
Health Benefits Of Whole Grains: A Literature Review

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Abstract

Whole grains are also rich sources of essential nutrients. The future years are going to see the numerous health benefits of eating whole grains. It is quite difficult to get a food material with almost all vital nutrients like whole grains. IP-6 from the whole grain extract is a promising drug of the future. Extensive research is going on, the role of phytoestrogens on breast cancer which is the killer cancer in the United States.

INTRODUCTION

According to the FDA's new guidelines, "whole grain" includes "cereal grains that consist of the intact and unrefined, ground, cracked or flaked fruit of the grains whose principal components -- the starchy endosperm, germ and bran -- present in the same relative proportions as they exist in the intact grain."

The major whole grains are Whole grain corn, Oats, Brown rice, Wheat, Millet, Rye and Barley. Dietary guidelines for Americans, 2005 advises to consume 3 or more ounce-equivalents of whole-grain products per day, with the rest of the recommended grains coming from enriched or whole-grain products. In general, at least half the grains should come from whole grains. But in spite of the beneficial effects of whole grains there consumption is low in the United States, mostly due to taste, cost and poor eating habits. The people must be exposed and made aware of the beneficial effects of whole grains and there health benefits. Grains remain an integral part of the recommended diet for the US population, as evidenced by their prominent position on the Food Guide Pyramid (US Department of Agriculture, Department of Health and Human Services, 1992) and a specific recommendation in the latest dietary guidelines (US Department of Agriculture, Department of Health and Human Services, 2000).

The Healthy People 2010 report (US Department of Health and Human Services, 2000) designates that a specific number of whole grain servings (three) be included in an individual's daily diet.

OVER VIEW OF NUTRIENT CONTENT OF WHOLE GRAIN CORN, OATS, BROWN RICE, WHEAT AND BARLEY

The potential biological components that may explain why whole-grain consumption is associated with a reduced risk for CHD and some cancers, include fermentable carbohydrates, antioxidants, lignans and phytoestrogens, anti-nutrients, fat and associated substances . Whole grains contain no cholesterol, are low in fat, and are high in dietary fiber, starch, protein, vitamins, and minerals. Whole grain Corn, Oats, Brown Rice, Wheat and Barley contain Phenolic acids. The potentially anticarcinogenic mechanism of phenolic compounds involves the induction of detoxification systems, specifically the phase II conjugation reactions. Ferulic acid, p-coumaric acid, and syringic acid are the principal phenolic acids. Oats contain a number of lipid-soluble esters of caffeic and ferulic acids that function as natural antioxidants. Of the phenolic acids in wheat bran, ferulic acid had the highest concentration. Wattenberg (1) classified caffeic and ferulic acids as inhibitors that act in 2 ways, by preventing the formation of carcinogens from precursor compounds, and by blocking the reaction of carcinogens with critical cellular macromolecules.

Apart from the chronic diseases Whole grains also protect against life style diseases like Hypertension and Diabetes.

The explored and un-explored health benefits of whole grain consumption are given below.

COMPONENTS OF WHOLE GRAIN CORN, OATS, BROWN RICE, WHEAT AND BARLEY

AND THEIR ACTIONS
BIOCHEMICAL CONSTITUENTS AND THEIR
BENEFICIAL ACTIONS

Figure 1

Component	Favorable lipid profile	Tumor suppression	Antioxidant	Hormone modulation	Cardio protective	Immunomodulation	Bone growth & mineralization
Omega 3 and 6 fatty acids	++++	+	++	-	++++		
Beta carotene	++	+	++			++++	
Selenium		++	+++		+++	+	
Phenolics		+	+++				
Phytoestrogens		+++	+++	++++			
Vitamin E	+++	++	+++	-	++	+++	
Riboflavin		+	++				
Thiamin					++		
Fiber	+++	+	+	+	+++		
Copper							++
Phosphates							++++
Phytates			+++			+++	
Avenanthramides			+++				
Fatty acids	+++		+		+++		

PHYTOESTROGENS IN WHOLE GRAINS AN INTRODUCTION

Phytoestrogens are a group of biologically active plant substances with a chemical structure that is similar to that of estradiol, an human estrogen. This structural similarity accounts for the ability of these compounds to bind to estrogen receptors in various cells and exert estrogenic or antiestrogenic effects (2,3,4) .

Phytochemicals are most varied and abundant in the outer layers of grains and include Lignans, Isoflavones and Coumestans. The major bioactive Isoflavons are Genistein and Daidzein which are derived from the precursors Biochanin A and Formononetin respectively. Two major Lignans, Enterolactone and Enterodiol are produced from Matairesinol and Secoisolaritresinol respectively. Coumesterol is the most important coumestan consumed by humans. Lignans Matairesinol and Secoisolaritresinol are converted in human gut to Enterolactone and Enterodiol. Production of Enterolactone relies on colon microflora (5) .

Lignans are compounds with a 2,3-dibenzylbutane structure (6,7) and have a diphenolic structure similar to that of estrogenic compounds, which has created interest in a possible estrogenic function for these compounds. These hormonally active compounds may protect against hormonally mediated diseases (6) .

Recently, some of the phytoestrogen Mammalian lignan production from plant foods was studied by Thompson et al (7) who used an in vitro fermentation method with human fecal microflora. Adlercreutz et al (8) found that total urinary lignan excretion in Finnish women was positively correlated with total fiber intake, total fiber intake per kg body weight,

and grain fiber intake per kg body weight. The traditional Finnish diet is believed to be richer in lignans than typical Western diets due to the relatively high intake of whole-grain products. A recently published study (10) says that whole grains and the bran are concentrated sources of lignans; which includes whole-grain wheat and whole-grain oats. Seeds also contain high amounts of lignans. Hence whole grains can protect against estrogen hormone mediated diseases due to there high Lignan Content.

