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A Review of the Benefits of Flax Supplementation

by

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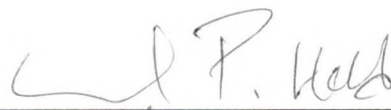
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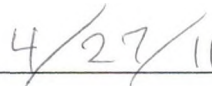
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Abstract

We have become a society of convenience. Healthy foods that were staples for thousands of years have become replaced by processed foods with long shelf lives. This has been done to the detriment of our nutrition and health. Flax is one such replaced food item. A staple food for hundreds of generations, flax had become scarce in our diet until recent interest spurred by research found flax to be one of the best sources on earth for alpha-linolenic acid an Omega-three fatty acid, plant lignans, and contains a large amount of dietary fiber. Potentially these constituents can have great health benefits for many health disparities such as cardiovascular disease including hypercholesterolemia, as well as, conditions such as cancer, inflammation, and bowel regulation.

The purpose of doing this review is to identify the proven benefits of flax supplementation to use in primary care. The main search engines used to search the literature included PubMed, CINAHL, and Google Scholar. The literature shows flax supplementation has proven LDL cholesterol lowering benefits, bowel regulation benefits, inflammatory marker reduction, and enormous potential for further research in many other areas. For this reason it is appropriate in primary practice to support flax supplementation to promote normal cholesterol levels, and for bowel regulation.

Key Words: lignans, flax, flaxseed, Omega-three Fatty acids, cholesterol, ALA, and cardiovascular disease

A Review of the Benefits of Flax Supplementation

Cardiovascular disease is prevalent in our society with 26.6 million diagnosed as having heart disease in the United States (CDC Fast Stats). This is due in part to diets high in Omega-six fatty acids found in animal derived meat and fats. During the past decade studies have found that supplementing the diet with foods rich in Omega-three fatty acids can help reduce the risk of cardiovascular disease. Fish oil is one such food that is high in Omega-three fatty acids; however there are concerns about the fish taste contained in fish oil supplements, industrial overfishing, and contaminants such as mercury found in fish. For those who want an alternative to fish oil, there is a common agricultural product that may also have cardioprotective Omega-three fatty acids, anti-inflammatory lignans, and beneficial fiber. This product is flax.

Flax is a grain that has been grown domestically since at least 8000 BC. (NDSU, 2007). It has been touted as a health food for hundreds of years; in the ninth century the Roman Emperor Charlemagne believed in the benefits of flax so much that he enacted a law to force its consumption among his constituents (Children's Better Health Institute, 2005). The seeds can be eaten whole or milled into flour, and the plant itself is very durable. In fact, flax has been used to make linen and is currently used to make cigarette paper, due to its durability in thin layers.

Flax seeds are very high in fiber, protein, magnesium, thiamine, plant lignans, and Omega-three fatty acids in the form of Alpha-linolenic-acid (ALA) (Buse, et al., 2009). ALA is one of only two essential fatty acids, meaning that it is needed by the body, however, the body is not able to produce it. In order to be utilized, ALA must be converted to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the body (Consumer Reports on Health, 2009). Fish oils are already high in the fatty acids EPA and DHA, but do not contain any fiber or plant

lignans. Current studies on ALA attempt to not only determine the amount of ALA that is able to be converted by the body, but also determine whether ALA has the benefits of EPA and DHA on its own. In addition, there are questions about the potential benefits of the fiber and plant lignans found in flax. This paper will attempt to identify the proven benefits of flaxseed product supplementation.

Purpose

This independent study on flax supplementation will review the current literature in order to fully understand the proven benefits of dietary supplementation with flaxseed and flax derived products. The health aspects looked at for the use of flax supplementation include cardiovascular health, type 2 diabetes mellitus, prostate cancer, inflammation, menopausal symptoms, and bowel management. ALA, fiber, and lignans are the three components of flaxseed that will be the focus of this review.

After completing this review, an educational pamphlet was created for use in clinical settings to discuss the research findings on flax supplementation (see Appendix B). If the findings are beneficial, methods in which to add flax to the diet, for example adding a tablespoon of ground flax to oatmeal or yogurt, or potential ways to use flax in baking, may be included. The potential recommendations for or against flax supplementation will be used for personal supplementation, as well as, for future patients, colleagues, and family members. If there is not sufficient evidence to support supplementation, or the evidence is not in favor of supplementation, flax supplementation will not be recommended.

Significance

This study has the potential to impact nursing science and practice in a positive way by improving the health of our patients. The science of nursing is a science that has health

promotion at its core. It focuses on taking a primary preventative approach to illness rather than a tertiary treatment approach. Dietary modification can affect several levels of prevention, it can be used to help prevent disease altogether, or it can be used to maintain and improve disease processes already at play. Flax supplementation could be one such dietary modification with preventative and treatment properties. Some of the potentially beneficial ingredients include a high amount of fiber, both soluble and insoluble, high concentrations of ALA omega-three fatty acid, and antioxidant plant lignans of which flax has 800 times the amount of lignans found in most other foods (Demark-Wahnefried, 2008). If flaxseed supplementation is effective at improving health or quality of life, it has the potential to affect all areas of health care for the prevention and treatment of disease.

