detrimental affect on TG (Dallongeville et al., 1995; Kim et al., 2000; Tremollieres et al., 1999) and others have shown no effect on TG (Do et al., 2000; Pasquali et al., 1997).

Other CHD risk factors that continue to be researched are Lp(a), homocysteine and C-reactive protein (CRP). Lp(a) is structurally similar to LDL-cholesterol and is considered an atherogenic particle; therefore, a CHD risk (Jenner et al., 1993). Several studies have found a relationship between Lp(a) levels and menopause (Kim et al., 2000; Sposito et al., 2001).

More recently elevated homocysteine has been linked to heart disease. The amino acid homocysteine results from dietary protein metabolism. Homocysteine forms as a result of the conversion of methionine to cysteine. This process involves folic acid, vitamin B6, and vitamin B12 (Malinow et al., 1999). One way homocysteine increases CHD risk is by negatively affecting endothelial cells (Kanani et al., 1999; Stamler et al., 1993; Woo et al., 1997). Hyperhomocysteinemia has also been linked to increased platelet accumulation leading to CHD (McCully et al., 1987; Stamler et al., 1993). Elevated homocysteine levels were found in healthy postmenopausal women; therefore, increasing their CHD risk (Knekt et al., 2001; Ridker et al., 1999). However, homocysteine studies involving women are limited. Increased homocysteine levels were associated with low folic acid, vitamin B6 and vitamin B12 intakes in elderly men and women in the Framingham Study (Selhub et al., 1995). Many research studies have shown significant decreases in homocysteine by increasing folic acid, vitamin B6 and vitamin B12 intake (Jacques et al., 1999; Malinow et al., 1998; Rimm et al., 1998).

Another CHD risk factor is CRP, which is a vascular inflammation marker. Inflammation can result from bacterial infection, trauma and/or tissue damage (Jialal & Devaraj, 2001; Koenig et al., 1999), which can promote atherosclerosis. When evaluating CHD risk one must take into consideration all risk factors including lipid levels and lifestyle factors.

Prevention and Treatment of Coronary Heart Disease in Women

Diet and Exercise

Lifestyle modification is the first step to decrease CHD risk. Modifications such as a low fat diet, high fiber intake, physical activity, smoking cessation and an increase in dietary omega-3 fatty acid intake have all been shown to decrease CHD risk .

The American Heart Association (AHA) and National Cholesterol Education Program (NCEP) recommend two different diets to treat hypercholesterolemia, depending on the severity of the individual (AHA Scientific Position, 2002). Step I and Step II diets are listed below:

NUTRIENT	STEP I DIET	STEP II DIET
Total Fat	30% or less	30% or less
Saturated Fat	7-10%	Less than 7%
Polyunsaturated Fat	Up to 10%	Up to 10%
Monounsaturated Fat	Up to 15%	Up to 15%
Carbohydrate	55% or more	55% or more
Protein	Approx. 15%	Approx. 15%
Cholesterol	Less than 300mg/day	Less than 200mg/day
Total Calories	To achieve and maintain desired weight	To achieve and maintain desired weight

In October 2000 the AHA decided to no longer use the Step I and Step II diets, instead they recommend maintaining appropriate body weight, overall healthy eating pattern, desirable cholesterol profile and desirable blood pressure for the general population. Therefore, it emphasizes the components of food and not percentages of these components (AHA Scientific Position, 2002).

There have been many research studies demonstrating the effectiveness of the AHA Step I and II diets. By following a Step I or Step II diet a person can significantly reduce their TC and LDL-cholesterol levels (Bunyard et al., 2002; Denke, 1994; Geil et al., 1995). Physical activity further benefits a person's lipid profile when added to a low-fat and low-cholesterol diet (Stampfer et al., 2000; Stefanick et al., 1998). The effects of the AHA diets and physical activity on HDL-cholesterol are mixed (Barnard, 1991; Schuler et al., 1992; Stefanick et al., 1998).

Cholesterol lowering diets also include increased intake of fiber, monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs). Good sources of MUFAs are olive, canola and peanut oil. PUFAs are found in corn, safflower and soybean oil. MUFAs and PUFAs, when combined or used independently, reduce LDL-cholesterol particle size (Kratz et al., 2002). A diet rich in PUFAs was found to decrease TC, LDL-cholesterol and TG, but had no effect on HDL-cholesterol (Wagner et al., 2001). MUFAs have also shown benefits on decreasing LDL-cholesterol susceptibility to oxidation (Kratz et al., 2002). This is important for postmenopausal women due to research showing that menopause decreases antioxidant enzyme activity (Krstevska et al., 2001).

Increasing fiber intake, especially soluble fiber, is beneficial in decreasing cholesterol levels. Human and animal studies have revealed that soluble fiber, such as

pectin or guar gum, significantly reduce TC and LDL-cholesterol levels (Arjmandi et al., 1992; Knopp et al., 1999). In a National Health and Nutrition Examination Survey epidemiological follow-up study, dietary fiber was found to significantly decrease CHD risk in men and women (Bazzano et al., 2001). Hunninghake et al. (1994) found a 5% decrease in TC and 9% decrease in LDL-cholesterol when supplementing 20 g of fiber (guar gum, pectin, soy, pea, corn bran) per day.

Current research is focusing on functional foods and their effect on serum cholesterol levels. A few of these functional foods are soy protein, flaxseed, oatmeal, garlic, and grapes (Frankel et al., 1998; Stein et al., 1999). However, the effect of dried plums on cholesterol has not been adequately investigated and was the focus of this study.

CHOLESTEROL-LOWERING DRUGS

Lifestyle changes do not always succeed in improving lipid profiles. There are a variety of drugs available that can improve lipid profiles by different mechanisms. The most common and widely used drugs are the statins also known as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. These drugs decrease LDL-cholesterol and TG and possibly increase HDL-cholesterol by inhibiting the rate of cholesterol synthesis (Branchi et al., 2001; Kuncl & Nelson, 2000). Numerous studies have demonstrated the effectiveness of statins on improving lipid profiles by decreasing TC and LDL-cholesterol, and increasing HDL-cholesterol (Pederson et al., 1996; Pfeffer et al., 1995; Shepherd et al., 1995). Even though statins are highly effective on lipids they can be expensive and interact with other medications (Chong et al., 2001).