Lignan compounds have been reported to possess a broad spectrum of biological properties, giving them the potential to reduce the risk of breast, prostate and colon cancers as well as cardiovascular diseases (11,12,13) .

ANTIESTROGENIC ACTION OF PHYTOESTROGENS OF WHOLE GRAIN- OATS

Due to structural similarities to endogenous estrogens, phytoestrogens acts as weak estrogens and compete with 17β-estradiol for binding to the intranuclear estrogen receptor protein to modulate gene transcription (14,15) . At least 2 distinct oestrogen receptors have been described and found to be expressed in various tissues (14) , including adipose tissue (16) .Phytoestrogens have been shown to bind to both estrogen receptors but bind more strongly to estrogen receptor α (17) .Whether phytoestrogens have an estrogenic or antiestrogenic effect may depend on the amount of endogenous estrogens present. Any significant increase in the overall cycle length would be potentially beneficial in lowering the risk for hormone-dependent cancers. Phytoestrogens may also exert their biological effects via non-estrogen receptor-mediated mechanisms by inhibiting the activity of several enzymes, including protein tyrosine kinases (18) , DNA topoisomerase I and DNA topoisomerase II (19,20) , and ribosomal S6 kinase (21) , which are involved in cell-signaling mechanisms and nuclear events such as cell proliferation and differentiation. Stoppage of these enzymes can protect against cancer by preventing cellular proliferation.

CONCERNS -CAN PHYTOESTROGENS CAUSE BREAST CANCER?

Due to the slight estrogenic action of Phytoestrogens questions have been raised on the procarcinogenic action of Phytoestrogens associated with whole grains. But Phytoestrogens appear to have little effect on breast cancer risk at the levels commonly consumed by non-Asian US women (22) .

PROTECTIVE ROLE OF WHOLE GRAIN PHYTOESTROGENS IN ENDOMETRIAL CANCER

Phytoestrogenic compounds, at the levels consumed in the typical American-style diet, are associated with reduced risk of endometrial cancer (23). Another beneficial action of Phytoestrogens in Whole grain Oats.

PROTECTIVE ROLE OF WHOLE GRAIN PHYTOESTROGENS IN THYROID CANCER

Epidemiological and pathological data suggest that thyroid cancer may well be an estrogen-dependent disease. Thyroid cancer prevention via dietary modification of phytoestrogen intake in other forms may be possible (24). Hence whole grain intake may well prevent Thyroid cancers especially Oats.

PROTECTIVE ROLE OF WHOLE GRAIN PHYTOESTROGENS IN PROSTATE CANCER

In human prostate cancer cell studies, Genistein and its precursor Biochanin A inhibit cell growth at relatively high concentrations. Genistein and Biochanin A are present in whole grains especially Oats (25). These effects on human prostate cancer cells in culture are confirmed and extended to isoflavones, lignans and flavones.

Diet in countries with low prostate cancer risk may contain higher amounts of cancer-protective compounds, such as Phytoestrogens (lignans and isoflavonoids),

affecting hormone metabolism or action (26). Additionally, phytoestrogens are known to have potent antioxidant activity.

WHOLE GRAIN PHYTOESTROGENS IN OSTEOPOROSIS

Lower levels of Isoflavanoids were found in Patients with Osteoporosis and hence whole grain Isoflavanoids may help in Osteoporosis(27).

WHOLE GRAIN PHYTOESTROGENS OTHER PROTECTIVE ACTIONS

In the Iowa Women's Health Study, the Nurses' Health Study, and the Health Professionals Follow-Up Study, people who consumed at least three servings a day of whole grains had a 20 to 30 percent lower risk of diabetes over the next decade or so than people who ate roughly one serving a week. Whole Grain Phytoestrogens especially from Oats inhibits Glucose uptake into brush border cells of Intestinal epithelium, Increases basal insulin secretion from Pancreas,

Decreases conversion of glucose into lipids and decreases number of insulin receptors in Liver, Inhibits glucose conversion into lipids, stimulates basal lipolysis and epinephrine-induced lipolysis, and inhibits insulin-stimulated glucose oxidation. Hence whole grains especially Oats lower the blood glucose levels in Diabetes.

ROLE OF WHOLE GRAIN PHYTOESTROGENS IN COLORECTAL CANCER

Dietary lignan intake was associated with a significant reduction in colorectal cancer risk, as was Isoflavone intake. This finding that phytoestrogen intake may reduce colorectal cancer risk is important, because dietary intake is potentially modifiable and hence the old known ability of fibers in Whole grains to prevent colon cancer may be reaffirmed (28).

WHOLE GRAIN PHYTOESTROGENS IN POST MENOPAUSAL WOMEN

There are many observational and epidemiological studies suggest the potential benefit of Isoflavones on the post menopausal symptoms, like hot flushes, osteoporosis, mood variations, cardiovascular system and the estrogen dependent cancers which are all common in the post menopausal age group (29).

FATS AND WHOLE GRAINS

Though grains have low fat, they have a favorable fatty acid composition of oleic and linoleic acid and the other essential fatty acids. Grains are rich in other compounds such as the Sterols, Tocotrienols, and Oryzanol, which were found to have hypocholesterolemic effects in animal studies (30). β-Sitosterol in grains reduced the incidence of tumors in rats (31).

ANTIOXIDANT PROPERTIES OF WHOLE GRAINS

Whole grains have significantly high Anti-oxidant content as any other food material. Whole grains are concentrated sources of vitamin E, Phytic acid, Riboflavin (vitamin B2), Phytoestrogens and Selenium which are powerful antioxidants, also tocotrienols. Wheat bran was shown to have antioxidant activity (32). Whole grain products contain biologically active antioxidants that could act independently or with fiber in them to reduce disease (33). Components in whole grains may bind carcinogens and thereby limit absorption by or contact with the gut.