This study is important in that it will demonstrate the potential benefits and or detriments of flax supplementation. With Cardiovascular disease consistently being a leading cause of mortality in the United States, a natural method of potential prevention is immensely important. This is especially true when the method of prevention is generally easy, such as eating or taking a supplement. If supplementation of flax may have the ability to help prevent cardiovascular disease like fish oil, but does not have the mercury contamination, bad taste, or allergenic affect, people may be more apt to adhere to a flax regimen. Also, there are a number of potential benefits of the fiber in flax. Much of the population requires fiber supplementation and or laxative use in order to maintain regularity of bowel movements and prevent constipation. Flax could potentially solve this problem without unnatural, and possibly detrimental, pharmacologic interventions. In addition, flax lignans have the potential to act as antioxidants that could prove to have many potential benefits, the extent of which are unknown.

While this study will not generate new results or uses for flax, it will compile the results already available making them easier to compare and contrast. In addition, it will help to determine the proven benefits of flax, the quality and reliability of the current information, and whether there is a need for further study before determinations on flax supplementation can be made.

Theoretical Framework

The theoretical framework used for this review is based on Betty Neumann's Systems model. This model uses the concepts of client wholeness, the goal of optimal health and utilization of primary prevention strategies to maintain wellness (Neumann & Reed, 2007). This model's focus is not only on prevention, but also on stress, reaction to stress, and the constant continuum towards and away from health and illness (Western Governor's University College of Health, 2011).

Neumann's continuum of illness and wellness is influenced by factors such as diet. Dietary intake can have positive or negative impact on health by influencing cholesterol, laxation, and inflammation. In the absence of disease, flax supplementation has the potential to provide a positive mode of primary prevention by maintaining normal cholesterol levels, normal healthy laxation, and potentially preventing inflammation and the numerous health disparities associated with inflammation. In the presence of disease, flax supplementation can provide tertiary prevention, which involves treating conditions such as hypercholesterolemia by reducing cholesterol, constipation by increasing ease of laxation, and conditions characterized and exacerbated by inflammation. In either circumstance, flax supplementation has the potential to help maintain or trend towards a healthier state (Western Governor's University College of Health, 2011).

Definitions

In writing this review there are several terms that require definition and clarification in order to achieve understanding of the concepts included. These terms include Omega three fatty acids, Alpha-linolenic acid (ALA), Eicosapentaenoic acid (EPA), Docosahexaenoic acid (DHA), fiber, and lignans.

1) Omega-three fatty acids: are polyunsaturated fats derived from fish and many plant sources such as flax, sunflower, corn, soybeans, olives, and canola.

2) ALA: Alpha-linolenic acid (ALA) is an essential omega-three fatty acid found in high concentrations in flaxseed oil. There are questions about whether or not ALA has any beneficial health effects in the body, or if it needs to be converted to EPA and then DHA before it can be beneficial.

3) EPA: Eicosapentaenoic acid is a beneficial Omega-three fatty acid found in fish oil. EPA can be converted to DHA, which is proven to be more beneficial than EPA. Some evidence exists that ALA is able to be converted to EPA and DHA.

4) DHA: Docosahexaenoic acid (DHA) is an Omega-three fatty acid, a polyunsaturated fatty acid, which studies show to be responsible for the antiatherogenic abilities of fish oil (Alternative Medicine Review, p. 391). It has also been established as the fatty acid responsible for raising HDL cholesterol, and lowering LDLs and triglycerides.

5) Fiber: fiber is found in most plant products. It is indigestible and helps prevent constipation by adding bulk to the stool and aiding in defecation. The fiber content of flax is 28% by weight, 33% of which is soluble fiber, which may have the potential to improve insulin sensitivity and lower cholesterol (Bloedon, 2008). Soluble fiber attracts water, turning into a gel in the GI tract which adds to bulk and aids motility of the stool.

6) Lignans: lignans are compounds that naturally occur in plants. Some plant lignans can be converted into enterolignans by intestinal flora and absorbed in the blood stream. Studies suggested that high serum concentrations of enterolactone, an enterolignan, are associated with a lower risk of acute coronary events. “Associations between enterolignans and cancer are less clear,” (Kuijsten, Arts, Van’t Veer, & Hollman, 2005, p. 2812). “Among foods consumed by humans, flaxseed contains the highest concentration of enterolignan precursors,” (Kuijsten, et al., 2005, p. 2812). Flax contains over 800 fold the dietary lignan than are contained in most other foods (Demark-Wahnefried, 2008)

Review of Literature

Purpose

The majority of flax supplementation research has been done with the focus on cardiovascular health. In 2008, Bloedon set out to research the effects of flax compared to the effect of wheat bran supplementation on fasting lipoproteins, insulin resistance, inflammatory markers, and oxidative stress. Patade (2008) has also conducted research to determine whether 30g of flaxseed would have an effect on the lipid profiles of postmenopausal Native American women. Lucas conducted a study in 2007 with the goal of comparing the cholesterol and lipid lowering cardiovascular benefits of 40g ground flax supplementation to the benefits of ground wheat. Lucas also set out to determine whether there were estrogenic or anti-estrogenic effects of the lignans, which potentially could have anti-osteoporotic benefits. Dodin, Lemny, Jacques, Legare, and Masse also attempted to find the effect of lignans on lipids, as well as, the phytoestrogenic effect from flaxseed supplementation (2005).