Another common drug used to improve lipids is bile acid sequestrants (inhibitors of bile acid transport). Bile acid sequestrants bind bile acids in the gut preventing enterohepatic cycling. Therefore, forcing the liver to make replacement bile acids from cholesterol, which increases LDL receptors drawing LDL-cholesterol from serum (Brown, 2001). Research has found bile acid sequestrants to decrease TC and LDL-cholesterol (Rifkind, 1984); however, increases in TG levels have been observed (O'Brien et al., 1990). Bile acid sequestrants can cause gastrointestinal disturbances and can be more effective when combined with HMG-CoA reductase inhibitors (Kuncl & Nelson, 2000).

Another possible option for people who cannot tolerate HMG-CoA reductase inhibitors is niacin. Niacin is used to decrease LDL-cholesterol and TG along with increasing HDL-cholesterol, but has been known to cause a number of adverse effects. Niacin stimulates the release of histamine and prostaglandins, which can cause itching and flushed skin. Niacin can be used concurrently with HMG-CoA reductase inhibitors or bile acid sequestrants. Fibric acid derivatives increase HDL-cholesterol and decrease TG; however, they have little effect on LDL-cholesterol. Derivatives of fibric acid are generally used to treat hypertriglyceridemia to prevent pancreatitis (Kuncl & Nelson, 2000).

Hormone Replacement Therapy

HRT may improve CHD risk in postmenopausal women by improving their lipid profiles. Several methods and combinations of hormones are administered to treat

menopausal symptoms. Estrogen is commonly given in combination with progestin or medroxyprogesterone to decrease possible side effects of estrogen alone.

There are several proposed mechanisms of how estrogen decreases CHD risk. Estrogen replacement therapy (ERT) has been shown to have antioxidant properties; therefore, decreasing oxidation of LDL-cholesterol resulting in decreased CHD risk (Krstevska et al., 2001; Shwaery et al., 1997). One mechanism of HRT benefiting CHD risk is by vasorelaxation of the arteries by increasing nitric oxide release from endothelial cells resulting in a decrease in blood pressure (Cicinelli et al., 1998; Collins et al., 1994). Animal and human studies have shown that estrogen can reduce coronary artery plaques, which can develop into atherosclerosis (Adams et al., 1997; Nathan & Chaudhuri, 1997). Plaques forming inside vessel walls can form a thrombus resulting in a heart attack or stroke (AHA, 2001). Atherosclerosis accounts for almost three-fourths of all CVD deaths. Estrogen has been shown to decrease atherosclerotic progression by lowering lipid levels (Dallongeville et al., 1995).

Research has shown that HRT has beneficial effects on CHD and is able to improve lipid profiles. Dallongeville et al. (1995) found that using estrogen combined with progestin resulted in significant decreases in TC, LDL-cholesterol, TG, apo B, and systolic and diastolic blood pressure. Another study evaluated the effects of ERT and combined HRT on surgical and natural menopause in over a thousand women. In this study estrogen only therapy resulted in significant decreases in TC, LDL-cholesterol and an increase in HDL-cholesterol. When conjugated equine estrogen was compared to transdermal estrogen, the transdermal method increased TG and HDL more than ERT

alone (Gokmen & Eyi, 1999). HRT is a highly researched topic since conflicting results of HRT and their beneficial affects on lipids have been found.

Three of the largest trials involving HRT and lipids are the Estrogen Replacement and Atherosclerosis study (ERA), the Heart and Estrogen/Progestin Replacement study (HERS) and the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial. HERS recruited 2763 postmenopausal women less than 80 years old who had a history of CHD. Participants were randomized into two groups: conjugated equine estrogen plus medroxyprogesterone acetate or placebo. After about four years on treatment no significant differences were found between the two groups, in fact an increase in thromboembolism occurred in the estrogen plus progesterone group. These results may have been related to prothrombotic effects of estrogen (Grady et al., 2000; Hulley et al., 1998). The ERA study was a randomized, placebo-controlled, double blind trial comparing estrogen with or without progestin versus placebo. Three hundred and nine postmenopausal women with atherosclerosis from five different sites took part in the study. Approximately three years after initiation of the study no benefit was found on the progression of atherosclerosis (Herrington & Klein, 2001). The PEPI trial was a randomized, double blinded, placebo controlled clinical trial that also evaluated the effects of ERT with and without progestin. The study evaluated three different progestin regimens on 847 postmenopausal women. Improvements in LDL-cholesterol and HDL-cholesterol levels were found. In fact women receiving estrogen alone showed a greater increase in HDL-cholesterol levels than women on one of the estrogen/progestin combinations (Barrett-Conner et al., 1997). Another study evaluating CHD risk factors and HRT involved 1746 postmenopausal women of which 369 were currently taking

combined (estrogen and progestin) HRT. Postmenopausal women taking combined hormone therapy had significantly lower serum TC, TG, apo B, and systolic/diastolic blood pressure when compared to non-HRT users (Dallongeville et al., 1995).

Most women seek HRT to relieve hot flashes and discontinue therapy when they no longer have hot flashes. More highly educated, Caucasian females are more likely to use HRT; therefore, some studies can be biased. It is estimated that approximately 30% of postmenopausal women in America take some form of HRT (Barrett-Conner et al., 2000). Noncompliance to HRT is largely due to possible side effects of HRT. Side effects include, but are not limited to, increased risk of endometrial and breast cancer, thrombosis and irregular menstrual bleeding (Lobo, 1995; Notelovitz, 1989). These side effects are very disturbing for some women; therefore, leaving them seeking other ways to decrease CHD and relieve menopausal symptoms.