Whole grain breakfast analyzed in a study contained from

2200-3500 TE. Fruits ranged from 600-1700 TE and vegetables averaged 450 TE, which clearly shows that whole grain breakfast had superior anti oxidant properties (34) .

PHYTIC ACID IN WHOLE GRAIN AS AN ANTIOXIDANT AND ANTICANCER AGENT

Whole grains, such as whole wheat, contain powerful phytonutrients whose activity has gone unrecognized and more research need to be undertaken. Phytic acid chelates with various metals, which suppress damaging iron-catalyzed redox reactions (35)

Dietary Phytic acid may suppress oxidant damage to the intestinal epithelium

IP-6 IN WHOLE GRAIN BROWN RICE AND WHEAT BRAN AS AN ANTICANCER AGENT

Inositol hexaphosphate (IP-6), is a naturally occurring carbohydrate found in brown rice, corn and wheat bran. It helps in the metabolism of Insulin and Calcium. It also helps hair growth, eye membrane development, bone marrow cell metabolism and helps the liver transfer fat. Fiber's health benefits may be due to the antioxidant, immune enhancing, and cardiovascular supporting activities of IP-6. P-6 has been reported to have in vivo and in vitro anti- cancer activity against numerous tumors, such as colon cancer, prostate cancer, breast cancer, liver cancer, chronic myeloid leukemia, pancreatic cancer, and rhabdomyosarcomas.

IP6 MODE OF ACTION

When administered IP6 is rapidly taken into the cells and dephosphorylated to lower-phosphate inositol phosphates, which further interfere with signal transduction pathways and cell cycle arrest. Enhanced immunity and antioxidant properties can also contribute to tumor cell destruction. IP6 enhances the anticancer effect of conventional chemotherapy, controls cancer metastases, and improves the quality of life. IP6 inhibits human platelet aggregation in vitro. IP-6 decreases cell proliferation of malignant cells, and increases differentiation of malignant cells, often resulting in a reversion to normal cell. The rate and pattern at which IP6 is metabolized by cancer cells varies depending on the cell type. Treatment of all the cell lines tested so far demonstrates that it is cytostatic and not cytotoxic. The actions of IP6 involve signal transduction pathways, cell cycle regulatory genes, differentiation genes, oncogenes and tumor suppressor genes. IP6 inhibits the growth of breast cancer cells and is effective against estrogen responsive alpha-negative cells and adriamycin-resistant cell lines.

IP-6 IN WHOLE GRAINS RECENT USES

Treatment of Pancreatic Cancer (36) ,Prostatic Cancer (37) ,Rhabdomyosarcoma (38) , Anti-HIV-1 activity (39) , Hypolipidemic action of IP-6 prevention of fatty liver (40) , IP-6, a natural substance found in whole kernel corn and brown rice, activates natural killer cell function - inhibits cancer (41) , Inositol hexaphosphate inhibits growth and induces G1 arrest and apoptotic death of androgen-dependent human prostate carcinoma LNCaP cells (42), Growth inhibitory and apoptotic effects of inositol hexaphosphate in transgenic adenocarcinoma of mouse prostate (TRAMP-C1) cells (43) ,Melanoma (44) .

VITAMIN E IN WHOLE GRAIN OATS AS AN ANTIOXIDANT ()

Vitamin E is an intracellular antioxidant that protects polyunsaturated fatty acids in cell membranes from oxidative damage. Vitamin E keeps Selenium in the reduced state. Vitamin E inhibits the formation of nitrosamines. Fat-soluble ferulic and caffeinic acid present in grains could function to protect lipid membranes These esters are equal to tocopherols as antioxidants that prevent lipid oxidation.

SELENIUM IN WHOLE GRAIN AS AN ANTIOXIDANT

The amount of selenium found in grain is proportional to the Selenium content of the soil in which the grain was grown. Selenium functions as a cofactor for glutathione peroxidase, an enzyme that protects against oxidative tissue damage. Selenium prevents neoplasia in cells.

ANTINUTRIENTS

Antinutrients found in grains include digestive enzyme inhibitors, Phytic acid, tannins Hemagglutinins, and. Protease inhibitors. Phenolic compounds, and saponins were shown to reduce the risk for cancers of the colon and breast in animals. Phytic acid, lectins, phenolic compounds, amylase inhibitors, and saponins were also shown to lower glucose, insulin, cholesterol, and triacylglycerol (46) . Protease inhibitors have inhibitory actions including both suppression of the expression of neoplasia in cells already exposed to a carcinogenic agent and inhibition of tumor promotion.

ANTICANCER PROPERTIES OF PHENOLIC ACIDS

Of the phenolic acids in wheat bran, Ferulic acid had the highest concentration. The potentially anticarcinogenic mechanism of phenolic compounds involves the induction of

detoxification systems, specifically the phase II conjugation reactions.

WHOLE GRAIN CARBOHYDRATES AND FIBER

Carbohydrates function like dietary fiber and enhance the intestinal environment and help to improve immune function (47). Whole grains contain high amounts of carbohydrates including dietary fiber, oligosaccharides and starch. Undigested carbohydrate is fermented by intestinal microflora to short-chain fatty acids. Undigested carbohydrates also increase fecal weight and speed of intestinal transit. Short-chain fatty acid production has been related to lowered serum cholesterol and decreased risk of cancer (48). Insulin sensitivity may be an important mechanism whereby whole-grain foods reduce the risk of type 2 diabetes and heart disease (49).

DIETARY FIBER FROM WHOLE GRAINS

Dietary fiber is generally divided into two categories, soluble and insoluble. Soluble fibers form a gel in water and is found in oats, oat bran, barley. Insoluble fibers are found predominantly in: Wheat bran. Whole-grain foods are a rich source of both insoluble and soluble dietary fiber. Soluble fibers have been shown to help lower LDL cholesterol levels and therefore reduces the risk of coronary heart disease. Insoluble fibers also have been associated with decreased cardiovascular disease risk (50).