Several other studies have been done on the efficacy of differing types of flax supplements. One such study by Austria et al. (2008) was focused on determining the efficacy of

absorption with the different modes of flax supplementation using 6g flax oil, 30g milled flax seed, or 30g whole flax seed. The intent was to determine the best method of supplementation with regards to ALA absorption, in addition to the effects of each product on cholesterol lipids and platelet aggregation. Some of the studies have been done using flax oil supplements alone. Barceló-Coblijn et al. (2008) conducted a study in Winnipeg, Manitoba with assistance from the University of North Dakota which compared the effects of fish oil to flaxseed oil in varying amounts. This study was done with firemen who were at risk for cardiovascular disease (CVD).

Flax studies have been done to determine benefits for conditions other than CVD as well. Demark-Wahnefried (2008) produced a study to determine the effect of flax supplementation on prostate cancer proliferation in patients diagnosed with prostate cancer awaiting prostatectomy. This arose because flax is a substantial source of fiber and plant lignans, which may have “antimitotic, antiangiogenic, antioxidant and phytoestrogenic effects” which could be beneficial to cancer patients (Demark-Wahnefried, 2008, p. 3577). Hallund studied the effects of plant lignan supplementation on markers for vasoconstriction and inflammation (2006). Another study regarding the benefits of flax lignans by Pan et al. was to determine the effects of flax lignans on people with type 2 diabetes mellitus, based on the protective antioxidant effects associated with lignans (2007). Dares-Dobbie conducted a study on bowel movement patterns and the need for pharmacologic laxative interventions while supplementing nursing home residents’ food with ground flax. This was done to see whether large amounts of fiber, both soluble and insoluble, would decrease the incidence of constipation (2006). Wang’s study focused on determining whether the bacteria in the human GI tract could effectively convert the lignans to a more bio-available form to be used in the body (2010).

Designs

Of the 12 clinical studies used in this review, all but two of them were double blind randomized controlled clinical trials in which a control group was used, as well as, at least one flax supplement group. Of these, one was a randomized, double-blind, cross-over study in which each group took an eight week stint of being the control group. The amount of flax supplemented in these studies ranges from 30-40g of whole flaxseed or ground/milled flax, or 1.2-6g flax oil and 360 -500 mg flax derived lignan supplement. In most of the studies, the flax products were used in baked goods to improve adherence and hide the identity of each groups' supplement. The durations of these studies varied; a presurgical study averaged 21 days, although most were 10-12 weeks, and one lasted a full year. All studies involved periodic blood sampling alone and some used urine collection in addition to measure lignan metabolites to determine adherence to the diet.

There were two studies in the review that were not randomized controlled trials, they were, however, repeatable clinical trials. One study involved the effect of incorporation of flax into the diet on bowel habits. For this study, the design was to record normal bowel habits and pharmacologic interventions for one month. Then, two months later, flax was added to the diet and bowel habits and interventions were recorded again for another month. This group was supplemented with two tablespoons of flaxseed every morning. Blood testing was not done in this study. The other non-randomized study took fecal samples from healthy young adults and colonized the bacteria, combining the bacteria with flax lignans to determine whether the GI flora could convert them to more potent and bio-available lignans.

Samples

According to Pan (2007), a sample of 67 was needed to maintain a one sided, 5% significance level for his crossover trial to allow for the chance of a 10% dropout rate. Sixty eight participants completed the Pan study. No other researchers reported the number of participants needed to maintain significance in their studies. Several of the studies had less than 55 participants; one was Austria's study in which there were only 30 participants separated into three groups, Dares-Dobbie's (2006) study on constipation which included only 12 participants, and Hallund, Tetens, Bugel, Tholstrup and Brunn's (2008) study which included only 22 healthy postmenopausal participants. The study by Dodin (2005) included the most participants with 199 healthy postmenopausal women starting the study and 179 finishing the study. Demark-Wahnefried (2008) had the second largest number of participants with 161 starting the study and 149 qualifying to finish the study. In several studies approximately 10% either did not return, dropped out, or were eliminated after being judged to have not adhered to the diet according to self reporting questionnaires and urine testing. The following inclusion criteria were used for many of the studies: age, menopausal status, cholesterol and lipid levels, health status, not currently using supplements, not using hormone replacement therapy, and one study included all subjects with prostate cancer scheduled for prostatectomy.

Measures

All but one of the studies used blood testing to determine the effects of the flax supplementation. For these studies blood was tested at induction and again at the end of the study, and most also tested blood at least once during the supplementation. One study by Barceló-Coblijn (2008) tested blood every two weeks for the 12 week period. In most studies, lipid panels were measured, but individually they also tested red blood cell fatty acid content,

insulin resistance (HOMA-ir), Hemoglobin A1C (HgA 1C), fasting glucose levels, insulin levels, inflammatory markers, oxidative stress markers, hormones, platelet aggregation, ALA levels, bone density tests, side effect journals, menopausal symptoms, and tumor proliferation markers. When urine was tested, it was tested for lignan metabolites to determine the amounts of flax consumed. Only one study, conducted by Dares-Dobbie (2006), did not measure blood or urine, but instead recorded bowel movements, reports of constipation, and use of pharmacologic interventions for bowel movements.