Selective Estrogen Receptor Modulators

Selective estrogen receptor modulators (SERMs) produce tissue-specific agonist or antagonist activity on estrogen receptors. There are two generations of SERMs: tamoxifen and raloxifene. The first generation SERM, Tamoxifen, was originally used to treat breast cancer since it is an estrogen antagonist in the breast; however, it is an estrogen agonist in the endometrium possibly causing endometrial cancer. Tamoxifen and raloxifene have shown similar results relating to CHD risk (Anthony et al., 2001). Raloxifene has shown beneficial effects on LDL-cholesterol, Lp(a) and homocysteine. SERMs have shown decreases in LDL-cholesterol and no change in TG or HDL, unlike HRT, which can increase TG and decrease HDL (Walsh et al., 1998; Walsh et al., 2000).

SERMs can have many adverse reactions such as: increasing risk of endometrial cancer, venous thromboembolic events, stroke, and increasing menopausal symptoms such as hot flashes (Anthony et al., 2001). After considering these risks, many postmenopausal women seek natural ways with fewer side effects to treat menopausal symptoms.

PHYTOESTROGENS

Phytoestrogens have shown beneficial effects on CHD risk, menopausal symptoms, osteoporosis and certain types of cancer. Phytoestrogens are naturally occurring plant compounds that are similar in function and structure to estradiol (E_2). It is thought that the mechanism phytoestrogens use is more related to SERMs than HRT, as far as producing estrogenic and antiestrogenic activity (Anderson et al., 1999). The most common phytoestrogens are isoflavones, lignans and coumestans. Isoflavones include genistein and daidzein. Coumestrol is the most important coumestan and it is commonly found in alfalfa. The major lignans are enterolactone and enterodiol, which are produced by colonic bacteria from their dietary precursors, which undergoes enterohepatic circulation. Grains are a good source of lignans. Commonly consumed sources of phytoestrogens are cereal, beans, flaxseed, fruits and vegetables (Adlercreutz & Mazur, 1997; Humfrey, 1998).

The isoflavone class of phytoestrogens is the most extensively researched class of phytoestrogens. Genistein and daidzein make up the majority of isoflavones, which appear to have estrogenic properties. Activity of estrogen depends on the affinity of estrogen binding to estrogen receptors. Genistein and daidzein bind to estrogen receptors with less affinity when compared to E_2; therefore, they produce a weak estrogenic effect.

Antiestrogenic effects of isoflavones are possibly due to competitive inhibition of the estrogen receptor (Adlercruetz et al., 1995).

One of the most common sources of isoflavones is the soybean. Intake of dietary phytoestrogens by postmenopausal women was studied in the Framingham Offspring study. Kleijn et al. (2001) found that dietary lignin intake was much higher than dietary isoflavone intake. Asian populations consume about 20-50 grams of soy protein per day, which is about 20-80 mg of phytoestrogens per day. The total intake found in the selected population from the Framingham Offspring study was less than 1 mg per day.

The Food and Drug Administration in the United States has allowed food companies to make the health claim that soy protein reduces the risk of heart disease by lowering cholesterol levels (Setchell & Radd, 2000). An average intake of 47 g/d of soy protein in humans has been found to decrease TC an average of 9%, LDL-cholesterol by 13% and TG by 10%. Greater improvements on lipid profiles were found in participants who had higher cholesterol levels at the beginning of the study (Anderson et al., 1995).

Possible mechanisms of the hypocholesterolemic effects of phytoestrogens are: increasing bile acid excretion therefore increasing LDL-cholesterol removal, creating a hyperthyroid state, and increasing removal of LDL-cholesterol by hepatocytes by altering hepatic metabolism (Forsythe, 1995). Evidence supporting a decrease in LDL-cholesterol has been seen, but less effect has been seen on HDL-cholesterol levels (Anderson et al., 1995).

Phytoestrogens can possibly be a better alternative to drug therapy to decrease CHD due to fewer side effects. Increased risk of breast and uterine cancer has been associated with HRT unlike with phytoestrogens. In fact phytoestrogens have been

associated with a decrease in some cancers; however, it is still not clear whether phytoestrogens impact hormone sensitive cancers and significantly improve lipid profiles (Nebres & Mark, 1996).

DRIED PLUMS

Dried plums (*Prunus domestics L.)* are an excellent source of fiber, potassium, iron, folic acid, and phytochemicals (Stacewicz-Sapuntzakis et al., 2001). Dried plums recently ranked the highest in antioxidant activity using the automated radical absorbance capacity (ORAC) assay (McBride, 1999). Another study ranked plums second to strawberries in antioxidant capacity using the ORAC assay (Wang et al., 1996).

Dried plums, also known as prunes, carry the stereotype of having an increased laxative effect; however, regular consumption has shown that an excessive laxative effect does not occcur. Dried plums can actually be beneficial in maintaining regular bowel habits. The minor laxative effect dried plums might have is possibly due to the high fiber or sorbitol content (Stacewicz-Sapuntzakis et al., 2001). One study evaluated 48 men consuming 100 g of dried plums per day for four weeks. Results showed the fecal wet and dry weights increased significantly after eating the dried plums. However, this did not result in diarrhea because the water content did not change between treatment groups (Tinker et al., 1991).

Dried plums are used in India to treat leukorrhea, irregular menstruation and weakness following miscarriage (Fang et al., 2002). Animal and human studies have shown beneficial effects of dried plums on bone, cardiovascular disease and management of blood glucose levels for diabetics (Arjmandi et al., 2001; Arjmandi et al., 2002; Lucas et al., 2000; Stacewicz-Sapuntzakis et al., 2001; Tinker et al., 1991; Tinker et al., 1994).

Polyphenolic compounds are believed to have antioxidant properties. The most predominant phenolic compounds in dried plums are neochlorogenic acid and chlorogenic acid. The phenolic compounds in dried plums have been found to inhibit in vitro oxidation of human LDL-cholesterol (Donovan et al., 1998; Meyer et al., 1998). Dietary antioxidants are beneficial by preventing oxidative damage that can occur in the body. By preventing or decreasing oxidative stress within the body one can possibly decrease their risk of cancer, heart disease and other age-related diseases (Fang et al., 2002). By inhibiting oxidation of cholesterol and fatty acids this can decrease atherosclerotic plaque formation; therefore, decreasing CHD risk. Plums are also a good source of copper, which is needed for oxidative and anti-oxidative enzymes to function properly; if balance is not maintained, unfavorable lipid levels can occur (Stacewicz-Sapuntzakis et al., 2001).