EFFECT OF DIETARY FIBER ON GASTROINTESTINAL SYSTEM OATS AND BARLEY

Increased fecal bulk and decreased transit time allow less opportunity for fecal mutagens to interact with the intestinal epithelium. Oats, and barley contain about one-third soluble fiber and two-thirds insoluble fiber. Soluble fiber is associated with cholesterol-lowering effects and improved glucose response, whereas insoluble fiber is associated with improved laxation. Wheat bran was the type of fiber most consistently shown to inhibit carcinogenesis.

WHOLE GRAIN FIBER AND DIABETES

Whole grain foods tend to have a low GI (glycaemic index). Consuming foods containing large amounts of dietary fiber like whole grains are lower blood sugar levels. High dietary fiber intake is better for patients with type 2 diabetes mellitus (51). Consumption of whole grains reduces glycemic response (52). Intact whole grains of barley, rice, oats, corn, and wheat have glycemic indexes of 36–81, with barley and oats having low values.

ANTINEOPLASTIC PROPERTIES OF WHOLE GRAIN FIBER

Fermentation of dietary fiber produces butyrate, that is antineoplastic (53). Fermentation of dietary fiber results in production of short-chain fatty acids, which lowers intestinal pH; this stops conversion of primary bile acids to secondary bile acids. At low pH, the solubility of free bile acids is reduced, so there is a decrease in carcinogenic activity (54). Intake of whole grains and the fiber derived from them may reduce risk of upper aerodigestive tract cancers (55).

PROBIOTIC EFFECT OF WHOLE GRAINS

Consumption of fructooligosaccharides increased bifidobacteria in the gut while decreasing concentrations of *Escherichia coli*, clostridia, and bacteroides (56,57).

WHOLE GRAIN FIBER AND WEIGHT GAIN

Whole grain products help in better weight control than refined grains. Weight gain is inversely associated with the intake of high-fiber, whole-grain foods. Refined foods tend to increase body weight. (58).

WHOLE GRAIN FIBER AND MORTALITY

The hypothesis that whole grain fiber consumption is associated with a reduced mortality risk in comparison to a similar amount of refined grain fiber was tested in 11,040 postmenopausal women enrolled in the Iowa Women's Health Study and those who consumed whole grains had 17% less mortality than those who consumed refined grains (59).

WHOLE GRAIN FIBER AND GALLSTONES

Eating foods high in insoluble fiber like whole wheat, can help women avoid gallstones due to Cholesterol lowering effect (60).

MINERALS

Minerals in whole grains are zinc, selenium, calcium, phosphates, sodium and potassium. Selenium in whole grains mainly benefits by its antioxidant properties. Phosphorous favours bone growth and bone mineralisation and prevents the development of osteoporosis.

ZINC IN WHOLE GRAINS

The zinc in whole grains is found in the germ and bran. Zinc is a co factor of alcohol dehydrogenase, which detoxifies ethanol. Zinc helps to maintain body levels of vitamin A. Through this action, zinc may help maintain healthy skin cells and thus may be helpful in generating new

skin after burns or injury. By helping collagen formation, zinc may also improve wound healing. Zinc aids the skin's oil glands and so may help in acne problems. Zinc in carboxypeptidase helps in protein digestion. Zinc is important for synthesis of nucleic acids. As part of superoxide dismutase (SOD), it protects cells from free radicals. Zinc maintains cell membrane structure and function. Zinc also supports immune function. Zinc improves antibody response to vaccines and can improve cell-mediated immunity. Zinc is necessary for Insulin activity and for normal taste sensation. Zinc has anti-inflammatory function, especially in the joints and artery linings. Zinc is needed for lactate and malate dehydrogenases, both important in energy production. Zinc is a cofactor for alkaline phosphatase, which helps maintain bones.

WHOLE GRAIN VITAMINS

The various vitamins present in whole grains include fat soluble vitamins like vitamin E and water soluble vitamins like B1(thiamine), B2(riboflavin), B5 (panthothenic acid) and folate.

THIAMINE (B1) IN WHOLE GRAIN RICE AND BENEFICIAL EFFECTS

The heart depends on vitamin B₁ for its proper function and Thiamine can be used as adjuvant in treatment of Cardiac failure. One double-blind study suggests that thiamine enhances mental function (61) and hence whole grains. Increased intake of vitamin B₁ might slow progression to AIDS and enhance overall survival rate. (62) and so HIV patients must increase the intake of Whole grains especially Rice. Vitamin B₁ may be helpful for Alzheimer's disease, Epilepsy and Fibromyalgia (63,64). Of all the whole grains Rice has highest amount of Thiamine.

RIBOFLAVIN (B2) IN WHOLE GRAIN AND BENEFICIAL EFFECTS

Riboflavin provides energy for the body and also works as an anti oxidant. Riboflavin protects the body from Cataract, Migraine headaches, Burn injury infection, Anemia and Depression. Low levels of riboflavin in the diet and/or riboflavin deficiency has been associated with rheumatoid arthritis, carpal tunnel syndrome, Crohn's disease, colon cancer, atherosclerotic heart disease, and multiple sclerosis. It still requires research to know whether supplementing Riboflavin can decrease Carpal Tunnel Syndrome. Whole Grain diets can be used as dietary supplements for patients with the above mentioned diseases but it requires further

research.

BETA GLUCANS IN WHOLE GRAIN OATS, BARLEY AND IMMUNITY

Beta-glucans can enhance the human immune system's response to bacterial infection. Beta-glucan helps neutrophils to navigate to the site of an infection quickly, it also enhances their ability to eliminate the bacteria. According to Jonathan Reichner of the Department of Surgery at Rhode Island Hospital and Brown University, priming neutrophils with beta-glucan helps neutrophils quickly locate the bacteria within infected tissue.