Approaches to Analysis

Analysis of variance (ANOVA) was used in the analysis of the data for six of the studies. The study by Bloedon (2008) was one of those; their study included both a primary and secondary stance. The primary stance was the information from all of the participants, the secondary was the findings of the participants who adhered to the diet more than 80% of the time, and the results were significantly different with adherence factored in. For most of the studies, only data from participants who finished the study were used. Several of the studies, however, did not mention the dropout rate, or possible nonadherence. The Dares-Dobbie (2006) study did not discuss their approach to analysis. Demark-Wahnefried's (2008) study analysis was based on intent to treat. Dodin (2005) and Hallund's (2006) studies used SAS statistical software.

Findings

Bloedon (2008) found ALA increased and omega-six fatty acid decreased in the flax group. At five weeks LDL was significantly reduced compared to the control group, and at 10 weeks, factoring in adherence, LDL levels were still significantly reduced. HDL levels reduced in men, but no change in HDL was found in women, and HDL levels were unchanged in the control

groups. There was no change in insulin sensitivity in either group. Flaxseed led to reduced inflammatory markers in those with hypertension, while inflammatory markers increase in the control group. With regard to inflammatory markers, 62% of the flax group vs. 32% of the control group responded favorably. Bloedon found there was a reduction in LDL at five weeks and it returned to baseline by 10 weeks, probably due to reduced dietary adherence. For this reason, the significance of this study was questioned. Further research should be done to repeat this study with greater methods of adherence testing, such as testing urine lignan metabolites.

Patade (2008) found that both flax groups had a total cholesterol level drop of 7%, without significant change in the control. LDL was reduced by 10% in the flax groups, without change in control group. HDL decreased by 17% in the control group, without change in the flax groups. Triglyceride levels increased by 18% in the control group, but only by 3% in the flax, and 8.5% in the flax and fiber group. Flax supplementation demonstrated no estrogenic effects. This study was sound, but concerns were noted. The study began with 55 subjects and ended with 42 subjects, which calls into question whether there were enough participants to be entirely valid. Also, there seems to be no method of determining the adherence of the individuals other than through random phone questionnaires.

Lucas (2002) found that the flax group had a 6% decrease in total and non-HDL cholesterol levels. LDL decreased by 4.7% (not significant), and triglycerides decreased by 12.8% (also not significant). HDLs were somewhat lowered by flax. APOa-one and APO-b (cholesterol precursors) were significantly reduced by flax and unchanged by wheat. No changes were found in markers of bone metabolism, which meant no benefits of the phytoestrogenic lignans on bone metabolism were found. This was a good study that found reductions in cholesterol and

cholesterol precursors. While LDL and Triglycerides were not reduced enough to be significant, their reduction is still beneficial. Lucas' study was good with sound subject numbers and criteria.

Austria et al. (2008) found that more ALA could be absorbed from ground flax than whole flax. Flax oil produced the highest rise in ALA, but milled flax was almost as effective. Milled flax had all the benefits of fiber and lignans, and produced a three fold increase in plasma ALA over baseline levels. EPA and DHA did not change in the plasma lipid panels. No changes in platelet aggregation or bleeding times were found. No changes in lipids or cholesterol were found in the healthy, young, normolipidemic, normocholesterolemic men. As far as ALA absorption, milled flax and flax oil are highly effective flax supplements. No changes in lipid panels were found, possibly due to healthy participants with normal lipid values.

Barceló-Coblijn (2008) found the consumption of ALA enriched supplements for 12 weeks was sufficient to elevate red blood cell levels of EPA and DHA, showing the effectiveness of ALA conversion. The amounts of ALA required to do this are easily achieved in the general population with dietary modification. There was no difference in lipid profile or plasma inflammatory markers between fish and flax oil groups. Fish oil groups had faster rises in Omega-three fatty acids in the bloodstream and the higher levels were maintained. This study illustrated that flax oil can produce much of the benefits produced by fish oil, however more research needs to be done on the effectiveness of ALA conversion to EPA and DHA, and whether intercellular EPA and DHA conversion in the red blood cells has the same effect as when dissolved in the plasma, which is measured by most lipid panels.

Demark-Wahnefried (2008) found the flax supplementation, rather than a low fat diet, showed positive effects in decreasing the tumor proliferation rates in men with prostate cancer. Tumor proliferation rates were measured by counting Ki-67 positive cells (an indication of

cancer growth) in the prostate specimens after prostatectomy. They found that those who ate flax and a low fat diet had 1.50% of cells Ki-67 positive, 1.66% in the flax and regular diet group, and 3.23% in the regular diet control group . Only low fat diets showed effects on cholesterol, which may potentially be due in part to the short duration of supplementation. This study included the highest number of participants and had some very significant findings, but was limited to the short duration of the presurgical timeframe average of 21 days. More research is needed on the full effects of lignans in order to utilize them to their full potential.

Pan (2007) found that by supplementing people with type 2 diabetes mellitus with flax derived lignans, they had significantly improved HbA1c levels, which is an indication of glycemic control. Homa-insulin resistance was reduced by 3.3% compared to baseline. Fasting glucose and insulin concentration levels were also reduced, but not significantly. There were no changes in the lipid panels, perhaps due to the lack of fiber and ALA found in flax, but absent from the isolated lignans. This study had enough participants and thorough analysis to be judged a reputable resource, however, more studies on the benefits of lignans are needed as there is currently very little available.