The cardiovascular benefits of dried plums involve improving hypertension and cholesterol levels. Dried plums contain 745 mg of potassium per 100 g (Food Processor version 7.50, ESHA Research, Salem, OR). Potassium helps maintain proper electrolyte balance and acts like a muscle relaxant, which can help prevent or control hypertension (McDonald et al., 1998). Not only do dried plums have the potential to alleviate high blood pressure but also hypercholesterolemia (Lucas et al., 2000; Tinker et al., 1991).

Dried plums are an excellent source of dietary fiber, both insoluble and soluble. Dried plums contain about 7 g of dietary fiber per 100 g (~3 g soluble fiber and ~4 g insoluble fiber) (Food Processor version 7.50, ESHA Research, Salem, OR). Various studies and methods of fiber extraction from dried plums resulted in varying amounts of different amount of fibers in dried plums. Studies have stated that 40 to 80% of dried

plum fiber is pectin (soluble fiber) with the rest mostly being cellulose and hemicellulose (insoluble fiber). Pectin, a soluble fiber, is beneficial in improving lipid profiles. Tinker et al. (1994), performed an animal study comparing different doses of fiber types and the effect on hyperlipidemic rats. Plasma LDL and liver cholesterol decreased when animals were fed pectin or dried plum; however, it was found not to be dose dependent. A similar study involving men found dried plums significantly lowered plasma LDL-cholesterol. Fiber is believed to decrease plasma cholesterol by increasing bile acid secretion (Tinker et al., 1991). Research studies involving dried plums are limited; therefore, research using dried plums is greatly needed.

DRIED APPLES

Dried apples like dried plums are also an excellent source of fiber and antioxidants. However, research is limited using apples to lower cholesterol levels. Wang et al. (1996) analyzed 12 fruits and five commercial fruit juices total antioxidant activity using the ORAC assay. When they analyzed the wet weight (edible portion) and dry weight of the fruits, apples ranked ninth out of 12 fruits; however, plums ranked second. This leads us to the conclusion that apples appear to have an antioxidant effect, which can be protective against heart disease.

One study fed healthy rats different doses of apple pectin and orange pectin for three weeks. They examined cholesterol concentrations in feces, serum, and liver. Their findings demonstrated a significant decrease in hepatic cholesterol in all pectin fed groups. Cholesterol concentration increased significantly only in the high dose apple and orange pectin fed groups. However, serum cholesterol decreased significantly only in the apple pectin fed groups (Gonzalez et al., 1998). Another animal study compared the

effect of two different dehydrated apple products on serum and liver lipids. After feeding the hamsters a high cholesterol, high fat diet the intervention of dehydrated apple pulp or dehydrated apple pomace was initiated. After two months both apple products decreased serum TC and TG by 40-70%. Hepatic cholesterol content decreased in both groups; however, only the apple pulp decreased TG. Even after six months on treatment the apple pulp continued to decrease cholesterol and TG in the serum and liver (Bobek et al., 1990). One human study included 25 men with mild hypercholesterolemia who drank 20 ounces of apple juice supplemented with fiber and 200 mg vitamin C. The fiber supplement consisted of apple fiber and gum arabic. The random, crossover study lasted for 12 weeks with no washout period. Fiber and vitamin C intake significantly increased among subjects during the study and dietary cholesterol intake slightly, but significantly decreased during the study. The fiber supplemented juice significantly decreased TC and LDL-cholesterol (Mee & Gee, 1997). Other apple products have also shown to decrease LDL oxidation in vitro (Pearson et al., 1999). Apples have been found to contain many bioactive constituents; however, we do not know exactly which component possibly exerts this possible cardioprotective effect (Justesen et al., 1998, van der Sluis et al., 2001; Wang et al., 1996). These studies demonstrate that more research on apples and other fruits are needed to see if they consistently exert a hypocholesterolemic effect.

CHAPTER III

METHODS AND PROCEDURES

SELECTION OF SUBJECTS

Fifty-eight postmenopausal women, who had not been on HRT for at least one year, were recruited though mass mailings and newspaper advertisements from the Oklahoma State University Campus, Stillwater, Oklahoma and communities nearby. The age of the participants was 54.3 ± 5.9 (mean ± SEM) years old. Postmenopausal status was determined by at least one year of amenorrhea. Exclusion criteria consisted of: less than 2 years or greater than 10 years postmenopausal; bone disorders (osteomalacia, osteoporosis, unexplained stress fractures), cancer, diabetes mellitus, gastrointestinal or chronic digestive disorders, hypertension controlled with thiazide diuretics, active liver disease, parathyroid disorders, renal disease or problems, thyroid problems, pelvic inflammatory disease, and/or endometrial polyps. Women who smoked ≥ 20 cigarettes per day were also excluded. Participants would not qualify for the study if they currently took or have taken these medications since onset of menopause: glucocorticoids, anabolic steroids, anticonvulsants, calcitonin, bisphosphonates, estrogens, oral contraceptives, HRT, or if they had been on thyroid hormones for less than six months. The primary reason for this study was to examine the effects of dried plums on bone. Because CHD was not the primary reason for the study, women taking lipid-altering medications were not excluded.

Participants were initially screened by a telephone interview. Qualified participants were then asked to attend their first appointment where they signed a consent

form after reviewing and discussing a description of the study. Subjects were asked to attend five appointments. Three appointments took place at the Human Environmental Sciences laboratories, Oklahoma State University (OSU). The other two appointments were held at Cimarron Women's Clinic in Stillwater, Oklahoma. Twenty women dropped out of the study, because of time constraints and gastrointestinal problems, leaving 38 women completing the study. Participants were asked to maintain their normal physical and dietary habits during the study. The OSU Institutional Review Board approved the study.