WHOLE GRAINS AND PERIODONTITIS

Increasing whole grain in the diet without increasing total energy intake may reduce periodontitis risk (65).

SUMMARY & CONCLUSIONS

In the oldest known book of Chinese medicine Classic of Internal Medicine first remedy for disease is a ten-day period during which the patient eats only rice. From this we can infer about the medicinal value of Whole grains especially rice. Below is a summary of the beneficial effects of Whole grain Corn, Oats, Brown Rice, Wheat and Barley

WEIGHT CONTROL

The dietary fiber found in whole grains helps promote a feeling of satiety, which reduces the amount of food eaten. The role that other components of whole grains contribute to weight management is not well defined. But, magnesium, a component of whole grains is found to have a role in reducing weight as well.

Whole-grain intake was inversely associated with body mass index, waist-to-hip ratio, total cholesterol, LDL cholesterol and fasting insulin.

Omega 3 and omega 6 fatty acids, thiamine and phosphorous prevent depression associated with eating disorders.

CARDIOPROTECTIVE ROLE

Dietary fiber found in whole grains (especially the soluble fiber found in oats and barley) may help reduce the absorption of dietary cholesterol. The bran and germ contribute a variety of substances, which also play a role in reducing the risk of heart disease, so also, trace minerals, and a variety of phytochemicals.

Observational findings suggest a beneficial effect of whole-

grain and fruit and vegetable consumption on the risks of total mortality and incident Coronary artery disease (CAD), but not on the risk of ischemic stroke ⁽⁶⁶⁾ .

Whole-grain breakfast cereal intake was found to be inversely associated with total and Cardiovascular disease-specific mortality, independent of age; body mass index; smoking; alcohol intake; physical activity; history of diabetes, hypertension, or high cholesterol ⁽⁶⁷⁾ .

Increased intake of whole grains may protect against coronary heart disease. Whole-grain consumption and risk of coronary heart disease: results from the Nurse's Health Study ⁽⁶⁸⁾ .

Long-term cohort studies have indicated that whole-grain consumption reduces the risk of both type 2 diabetes and cardiovascular disease ⁽⁶⁹⁾ .

Increased intake of whole-grain foods has been related to a reduced risk of developing diabetes and heart disease. In men, a diet high in whole grains is associated with a reduced risk of type 2 diabetes ⁽⁷⁰⁾ .

An inverse association was observed between whole grain intake and ischemic stroke risk. This inverse association remained essentially unchanged with further adjustment for known CVD risk factors, including saturated fat and trans fatty acid intake. These prospective data support the notion that higher intake of whole grains may reduce the risk of Ischemic stroke ⁽⁷¹⁾ .

DIABETES MELLITUS

Consuming whole grains, within an overall balanced diet, is one way to reduce the risk of developing diabetes. Dietary fiber (especially soluble dietary fiber found in whole oats and barley) helps reduce the rate of carbohydrate absorption and supports appropriate insulin response to carbohydrate in the diet.

Whole-grain intake is favorably associated with metabolic risk factors for type 2 diabetes and cardiovascular disease in the Framingham Offspring Study ⁽⁷²⁾ .

Substituting whole- for refined-grain products may decrease the risk of diabetes mellitus ⁽⁷³⁾ . Whole-grain intake is favorably associated with metabolic risk factors for type 2 diabetes and cardiovascular disease in the Framingham Offspring Study ⁽⁷⁴⁾ .

GASTROINTESTINAL HEALTH

Increased intake of whole grains with higher contents of insoluble fiber (such as whole wheat or brown rice) can prevent or treat constipation. Both the soluble and insoluble fibers found in a variety of whole grains promote overall bowel health, including a reduction in the risk of colon cancer. They prevent the development of gallstones by reducing absorption of cholesterol.

CANCER

Phytochemicals (antioxidants and phytoestrogens) and trace minerals (such as selenium) found in whole grains are found to inhibit the development or progression of various types of cancer. Insoluble fiber (found in large amounts in whole wheat and brown rice) increases fecal bulk and speeds up transit in the colon. Cancer-causing agents thus have less time in contact with cells lining the large intestine.

Bacteria break down soluble fibers (found in large amounts in oats and barley) in the large intestine and helps enhance the health of colon cells and reduced the co carcinogenic effects of bacteria and bile. Other potential mechanisms whereby whole grains may protect against disease include binding of carcinogens and modulation of the glycemic response ⁽⁷⁵⁾ .

Whole grain ones a favourable indicator of the risk of upper aerodigestive and respiratory tract neoplasms ⁽⁷⁶⁾ .

Substitution of whole for refined grain may reduce chronic disease risk in the United States ⁽⁷⁷⁾ .

Higher frequency of whole grain food intake is an indicator of reduced risk of several neoplasms ⁽⁷⁸⁾ .

Nevertheless there is a striking consistency in reduced risk for colorectal and gastric cancers associated with intake of whole grain, also found in isolated studies of endometrial cancer and coronary heart disease. Because reduced risk was not associated with refined grain intake, these findings do not appear to be confounded by participant confusion concerning refined vs. whole grains ⁽⁷⁹⁾ .

The case-control evidence in the study conducted by Jacobs et al is supportive of the hypothesis that whole-grain intake protects against various cancers ⁽⁸⁰⁾ .

IMMUNITY

Zinc has also been shown to support immune function. Zinc will improve antibody response to vaccines and can improve cell-mediated immunity by helping regulate the function of

the white blood cells. A somewhat higher amount of zinc has caused an increase in production of T lymphocytes, important agents in cell-mediated immunity.

Beta glucan enhances the body's response to bacterial infections. It helps in the chemotaxis and phagocytosis of neutrophils. Selenium and vitamin A enhance immunity.