Dares-Dobbie (2006) found that during the flax supplementation phase there were no reports of constipation. During supplementation there was a 95% decrease in laxative use and 42% of participants increased frequency of bowel movements, while 48% had decreased frequency of bowel movements. Results showed that, in these patients, adding flax often decreased bowel movements but increased ability to have bowel movements without intervention. This study was very limited in its resource value. While the concept is good, and the information is good, there was no discussion of necessary sample size, and this study was small with only 12 participants. More research with larger samples and more analysis is needed for flax and bowel care.

Dodin's (2005) study is the largest of the group, with 199 postmenopausal women spanning one year of supplementation. While they did not demonstrate any change in bone mineral density or menopausal symptoms, the women in the flaxseed group had a significant decrease in total cholesterol of 0.2mmol/L (or 8 mg/dL). Initially systolic and diastolic BP were both reduced by 4 mm/Hg to 5 mm/Hg in the flax group, with no change in the placebo, but these numbers did not carry through to the end of the study. In addition, this study showed a slight decrease in HDL of 0.08mmol/L or about 3 mg/dL as well (Dodin, 2005). More study is needed in the effect of flax on hypertension.

Hallund (2006; 2008) produced two studies with the same study group, through testing for different factors; one for inflammation, and one for vascular endothelial constriction. While they found the C-reactive protein, a marker of inflammation, decreased by 15% through flax supplementation, they did not find any significant change in markers of constriction. This sample size was small, at 22 participants, but the results are significant and warrant further study.

In order to determine the bioavailability of the lignans found in flax, as well as, to determine whether the flora found in human intestinal tracts are sufficient to convert lignans into their usable forms, Wang et al. conducted a study in 2010. They found through culturing and isolating human fecal bacteria, it was possible to isolate groups of bacteria that convert flax lignans into potent bioavailability lignans. These bacteria were found to be more efficient and effective at converting flax lignans than can currently be done synthetically. This study has proven the effectiveness of the conversion of flax lignans in the human GI tract, as well as, the possibility of future commercial production of lignans through bacterial conversion.

Findings of Reviews

Bassett, Rodriguez-Leyva, and Pierce (2009), in doing a systematic review on flax supplementation, reviewed 53 articles on the subject. They found that ground flaxseed could reduce total cholesterol 6-11%, LDL by 9-18%, and could lower markers of atherosclerotic cardiovascular disease. The hypocholesterolemic effect was most likely associated with the fiber and lignan content of the ground flax. There were also anti-inflammatory, antiatherogenic and antiproliferative effects of flax supplementation which were attributed to the ALA Omega-three fatty acids. This review supported the idea that ALA is a cardioprotective Omega-three fatty acid, like EPA and DHA from fish oil. This review also suggested further study of flax supplementation in patients with atherosclerosis.

Prasad et al. completed a review of flax supplementation in 2009 which references 96 articles on the subject of flax supplementation and cardiovascular disease. Their findings suggested that flaxseed constituents such as fiber and lignan, but not flax oil, can suppress atherosclerotic heart disease, but can't regress it. They linked the suppressive effects to the lignan rather than the ALA content of flax. They found that flax that is low in ALA, and lignans can significantly lower lipid levels, but these effects are variable. ALA in high doses suppressed inflammation, decreased platelet aggregation and increased bleeding time. Their findings suggested that the components of flaxseed may be effective in cardiovascular health.

Pan, Yu, Demark-Wahnefried, Faranco, and Lin, in their 2009 review, critiqued 28 studies spanning the last 20 years in order to compile the proven effects of flax derived supplements on lipids. This review found whole flaxseed reduced LDL by 0.21 mmol/L and 0.16 mmol/L, flax lignans reduced LDL by 0.28 mmol/L and 0.16 mmol/L, but flaxseed oil showed

no effect on LDL. They did not find that any flax derived intervention effected HDL or triglycerides significantly.

Characteristics of individual studies included in this paper are presented in Table A1 *Summary of Study Characteristics* (Appendix), which lists studies by author and includes the types of study designs used, conclusions of each of the studies, and comments and opinions about each of the studies.

Methods

This review began with searches on several databases, mainly CINAHL, PubMed, and Google Scholar. Keywords used in the search included flax, flaxseed, Omega-three Fatty acids, cholesterol, ALA, and cardiovascular disease. When possible, the limitations of Peer Reviewed, PDF full text available, human studies, trial studies and English language were used. The initial searches in CINAHL resulted in very limited results yielding only five usable articles, however, PubMed had many more. Google scholar results brought up many of the same articles from PubMed and CINAHL, but few were able to be accessed. Through the searches, many relevant articles were found. Using the references from several of those articles led to the retrieval of several others that had not originally shown up in the searches.

Researching flax supplementation the main focus was on articles and studies that, in general, compared flax to a control which consisted of substances known to have little benefit in cholesterol management, such as wheat bran. In using these studies, any effects of the flax should be clear when compared against the control, as the control should have no significant effect of its own. Few studies were included that compared flax to another treatment modality such as fish oil. One such study did compare the two, but had flax as the primary focus and did not diminish the flax oil effects. Only human trials were included. Not all studies had a control,

but the ones selected for this review were current, and involved flax supplementation in the form of whole flaxseed, ground flax, flax oil, or flax derived lignan.