EXPERIMENTAL DESIGN

This study was a randomized, controlled trial in which qualified subjects were assigned to receive either dried plums or dried apples daily for three months. Each participant consumed 100 grams of dried plums supplied by the California Prune Board, which were vacuum-sealed into individual packages. Dried apples were packaged at OSU into 75-gram vacuum-sealed packages. Study participants were asked to take into consideration the extra caloric consumption, from the study food, and adjust their diet accordingly. The dried fruit regimens were dispensed to the participants on a monthly basis. Participants returned any unused dried fruits and a self-recorded log at the end of each month to determine compliance. Seventy-five grams of dried apples was chosen as the control because it is comparable to 100 grams of dried plums in calories, carbohydrates, fat and fiber as analyzed by food analysis software (Food Processor version 7.50, ESHA Research, Salem, OR). Nutrient analysis of dried plums and dried apples is given in Table II.

DIETARY ASSESSMENT

All participants answered questions regarding their medical and nutrition histories at the beginning of the study. At the beginning and end of the study, a registered dietitian interviewed the subject and filled out a seven-day food frequency questionnaire (Thompson & Byers, 1994). Foods were then coded and analyzed by food analysis software (Food Processor version 7.50, ESHA Research, Salem, OR).

ANTHROPOMETRIC MEASUREMENTS AND BODY FAT ANALYSIS

At baseline each participant's age, weight, height, waist circumference, hip circumference, wrist circumference, knee height and body fat percentage were obtained (Table I). Weight was determined using a standardized weighing scale (Healthometer, Continental Scale Corporation, Chicago, IL). Participants weighed in street clothes without shoes. Height was obtained using a stadiometer (Shorr Productions, Olney, MD). BMI was then calculated using the Quetelet's index equation:

$$BMI = \text{weight (kg)} / \text{height}^2 \text{ (m)}$$

A trained staff member took waist and hip measurements using a measuring tape. Waist to hip ratio was calculated using waist and hip circumferences. Body fat was estimated by bioelectric impedance (Jackson et al., 1988) (Biodynamics Model 310, Biodynamics Corp., Seattle, WA).

BLOOD COLLECTION AND PROCESSING

A phlebotomist obtained a fasting 20 ml venous blood sample from each participant at baseline and at the end of three months. Blood samples were drawn into

nonheparinized vacutainer tubes and placed in ice. Samples were centrifuged at 2000g for 15 minutes at 4°C. Serum and plasma were then aliquoted into smaller microcentrifuge tubes and stored at -20°C. All blood samples were analyzed at the same time at the completion of the study.

ANALYSIS OF SERUM LIPIDS AND LIPOPROTEINS

A Cobas-Fara II Clinical Analyzer (Monclair, NJ) was used to analyze total cholesterol, HDL, Lp(a), apo A-1, apo B, TG, and CRP. Calibration of the Cobas-Fara II Clinical Analyzer was performed before each test using a Roche Calibrator (Roche Diagnostic Systems; Somerville, NJ; Nutley, NJ; Branchburg, NJ) with the exception of Lp(a) and CRP. Lp(a) and CRP were calibrated using SPQ Calibration sets (Stillwater, Minnesota). BioRad QCS Level 1 and Level 2 controls were used in all tests except apo A and apo B, where Roche Apolipoprotein Standard was used.

The process of quantitative measurement of total cholesterol occurs by cholesterol esterase acting upon cholesterol esters resulting in free cholesterol and fatty acids. The free cholesterol is then oxidized by cholesterol oxidase forming hydrogen peroxide, which is combined with 4-aminoantipyrine and phenol resulting in quinoneimine. The cholesterol concentration was measured photometrically at 500 nm. A direct relationship occurs between the increase in absorbance and cholesterol amount (Roche Diagnostics, Branchburg, NJ).

HDL-cholesterol concentrations were determined directly by adding phosphotungstic acid and magnesium chloride to serum samples and centrifuging leaving

the HDL fraction in the supernatant (Roche Diagnostic Systems; Nutley, NJ). The following equation was used to calculate LDL-cholesterol (NCEP, 1993):

LDL = total cholesterol – [HDL-cholesterol + (TG/5)]

Triglycerides are hydrolyzed by lipoprotein lipase forming glycerol and fatty acids. Adenosine triphosphate phosphorylates glycerol with the action of glycerol kinase resulting in glycerol-3-phosphate. Oxidation occurs forming dihydroxyacetone phosphate and hydrogen peroxide. A quinoneimine complex forms after hydrogen peroxide reacts with 4-chlorophenol and 4-aminophenazone. This complex was read at 490-550nm. As absorbance increases as the concentration of triglycerides proportionately increases (Roche Diagnostics; Nutley, NJ).

Apo A-1 and apo B were measured by forming a precipitate with a specific antiserum from sheep and rabbits respectively (Roche Diagnostics; Somerville, NJ). Samples were measured at 340 nm after a set amount of time. Apo A-1 and apo B levels were proportional to the degree of turbidity.

Quantitative determination of Lp(a) was performed by automated immunoprecipitin analysis (DiaSorin Inc.; Stillwater, MN). A polymeric enhancer was added to the samples prior to incubation. Antiserum was then added to the samples and insoluble complexes started forming, resulting in increased turbidity. Another incubation period occurred and Lp(a) was measured by the amount of absorbance of the solution.

CRP was determined by immunoprecipitin analysis (DiaSorin Inc.; Stillwater, MD). Antiserum was added to samples after an initial incubation period. Insoluble complexes form, which increased turbidity. Another incubation period of about five minutes occurred and the absorbance of the solution was measured.

DATA COLLECTION AND STATISTICAL ANALYSES

A trained graduate assistant entered data from the questionnaires and serum analyses into a spreadsheet. Data were analyzed using SAS (version 8.0, SAS Institute, Cary, NC). PROC MIXED was used to calculate the least square means and analysis of variance (ANOVA). The least square mean ± standard error was reported. A p value < 0.05 was considered significant.

CHAPTER IV

RESULTS

Subject Participation

Demographics of participants are given in Table I. Fifty-eight women enrolled in the study with 38 completing the study (18 on dried plum regimen and 20 on the dried apple regimen). Nine women quit the study due to noncompliance, one women thought it was too time consuming, four women dropped out because of medical conditions, and one woman quit for personal reasons. Five women in the dried plum group did not finish because of gastrointestinal problems: one stated loose stools and another stated increased flatulence, and two said the dried plums caused constipation and another stated abdominal pain. The women who completed the study stated that the study food was a reasonable amount to be consumed on a daily basis.