CONCLUSIONS

The following conclusions were reached after a thorough estimation of the various aspects of whole grains.

1. Wheat has the lowest total calories per 100gram weight and is recommended for obese, those with metabolic syndrome and type 2 diabetes mellitus.
2. Dietary fiber is maximum in barley among the whole grain products and regular consumption of one cup of barley a day (contains 30 grams of dietary fiber) is likely to prevent constipation, hemorrhoids and diverticulosis.
3. Vitamin E is maximum in 100 gram of brown rice when compared to other whole grains and consumption of around 6 and half cups of brown rice a day gives sufficient vitamin E. Tocotrienol(vitamin E) in barley suppresses HMG co A reductase enzyme and thereby reduces LDL (bad cholesterol).
4. Omega 3 and omega 6 fatty acids are present in huge proportions of oats when compared to other grains and it has cardio protective and anti inflammatory properties. Omega three and omega six fatty acids in oats has been shown to have the ability to prevent depression.
5. Maximum proteins are present in oats, which is 17times that in brown rice and double that in corn and barley. Next to oats in protein is wheat, which has 14 times the amount of protein in rice. Consuming 2 cups of oats/ 2 and half cups of wheat a day can adequately meet the recommended dietary allowance of protein.
6. Vitamin A(beta carotene) is present in small amounts in barley and wheat though carotene is present only in yellow maize.
7. Maximum amount of thiamine is present in 100-gram oats compared to the other whole grains. Consumption of three fourth cup of oats or one and a quarter cups of wheat/corn/brown rice a day improves memory and cognition significantly.
8. Consuming one-fourth a cup of wheat/corn or half cup of rice/oats/barley can provide sufficient amount of vitamin B2, which prevents the development of cataract.
9. Maximum amount of niacin is present in wheat barley and brown rice, which is vital for healthy skin, absorption of amino acids, good cognition and memory. One and a half cups of wheat/brown rice a day can provide sufficient niacin.
10. Panthothenic acid which is found most in brown rice, oats and wheat in that order is found to be an anti stress vitamin which modulates the function of the adrenal glands. One and a half cup of brown rice/oats will meet the RDA requirements of panthothenic acid.
11. Maximum amount of calcium is present in wheat, though the amount is not very significant.
12. Phosphorous is present in very high proportions in oats and consuming three-fourth cup of oats will adequately meet the RDA requirements of phosphorous which is essential for normal bone mineralisation, skeletal muscle function and to prevent lethargy. One cup of rice/wheat and 2 cups of barley and corn will provide similar effects.
13. All of the whole grains no cholesterol, which helps in lowering the incidence of atherosclerosis, coronary heart diseases, stroke and gall stones.
14. Selenium is maximally present in wheat that is a very powerful antioxidant and it prevents the development of cardiomyopathy and ageing and it also protects against various tumors.
15. Maximum folate, though not in very significant amounts, is present in oats.
16. Vitamin B6 is maximal in corn and brown rice.
17. Potassium is present maximally in wheat and oats, three and a half cups of which can provide adequate potassium as per the RDA requirements.
18. Sodium is minimally present in wheat and oats the excess of which can cause the development of edema and aggravation of hypertension.
20. Total fat is minimum in barley and wheat and maximum in oats and the saturate fat is maximum in oats/rice and minimum in wheat/barley.
21. Whole grains contain much more nutrients and fiber when compared to processed food materials.

22. Phytoestrogens and lignan levels are significantly elevated in the urine of people consuming whole grains when compared to those on processed food. Corn, wheat and oats are rich in phyto estrogens.

23. Consumption of phytoestrogens which are present significantly in corn and wheat on a regular basis reduces the risk of endometrial cancer in women.

24. Studies suggest the potential of phytoestrogens to lower the risk of developing thyroid cancer in all age groups and both sexes.

25. Phyto estrogens have oestrogenic and antioestrogenic properties and are of doubtful benefit in preventing and curing breast cancer. Lignans (phytoestrogens) have been shown to reduce breast cancer by their antioxidant action. These findings are contradictory and a final conclusion is yet to be reached due to lack of further evidence.

26. Preliminary evidence suggests that phytoestrogens inhibit the growth of prostate cancer cells, however further research needs to be done before conforming the association. Flavenoids have been shown to limit the growth of bronchial tumor cells.

Whole grains are found to prolong the survival rate of patients (smokers and non smokers) with bronchial carcinoma as per a large case control study. Some studies suggest that this might be due to the action of lignans. However, solid clinical evidence is lacking.

27. Phyto estrogens like isoflavanes and lignans have beneficial effects on diabetes mellitus type 2 and obesity. This calls for further studies to find the mechanisms of action of these agents in lowering blood sugar and body weight.

28. People with osteoporosis have been found to have lower levels of isoflavanoids when compared to healthy individuals. There is scope for further research regarding the beneficial effects of isoflavanoids in whole grains in lowering the risk of developing osteoporosis.

29. Regular consumption of whole grain containing lignans and isoflavanoids was found to significantly lower the risk of developing colon cancer. This is an important finding as dietary intake is potentially modifiable. However, there is not many studies have been conducted on the anti tumerogenic properties of isoflavanoids and lignans.

30. Isoflavanes have been found to alleviate the symptoms of

post menopause like hot flushes, mood variations, cardiac symptoms and osteoporosis associated with menopause.

31. Consumption of corn, wheat and oats is associated with significant decrease in oestrogen levels.

32. Whole grains are abundant in anti oxidants like selenium, riboflavin, tototrienol, lignans, phytic acid and vitamin E.

33. Antioxidants, along with other components in whole grains act to reduce many chronic diseases as discussed in many observational studies conducted world-wide.