A poster was created which basically provided a summary of the review as of April 2010. This poster was completed with an overview of the reasons that flax is being studied, which included the potential benefits of ALA, lignans, the soluble and insoluble fiber, and the best form in which to supplement flax. An in-depth review of the studies reviewed was also included. The proven benefits of flax supplementation were highlighted along with considerations for practice and intentions for a final product.

Results

In order to determine the effectiveness of the pamphlet, it was posted to an evidence based practice graduate level nursing class blog. The purpose of this was to obtain peer reviews of not only the pamphlets presentation, but of the content as well. In total, five peers viewed and commented on the pamphlet. Most comments were very positive, with several constructive comments on the need to reduce the information posted in the body of the pamphlet. These comments were taken into consideration and edits were made to make the pamphlet easier to read and comprehend.

Using the information found in this review and the pamphlet created, education will be provided to both patients and colleagues on the benefits and indications for flax supplementation. This information will be introduced into practice and both this review and the pamphlet will be available for patients and practitioners to use at their discretion. Also, this information can be used to create and present a presentation about flax supplementation geared towards either patients or providers.

Discussion and Implications for Nursing

Practice

The findings of the studies reviewed indicated there is great potential for flax supplementation with regards to cholesterol management. Studies have shown modest improvement in both total cholesterol, and LDL cholesterol through flax supplementation. For this reason practitioners should advise the addition of flax in the diets of patients who wish to maintain a normal cholesterol level, as well as, those who need to reduce their LDL cholesterol.

For patients who use pharmacologic bowel regulation measures, trialing flax supplementation in lieu of pharmaceutical methods could be suggested. While the bowel health study reviewed was limited in its size and analysis, the findings were valid. Personal experience supplementing the diet with ground flax can have tremendous abilities in the prevention of constipation, with fewer episodes of gastronomic disturbance and flatulence than many high-fiber foods on the market today.

Research

While the findings of the studies have proven there are benefits to flax supplementation, the full extent of the benefits are not fully understood. This is especially true of the benefits of lignans found in the flaxseed. Flax has the highest concentration of lignans of any organic food source. Additional questions regarding flax lignans include: how beneficial are lignans? What health conditions can lignans provide protection from? and what conditions are they able to treat? In order to answer these questions more research is required.

In addition, the full effects of the ALA found in flax are still not fully understood. More research is needed in order to determine the body's abilities to utilize ALA for a significant benefit. Debate also continues about the cholesterol lowering abilities of flax being either an

ALA or lignan/fiber benefit. These questions need to be answered and the only way to accomplish that is through more research.

The final area of flax supplementation that has greatly overlooked potential is the bowel management properties of the fiber found in flax. The one study reviewed was very small in sample size and low in analytical discussion, the results were very clear, but more study is needed to determine just how effective flax supplementation is in treatment of constipation and bowel regulation. From personal experience supplementing a diet with flax, it has tremendous abilities in the prevention of constipation. However more research showing its full effectiveness would be very beneficial.

Education

Education on dietary modification is necessary in order to promote inclusion of flax in the diet. Ground flax has a relatively short shelf life, and must be used or frozen within a month after grinding or opening. Also, it is necessary to start with a small amount of flax and increase to a total of two to four tablespoons per day in order to acclimate to the large amount of fiber without abdominal discomfort. Adequate hydration is necessary with all high-fiber diets in order to prevent constipation.

Ways in which to include flax in the diet are often simple, such as adding ground flax to yogurt, cereal, or oatmeal. It can also be mixed in condiments such as mustard or mayonnaise and used in a sandwich. It can be used in baking as well, either as an addition to the ingredients, or as a substitute for eggs or cooking oil. One tablespoon of ground flax with three tablespoons of warm water, when mixed and allowed to sit, can be substituted for an egg (Buse et al., 2009). One cup of flax flour can replace one-third cup of cooking oil (Children's Better Health Institute, 2005). Imagine the health benefits of using less cooking oil and more flax in our everyday diet.

Flax should be a mainstay in baked goods; all it takes is a little education on our part and the parts of dieticians in order to get more people to consume more flax.

Health Policy

Flax supplementation would not require much in the way of health policy change, rather the extent of its benefits are in need of further study, and more dietary inclusion. Once flax benefits are fully known, it could become a staple health food that would be recommended in many areas of healthcare. Policy should not be affected except in facilities whose policies would change in order to include flax in their diet.

Summary/Conclusions

In conclusion, flax supplementation is a topic of debate for good reasons. It has been linked to improved cardiovascular health through the anti-inflammatory, antiatherogenic and antiproliferative properties of ALA. Also, it has anticholesterolemic properties through ingestion of the lignans and fiber. The full benefit of ALA and lignans in humans is still not fully understood, but additional research should determine the full extent of ALA function and use.

The cardiovascular effects of flax supplementation are only the tip of the iceberg as far as the potential benefits of flax goes. Flax also has tremendous potential for beneficial effects on bowel management, diabetes management, and reduction of tumor proliferation rates. Some of these benefits are not fully understood and will require additional research in order to determine the extent of the benefits and what conditions may benefit from flax supplementation.