Nutrient Intake

The 7-day food frequency questionnaire analysis revealed no significant differences in food intakes between treatment groups or between baseline and final (Table III). This questionnaire included the dried plum and dried apple supplement. There were slightly higher intakes of total energy, protein and carbohydrate in the dried plum group at the end of the study in comparison with their baseline values, but they were not significantly different. Both groups also appeared to slightly increase their fiber intake during the study.

DEMOGRAPHICS AND ANTHROPOMETRICS

Table I gives the demographic and anthropometric characteristics of the participants. The mean age for the dried plum group was 53.6 ± 1.6 and the dried apple group's mean age was 55 ± 1.2 years. Years since menopause was 7.9 ± 1.8 and 9.1 ± 1.8 for the plum and apple groups respectively. No significance was found between the two groups at baseline for age, years since menopause, weight, BMI, waist to hip ratio or body fat percentage. There were no significant changes in weight, BMI or waist to hip ratio in either group, when baseline and final visit were compared. There were no significant changes in body fat percentage in either group; however, the dried apple group demonstrated a trend ($P = 0.0551$) of decreasing body fat percentage.

SERUM ANALYSES

Serum analyses were ran only on the participants that completed the study. Consumption of dried plums resulted in a significant increase in TC ($P < 0.05$) (Table IV), while the dried apples demonstrated a trend ($P < 0.07$) in lowering TC. LDL-cholesterol significantly decreased and HDL-cholesterol significantly decreased in the dried apple regimen, but no difference was found in the dried plum regimen. No significance was found in TG, apo A-1, apo B, Lp(a) or CRP. However, a trend ($P = 0.07$) was found in increasing TG with the dried plum regimen. Mean changes from baseline values in serum lipid parameters and body fat percentage after 3-months of dried plum and dried apple regimens is shown in figure 1.

CHAPTER V

DISCUSSION

The hypocholesterolemic effects of dried plums have not been adequately investigated. To our knowledge, there is one published human study (Tinker et al., 1991) which has shown the effectiveness of dried plums in lowering serum total cholesterol in men. The present study is the first trial to examine the hypocholesterolemic properties of dried plums in postmenopausal women. We conducted this study because the findings of our earlier animal study (Lucas et al., 2000) demonstrated the favorable effects of dried plums on lipid profiles in ovarian hormone deficiency. In that study (Lucas et al., 2000), ovariectomized rats were given diets containing either 5% or 25% dried plums for 45 days. Although both dried plum diets were effective in preventing the ovariectomy-induced rise in serum total cholesterol, only the 25% dried plum diet was able to significantly prevent the rise in serum total cholesterol.

Though elevated serum total cholesterol is a risk factor for the development of CHD, measurement of other lipoprotein particles may be necessary to adequately assess a person's risk for CHD (Branchi et al., 1994). It is well recognized that increased total cholesterol, LDL-cholesterol, TG and decreased HDL-cholesterol increase a persons' CHD risk. Other parameters that can be evaluated include apo A-1, apo B, Lp(a), CRP and body fat percentage (Kim et al., 2000; Tremollieres et al., 1999).

Our findings that dried plum regimen increased serum cholesterol contradict Tinker and colleagues' results (1991). However, in the current study we cannot offer an explanation as to why women who consumed dried plums experienced an increase in

their serum total cholesterol. Nonetheless, we can speculate that this unexpected increase in total cholesterol might have been due to high sugar content of dried plums, as sucrose has been shown to increase serum total cholesterol (Stacewicz-Sapuntzakis et al., 2001). Our findings that dried plums tended to increase TG are in agreement with Tinker and colleagues' findings (1991) where they also noticed an increasing trend in serum TG. Our results lead to the question as to whether dried plums' beneficial effects on bone in postmenopausal women (Arjmandi et al., 2002) outweigh the risk of increasing serum total cholesterol. Dried plums are a rich source of dietary fiber and antioxidants. Both dietary fiber and antioxidants have been demonstrated (Donovan et al., 1998; Stacewicz-Sapuntzakis et al., 2001; Wolk et al., 1999) to be effective in decreasing cholesterol and risk of CHD. Therefore, we cannot totally rule out the beneficial effects of dried plums in spite of our negative findings.

However, our comparative control dried apple regimen lowered ($P = 0.066$) total cholesterol concentration in comparison with corresponding baseline values. The apple regimen also significantly ($P < 0.05$) reduced serum LDL-cholesterol. More interestingly, dried apples increased ($P < 0.02$) serum HDL-cholesterol concentrations. These favorable effects of dried apples on lipid profiles may be in part due to apples' pectin and antioxidant contents. Decreasing LDL-cholesterol and increasing HDL-cholesterol is considered to be cardioprotective; therefore, CHD risk could possibly decrease among postmenopausal women using dried apples. Apples have been reported to have beneficial effects on cholesterol levels in animals and humans (Bobeck et al., 1990; Mee and Gee, 1997). Gonzales et al. (1998) conducted a study feeding rats 2.5% or 5% apple pectin, orange pectin or a control for 3 weeks. Their study found that hepatic cholesterol

concentrations were significantly decreased in all groups; however, serum total cholesterol only significantly decreased in the apple pectin fed rats.

Another interesting point in the current study is that postmenopausal women who consumed dried apples experienced a decrease in percent body fat. Postmenopausal women usually have increased central adiposity and hence the findings of our study if confirmed in future studies with larger sample size should have public health implications.

In summary, the results of the present study show that even though dried plums have shown the possibility of decreasing bone loss associated with menopause it might increase serum total cholesterol, a risk for CHD. In contrast, dried apples, as expected have not only lowered total- and LDL-cholesterol but at the same time elevated serum HDL-cholesterol, confirming the notion that apples are good fruits for health promotion. However, as to what components of apples exert the beneficial effects on lipid profiles merit investigation.