34. Phytic acid (IP6) in whole grains is found to be useful in inhibiting the growth of breast cancer, rhabdomyosarcoma, prostate cancer and pancreatic cancer cells, there is still lacking solid clinical evidence in these areas. It has been found that IP6 effectively kills the cells of rhabdomyosarcoma both in vivo and invitro. Animal studies are underway to establish phytic acid as an anticancer agent in the treatment of androgen dependant prostatic cancer and malignant melanoma on the assumption that the anticancer effects are due to the apoptotic properties of phytic acid. It has been found to reduce mammary tumor in rats.

35. It has been proposed that phytic acid has anti HIV properties (inhibits the replication of HIV virus). Studies are underway to develop newer drugs in HIV treatment and the addition of phytic acid as an adjuvant is being considered.

36. Phytic acid prevents fatty liver by its hypolipedemic actions as suggested by preliminary studies and is thought to prevent the progression of acute hepatitis to chronic hepatitis. So far, there is no strong clinical evidence to support this hypothesis.

37. IP6 (Phytic acid) found in whole kernel corn and brown rice has been found to activate natural killer cell function and thereby inhibit cancer.

38. Vitamin E as a cancer inhibitor exerts its effect by preventing the formation of carcinogens from precursor compounds.

38. Selenium in wheat, barley and brown rice is a powerful antioxidant that keeps glutathione in the reduced state, as well as a suppressing agent, or inhibitor, that prevents the expression of neoplasia in cells that have been exposed to a carcinogen previously.

39. A phenolic acid in wheat bran, ferulic acid, exerts

antitumour effects by means of its detoxification reactions like the phase II conjugation reactions, preventing formation of carcinogens from precursors and by acting at the cellular level. It is proposed that phenolic acids might have a role in preventing and treatment of early stages of colon cancer.

40. Short-chain fatty acid in whole grains has been related to lowered serum cholesterol and decreased risk of cancer.

41. Soluble dietary fiber in oat bran, rolled oats and barley has been shown to help lower LDL cholesterol levels (the bad cholesterol), and therefore reduces the risk of coronary heart disease.

42. Insoluble dietary fiber in wheat bran also has been associated with decreased cardiovascular disease risk.

43. Oats, rye, and barley contain about one-third soluble fiber and two-thirds insoluble fiber. Soluble fiber is associated with cholesterol-lowering effects and improved glucose response, whereas insoluble fiber is associated with improved laxation. Wheat is lower in soluble fiber.

44. Coarse bran delays gastric emptying and accelerate small bowel transit.

45. Whole grain foods tend to have a low glycaemic index because of the larger particle size and high content of viscous fiber. Intact whole grains of barley, rice, oats, corn, and wheat have glycemic indexes of 36–81, with barley and oats having the lowest values (18). Foods with low glycemic index are best for patients with type 1 and type 2 diabetes mellitus.

46. Wheat bran has been found to be the type of fiber most consistently shown to inhibit carcinogenesis.

47. Consumption of fructooligosaccharides in whole grains increased bifidobacteria in the gut (beneficial to humans) while decreasing concentrations of *Escherichia coli*, *clostridia*, and *bacteroides* (harmful bacteria).

48. High intakes of dietary fiber were associated with a lower risk of colorectal adenoma, after adjustment for potential dietary and non-dietary risk factors.

49. Whole grain has a favorable effect in reducing the risk of upper aero-digestive and respiratory tract neoplasms. However, there is only preliminary evidence to support this hypothesis.

50. A large prospective cohort study pointed out that

consumption of dietary fiber in barley, oats and wheat has shown to reduce the risk of mortality.

51. Cereals and breads made from whole wheat can help prevent the development of cholesterol gallstones as pointed out in various studies.

52. Phosphorous in oats, rice and wheat favors bone growth and bone mineralisation and prevents the development of osteoporosis.

53. Zinc in oats and wheat is also thought to help utilize and maintain body levels of vitamin A. There is future scope for research in this field and whether vitamin A – zinc combinations are a better alternative for treatment of vitamin A deficiency than vitamin A alone.

54. By helping collagen formation, zinc may also improve wound healing. This calls for clinical trials involving zinc - oral and topical in non-healing ulcers and post operative wound dressings.

55. Zinc aids the skin's oil glands and so may help in acne problems. This might account for the use of zinc in talcum powders.

56. Zinc is important in male sex organ function and reproductive fluids. It is in high concentration in the prostate gland as well as in the eye, liver, and muscle tissues suggesting its functions in those areas. Zinc can be tried in the future in preparations for treating impotence infertility in males.

57. Zinc is a powerful antioxidant and is therefore an anticancer agent. Studies are underway to use zinc as an adjuvant in treating cancers of breast, bronchus and colon.

58. Zinc has been shown to improve cell-mediated immunity by increasing the number of T lymphocytes and there is scope for using zinc as an adjuvant in anti HIV therapy where, many symptoms are due to a decrease in cell mediated immunity.

59. Zinc in oats improves memory and cognition.

60. Thiamine in oats, wheat, corn and brown rice can improve symptoms of congestive heart failure and enhance cognition and memory.

61. Studies have shown that thiamine in oats can slow down the progression of HIV to AIDS and enhance the overall survival rate of HIV patients.

62. Weak and contradictory evidence hints that thiamine may be helpful for Alzheimer's disease. However, this theory lacks solid supporting clinical evidence. A proposed mechanism of action is via acetylcholine.

63. Vitamin B1 (thiamine) has also been proposed as a treatment for epilepsy, canker sores, and fibromyalgia. No significant clinical evidence exists so far in support of this proposal.

64. Preliminary evidence suggests that riboflavin in whole grain wheat and corn has antimigraine properties comparable to those in the conventional antimigraine drugs.

65. B-complex vitamins in oats, wheat, rice bran and barley may help alleviate stress and reduce symptoms of depression, frequently associated with eating disorders.