Phytoestrogenic effects were not shown in any of the studies reviewed, so flax should neither be used for nor contraindicated by phytoestrogenic effects.

Flax supplementation shows great promise. Currently there is sufficient evidence showing that flax has benefits for both cardiovascular health, in the form of cholesterol management, and

bowel health, in constipation management. Among flax supplementation, ground flax is considered the best medium of supplementation due to the availability of the ALA to be absorbed easily, as well as, the presence of the fiber and lignans.

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Appendix

Table A1

Summary of Study Characteristics Table

Author(s), Year	Description of Study	Conclusions	Comments
Bloedon, L., et al. (2008).	Randomized clinical trial using 62 men and postmenopausal women. Randomly given 40g/day of flax supplementation.	Ground flaxseed has a modest but short lived LDL-C lowering effect, yet reduces inflammatory markers and improves insulin sensitivity in hyperlipidemic adults. The HDL-C lowering effect of flaxseed in men warrants additional study.	Good study with clinical testing but indicates further need for testing.
Patade, A. (2008)	Randomized clinical trial 55 female Native American postmenopausal women with hypercholesterolemia given 30g flaxseed, oat bran+ flaxseed, or a control supplementation for three months.	Results in flaxseed group showed a 7-10% decrease in LDL levels. HDL and triglycerides remained unchanged.	Good article, good sample, and good time frame.
Lucas, E., et al. (2002).	Randomized clinical trial, 58 postmenopausal women consumed 40g of flax or wheat substitute daily for three months.	Flaxseed supplementation lowered total cholesterol, and non-HDL. The control regimen had no effect. Flaxseed regimen reduced serum levels of both LDL and HDL. Bone formation markers not affected by phytoestrogenic effects of flaxseed supplementation.	Good study covering a longer study period and higher number of subjects than the study by Hallund.
Austria, J. et al. (2008)	30 healthy volunteers ages 18-49 randomly assigned to three treatment groups, ingesting whole flax seed, milled flax seed and flax seed oil in baked goods. Over a period of 12 weeks.	Were able to extract more ALA from ground flax than flax. Oil produced highest rise in ALA, but has low shelf life. Milled flax has all the benefits of fiber and lignans with three times the increase in	Gastrointestinal disturbances found to hinder compliance in whole seed group.

		plasma ALA. EPA and DHA did not change. No change in platelet aggregation or bleeding times. No change in lipids or cholesterol.	
Barcelo-Coblijn, G. (2008)	Study involving six groups consisting of 9-12 Winnipeg firefighters over age 40 not on medication, exercising, and eating a high fat diet. Control group had 1g sunflower oil supplement. Flax oil groups were supplemented with 1.2g/day, 2.4g/day, or 3.6 g/day. Fish oil groups supplemented with 0.6g/day or 1.2g/day. Blood was tested every two weeks for 12 weeks. Study protocol approved by UND and blood samples tested at UND.	The consumption of ALA enriched supplements for 12 weeks was sufficient to elevate red blood cell levels of EPA and DHA showing the effectiveness of ALA conversion. The amounts of ALA required to do this are easily achieved in the general population with dietary modification. There was no difference in lipid profile or plasma inflammatory markers between fish and flax oil groups.	Shows that ALA can be effective like fish oil. However, found fish oil increases levels more quickly and maintain levels higher than flax oil.
Demark-Wahnefried, W. (2008)	Randomized controlled clinical trial to test effects of a regular diet, a low fat diet, low fat diet with flax seed supplementation or flax seed supplementation with a regular diet on 161 individuals with prostate cancer prior to prostatectomy. Average 30 days from initiation to end point. Levels were measured for PSA, LDL, cholesterol, testosterone, insulin-like growth factor-one, and the tumor marker Ki-67. 149 participants finished the study.	The flax groups had significantly lower tumor proliferation rates which were 1.5 For flax and low fat, 1.66 for regular diet and flax, 3.2 for the regular diet without flax, and 2.56 for the low fat diet without flax. Cholesterol decreased in low fat diet. Flax may be protective against prostate cancer.	Large study sample, short time frame, good results and repeatable study.
Dares-Dobbie, E. (2006)	Non randomized clinical trial of flax supplementation in food cooked in a nursing home for willing	Laxative use decreased by 95% during flax supplementation. Half had increased bowel	Very interesting study with enormous potential for impact in the elderly