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TABLE I

Summary of Participant Demographics and Anthropometrics[a]

	Dried Apples			Dried Plums		
	Base	**Final**	***P*** [b]	**Base**	**Final**	***P*** [b]
Age (years)	55 ± 1.2	----	----	53.6 ± 1.6	----	----
Time since menopause (years)	9.1 ± 1.8	----	----	7.9 ± 1.8	----	----
Weight (lbs)	163.9 ± 7.6	164 ± 7.6	0.40	171.6 ± 8.0	172.9 ± 8.0	0.32
BMI (kg/m^2)[b]	28.3 ± 1.3	28.5 ± 1.3	0.40	28.9 ± 1.3	29.1 ± 1.3	0.31
Waist/hip ratio	0.81 ± 0.02	0.81 ± 0.02	0.81	0.81 ± 0.02	0.80 ± 0.02	0.24
Body Fat (%)[c]	37.6 ± 1.1	36.7 ± 1.1	0.06	35.6 ± 1.0	36.2 ± 1.2	0.20

[a]Values are mean ± SE; n=18 for dried plum regimen, n=20 for dried apple regimen.
[b]BMI – body mass index
[c]Body fat percentage determined by bioelectric impedance (Biodynamics Model 310).

TABLE II

Concentration of selected nutrients in dried plums and dried apples[a]

Component	Dried Apples (per 75g)	Dried Plums (per 100g)
Calories	259.5	239.0
Protein (g)	0.99	2.61
Dietary Fiber (g)	9.30	7.10
Soluble Fiber (g)	--[b]	2.98
Insoluble Fiber (g)	--[b]	4.12
Total Fat (g)	0.43	0.52
Saturated Fat (g)	0.07	0.04
Monounsaturated Fat (g)	0.02	0.34
Polyunsaturated Fat (g)	0.13	0.11
Total Sugar	58.15	42.95
Vitamin A (IU)	60.75	1987.0
A-Carotenoid (RE)	6.00	199.0
A-Beta Carotene (mcg)	24.48	1075.0
Niacin (Vitamin B3) (mg)	0.51	1.96
Vitamin B6 (mg)	0.21	0.26
Vitamin B12 (mcg)	0	0
Vitamin C (mg)	1.65	3.3
Vitamin E (IU)	4.00	2.16
Folate (mcg)	0.75	3.70
Potassium (mg)	480.0	745.0
Iron (mg)	1.5	2.48

[a]Nutrient analysis assessed by Food Processor version 7.50 (ESHA Research, Salem, OR).
[b]Not available.

TABLE III

Daily nutrient intake calculated from 7-day food frequency questionnaires of women before and after 3-month supplementation with 100 g dried plums or 75 g dried apples daily[a]

Daily intake	Dried Apples		Dried Plums	
	Before Treatment	**After Treatment**	**Before Treatment**	**After Treatment**
Total energy (kcal)	1738± 422	1785± 498	1604± 364	1989± 493
Macronutrients (g)				
Protein	73. 8 ± 20.7	64.7 ± 18.1	62.5 ± 13.4	71.7 ± 20.9
Carbohydrates	239 ± 69	252 ± 68	204 ± 47	279 ± 62
Dietary fiber	19.2 ± 6.8	24.0 ± 7.3	19.3 ± 6.0	26.9 ± 8.7
Total fat	56.9 ± 18.4	62.0 ± 28.4	59.9 ± 20.5	70.1 ± 31.6
Saturated fatty acids	19.4 ± 6.8	20.0 ± 9.8	21.5 ± 8.2	23.8 ± 9.6
Polyunsaturated Fatty acids	10.1 ± 3.9	10.8 ± 5.2	10.5 ± 4.6	13.0 ± 8.8
Alcohol (g)	1.4 ± 2.6	2.3 ± 3.4	4.8 ± 9.0	3.0 ± 7.2
Vitamins				
Vitamin A (IU)	12592 ± 9430	12830 ± 7044	15526 ± 15523	15961 ± 11978
Vitamin C (mg)	116 ± 79	107 ± 62	122 ± 79	135 ± 87
Vitamin D (IU)	165 ± 114	127 ± 78	121 ± 83	117 ± 60
Vitamin E (IU)	9.3 ± 4.2	10.5± 5.6	9.5 ± 2.9	14.4± 14.0
Vitamin K (μg)	68.7 ± 59.8	94.2 ± 82.4	121.8 ± 96.7	101.1 ± 64.9
Minerals (mg)				
Calcium	941 ± 455	710 ± 275	695 ± 273	803 ± 266
Iron	13.4 ± 6.4	13.3 ± 4.2	12.2 ± 2.8	16.3 ± 4.5
Magnesium	287 ± 77	286 ± 116	280 ± 69	353 ± 137
Phosphorus	1224 ± 364	1069 ± 335	1049 ± 272	1207 ± 401
Potassium	3029 ± 1086	2883 ± 902	2714 ± 706	3399 ± 940
Zinc	10.2 ± 3.2	9.0 ± 2.8	8.9 ± 2.0	11.0 ± 4.2

[a]Values are mean ± SE; n= 20 for dried apple regimen and 18 for dried plum regimen.