	participants, comparison of bowel movements, PRN laxative use, over a month's time before and after flax supplementation.	movements with flax, half had fewer. None reported constipation during the flax supplementation.	population. Also a great benefit for those with bowel irregularity. Good study on secondary benefits of flax.
Pan, A., et al. (2007)	Randomized, double-blind, cross-over trial for the use of flax lignan supplement on type two diabetics. 37 took a 360mg flax lignan pill and 36 took a placebo for 12 weeks, took eight weeks off then the groups switched for 12 weeks. Urine tests validated adherence in lignan group.	Lignans reduced Homa-insulin resistance by 3.3% compared to baseline. Fasting glucose and insulin concentration were also reduced, but not significantly. By week 12 HgA1c was significantly reduced.	Study had good findings, and information regarding why they chose the number of participants and how they chose the amount of lignan.
Dodin, S., et al. (2006)	A randomized double-blind clinical study in which 199 healthy menopausal women were assigned to 40 g flax or wheat germ placebo for 12 months. Menopausal symptoms, lipids, and bone mineral density at were recorded at onset and at 12 months.	Flaxseed reduced total cholesterol, 0.2 mmol/L, and HDL 0.08 mmol/L. There was no change in bone mineral density. Similar reductions in menopausal symptoms were found in both placebo and flax groups.	Good size and duration of study, shows good decrease in total cholesterol.
Hallund, J., et al. (2006)	Randomized, double-blind, placebo controlled crossover study in which 22 postmenopausal women ate muffins daily with or without the flax derived lignans. Blood draws were taken to measure markers of vascular endothelial constriction.	This study showed no significant change in the markers of vascular constriction.	Small sample size, but otherwise good study, shows that lignans probably do not reduce endothelial inflammation.
Hallund, J., et al. (2008)	Randomized, double-blind, placebo controlled crossover study in which 22 postmenopausal women ate muffins daily with or without the flax derived lignans. Blood draws were taken to measure C-reactive	This study did show a significant difference of 15% in CRP levels from the flax lignan group in comparison to the placebo group.	Small sample size, but otherwise good study, shows that lignans probably do reduce inflammation.

	protein (CRP) a marker of inflammation.		
Wang, C., et al. (2010)	Clinical trial of producing enterodiol, an effective antioxidant from defatted flax seeds by using human intestinal bacteria.	This study found that the intestinal bacteria cultured from fecal matter of healthy young adults, is an effective, efficient and eco-friendly way to convert flax lignans to enterodiol, a potent antioxidant.	This clinical trial isolated the bacteria in order to determine which combination of bacteria yields enterodiol.
Pan, A., et al. (2009)	Literature review including 28 studies dating from 1990-2008. Review covered whole flax seed, flax derived lignans and flax seed oil supplements effect on adult lipid profiles.	Flaxseed interventions reduced total LDL concentrations by 0.1 and 0.08 mmol/L, Whole flaxseed by 0.21 and 0.16 mmol/L, flax lignans by 0.28 and 0.16 mmol/L, but flaxseed oil showed no effect on LDL. No flax derived intervention had significant effect on HDL or triglycerides.	This review was fairly comprehensive and used the Jadad score in order to determine validity of the studies.
Bassett, C. (2009)	Review of clinical dietary intervention trials. 53 references.	Evidence suggests that ALA and lignans provide hypercholesterolemic action. ALA contributes to the antiatherogenic effects of flaxseed via anti-inflammatory and antiproliferative mechanisms.	Good review covering many of above articles as well as many more that were unavailable to me.
Prasad, K. (2009)	Review of studies on the effectiveness of flax seed supplementation on cholesterol in humans and animals. Discusses contents of flax including cyanide. Eating one kg per day could cause problems in regards to cyanide toxicity.	Flaxseed, not flax oil can suppress the development of atherosclerosis, but do not regress atherosclerosis. Flaxseed oil in large quantities can suppress inflammatory mediators and decreases platelet aggregation. Flaxseed oil may interact with anticoagulants. Review finds flax may be	Very thorough review. 96 references. States good and bad qualities of flaxseed supplementation.

		good for cardiovascular health.	
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Appendix B

Why consider flax supplementation?

- Like fish oil, flax is high in omega-3 fatty acids. However flax also contains fiber, lignans which can act as antioxidants, and are a good option for those allergic to fish.
- Flax can help lower cholesterol.
- Flax can help prevent constipation.
- Flax has potential to reduce systemic inflammation.
- Easy to supplement and incorporate in diet.



Flax Bread

North Dakota Flax Field



FLAXSEED SUPPLEMENTATION

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FLAXSEED SUPPLEMENTATION

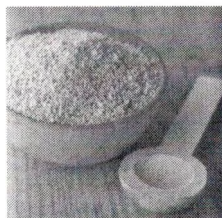
How flaxseed can benefit your health.



Whole Flax Seed

Benefits of flaxseed supplementation.

- Ground flax supplementation is proven to:
- Lower total cholesterol by as much as 6-11%.
- lowers LDL cholesterol by as much as 6-18%.
- Reduce incidences of constipation and need for laxative use.
- Improve markers of systemic inflammation.



Ground Flax.



Flaxseed before and after grinding.

How to supplement with flaxseed.

Flax is best supplemented as ground flax and flax flour as it has a fibrous shell that must be broken before the contents can be digested.

Flaxseed contains a large amount of fiber, when you start to use flax start with one teaspoon of flax flour, and gradually increase up to 2 tablespoons to avoid gas or abdominal discomfort.

Flax flour can go rancid faster than regular flour, for this reason it may be best to buy whole flaxseed which has a long shelf life then grind it in a coffee grinder prior to use.

Flax flour will last longer if stored in the freezer.

Tips for supplementing with flaxseed.

Add ground flax or flax flour to cold cereal, yogurt, oatmeal, or condiments such as ketchup, mustard, or mayonnaise.

Replace 1/3 cup of oil with one cup of flax flour in baked goods.

Replace Eggs in baked goods by combining 1 tablespoon of Ground Flax with 3 tablespoons of water, let it sit for a few minutes before adding.



Flax Buns

FLAXSEED SUPPLEMENTATION

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