TABLE IV

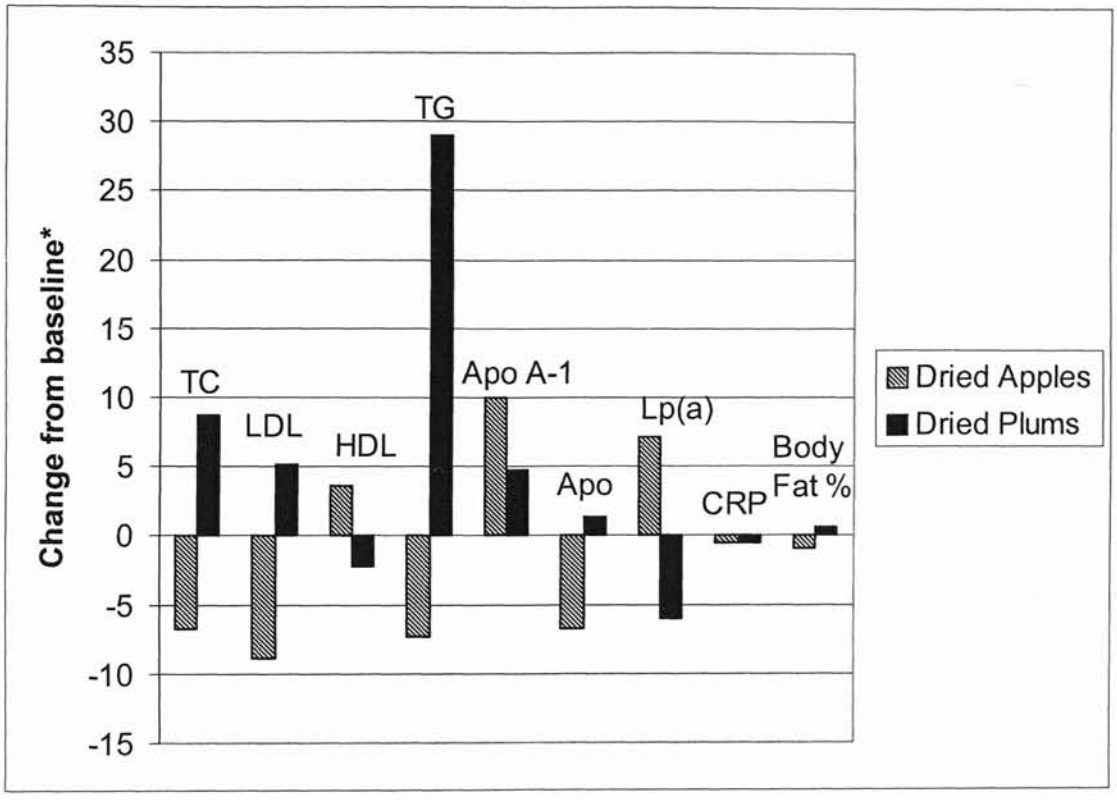
Effect of 3-month supplementation with dried plums or dried apples on serum parameters[a]

	Dried Apples			Dried Plums		
	Base	**Final**	***P*** [b]	**Base**	**Final**	***P*** [b]
Serum measurement						
Total cholesterol (mg/dL)	236.95 ± 8.49	230.15 ± 8.49	0.066	214.78 ± 8.95	223.44 ± 8.95	0.028
HDL-cholesterol (mg/dL)	37.55 ± 3.07	41.15 ± 3.07	0.016	44.31 ± 3.24	42.08 ± 3.24	0.146
LDL-cholesterol (mg/dL)	158.32 ± 8.04	149.40 ± 8.04	0.045	140.62 ± 8.48	145.69 ± 8.48	0.269
Triglycerides (mg/dL)	205.42 ± 25.73	198.0 ± 25.73	0.618	149.28 ± 27.13	178.33 ± 27.13	0.070
Apolipoprotein A-1 (mg/dL)	153.19 ± 7.73	163.6 ± 7.61	0.138	155.03 ± 8.33	161.33 ± 8.02	0.401
Apolipoprotein B (mg/dL)	129.0 ± 5.59	122.18 ± 5.59	0.256	113.94 ± 5.89	115.33 ± 5.89	0.825
Lipoprotein a (mg/dL)	47.27 ± 14.18	54.91 ± 14.14	0.134	36.24 ± 14.53	30.15 ± 14.53	0.230
C-reactive protein (mg/L)	6.77 ± 1.14	6.79 ± 1.17	0.987	5.09 ± 1.24	4.39 ± 1.20	0.647
Estradiol (pg/mL)	8.91 ± 2.42	9.33 ± 2.5	0.793	11.02 ± 2.58	9.48 ± 2.56	0.344
Estrone (pg/mL)	21.83 ± 3.84	22.37 ± 3.84	0.815	24.07 ± 4.09	21.85 ± 4.05	0.379

[a]Reported values are mean ± SE; n=20 for dried apple regimen and 18 for dried plum regimen.
[b]*P* values represent comparison within groups between baseline and corresponding final values after treatment.

FIGURE I

Mean changes from baseline values in serum lipid parameters and body fat percentage after 3-months of dried plum and dried apple regimens.



Compared with dried plums, dried apples significantly reduced total cholesterol (TC; $P < 0.01$), LDL-cholesterol ($P < 0.05$), and body fat percentage ($P < 0.05$). Dried apples significantly increased HDL-cholesterol ($P < 0.01$) and Lp(a) ($P < 0.05$). A trend was also found with dried apples decreasing triglycerides ($P < 0.1$). *Unit for TC, LDL, HDL, TG, Apo A-1, Apo B, and Lp(a) is mg/dL. Unit for CRP is mg/L and body fat is reported as a percentage.

OKLAHOMA STATE UNIVERSITY
INSTITUTIONAL REVIEW BOARD

Date:	July 1, 1999	IRB #:	HE-99-102
Proposal Title:	"EFFECT OF PRUNE ON INDICES OF BONE STATUS IN POSTMENOPAUSAL"		
Principal Investigator(s):	Bahram Arimandi Barbara Stoecker		
Reviewed and Processed as:	Expedited		

Approval Status Recommended by Reviewer(s): Approved

Signature:

Carol Olson, Director of University Research Compliance

July 1, 1999
Date

Approvals are valid for one calendar year, after which time a request for continuation must be submitted. Any modification to the research project approved by the IRB must be submitted for approval. Approved projects are subject to monitoring by the IRB. Expedited and exempt projects may be reviewed by the full Institutional Review Board.

VITA 2

Amanda Marie Georgis-Trolinger

Candidate for the Degree of

Master of Science

Thesis: HYPOCHOLESTEROLEMIC EFFECTS OF DRIED PLUMS IN POSTMENOPAUSAL WOMEN

Major Field: Nutritional Sciences

Biographical:

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Experience: Employed as a dietetic technician during the summers of 1997-1998. Worked as a graduate research assistant; Oklahoma State University, 2000-2001. Currently employed as a renal dietitian at two dialysis clinics and teach aerobics at a medical center.

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