66. Lower levels of riboflavin are associated with inflammatory arthritis, carpal tunnel syndrome, Cohn's disease and atherosclerosis. However, conclusive evidence is still lacking except that for carpal tunnel syndrome.

67. Beta glucans in wheat and oats increases the body's immune response to bacterial infections. It has been proven to help the chemotaxis of neutrophils towards the bacteria and in the phagocytosis of the bacterial pathogens

68. Substitution of whole for refined grain has been suggested to reduce chronic disease risk in the United States.

69. Whole-grain breakfast cereal intake was found to be inversely associated cardiovascular disease-specific mortality, independent of age; body mass index; smoking; alcohol intake; physical activity; history of diabetes, hypertension, or high cholesterol; and use of multivitamins.

70. Whole-grain intake was inversely associated with body mass index, waist-to-hip ratio, total cholesterol, LDL cholesterol and fasting insulin.

71. An inverse association was observed between whole grain intake and ischemic stroke risk. Three studies have shown that serum homocysteine is found to be lower in people consuming whole grains and is a contributory factor in preventing the development of stroke.

72. Substituting whole for refined-grain products may decrease the risk of developing type 2 diabetes mellitus. This information is helpful in the primary prevention of diabetes mellitus.

73. Increase in the consumption of whole grain fiber in oats and barley has been shown to reduce the carcinogenic effects of bacteria and bile in the colon by forming bulk in stools and decrease in bile acid production and prevents constipation.

Insoluble fiber (found in large amounts in whole wheat and brown rice) increases fecal bulk and speeds up transit in the colon. Cancer-causing agents thus have less time in contact with cells lining the large intestine.

74. Butyric acid and propionic acid produced during the degradation of dietary fiber has been found to protect against bowel cancer in rats.

75. Avenanthamides in oats prevents free radical injury by LDL cholesterol.

76. Dietary fiber has been shown to reduce estrogen levels and thereby reduce the incidence of estrogen dependant tumors. Fibers also decrease bacteria that help to absorb estrogen into the body.

77. Vitamin B12 (cyanocobalamine) in barley, whole grain corn and brown rice is found to improve the functioning of the nervous system.

78. Niacin in wheat, brown rice and barely helps reduce total cholesterol and lipoprotein A levels, LDL, VLDL (bad cholesterol) and increases HDL (good cholesterol) and prevents platelet aggregation, which is useful in prophylaxis of myocardial infarction

79. By reducing blood sugar levels in patients with type 2 diabetes mellitus, whole grains while consumed without processed food, reduces the incidence of periodontitis and provides healthy gums. It is yet to be proven whether this benefit occurs in non-diabetic individuals also and if this effect might also be due to some other mechanisms like local action of fiber causing removal of plaques.

80. Copper, present maximally in oats, is found to reduce inflammation in arthritis, and further evidence is awaited to prove this fact conclusively.

81. Phenolics are found to cause acidification of urine and are found to have the property of reducing the occurrence of urinary tract infections. This needs further evaluation as no studies have been conducted so far in this area.

82. Whole grains lack vitamin C .

83. Magnesium in oats, wheat and rice acts as a co-factor for insulin secretion, and this might be attributed to its role in prevention and management of diabetes mellitus. However, this has not been proved by clinical trials.

84. It is proposed that phytic acid/IP 6 can fight fungal infections though this yet remains to be put into practice.

85. IP 6 (phytic acid) potentiates the action of adriamycin and tamoxifen in the treatment of breast carcinoma. This might emerge as a future breakthrough in the management of drug resistant breast cancers.

86. Propionic acid produced by insoluble fiber is partly responsible for the cholesterol lowering properties of fiber due to inhibition of HMG Co A reductase.

87. Beta glucan helps to lower cholesterol by binding to bile acids and removing them from the body via feces

88. Iron concentration is maximal in wheat among the various whole grains, two cups of which can protect against nutritional iron deficiency anemia.

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References

1. Wattenberg LW. Chemoprevention of cancer. *Cancer Res* 1985;45:1-8.[Medline]
2. Martin PM, Horwitz KB, Ryan DS, McGuire WL. Phytoestrogen interaction with estrogen receptors in human breast cancer cells. *Endocrinology* 1978;103:1860-7
3. Wang TTY, Sathyamoorthy N, Phang JM. Molecular effects of genistein on estrogen receptor mediated pathways. *Carcinogenesis* 1996;17:271-5.
4. Kuiper GGJM, Lemmen JG, Carlsson B, et al. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor β . *Endocrinology* 1998;139:4252-63.
5. Borriello, S. P., Setchell, K. D., Axelson, M. & Lawson, A. M. (1985. Production and metabolism of lignans by the human faecal flora. *J. Appl. Bacteriol.* 58:37-43.[Medline]
6. Adlercreutz H. Does fiber-rich food containing animal lignan precursors protect against both colon and breast cancer? An extension of the "fiber hypothesis." *Gastroenterology* 1984;86:761-6.[Medline]
7. Thompson LU, Robb P, Serraino M, Cheung F. Mammalian lignan production from various foods. *Nutr Cancer* 1991;16:43-52.[Medline]
8. Adlercreutz H, Fotsis T, Bannwart C, Hamalainen E, Bloigu A, Ollus A. Urinary estrogen profile determination in young Finnish vegetarian and omnivorous women. *J Steroid Biochem* 1986;24:289-96.[Medline]
9. Adlercreutz H, Mazur W. Phyto-oestrogens and western diseases. *Ann Med* 1997;29:95-120.[Medline]
10. Thompson, L. U. (1998. Experimental studies on lignans and cancer. *Baillieres Clin. Endocrinol. Metab.* 12:691-705.[Medline]
11. Adlercreutz, H. (2002. Phyto-oestrogens and cancer. *Lancet Oncol* 3:364-373.[Medline]
12. Adlercreutz, H. & Mazur, W. (1997. Phyto-oestrogens and Western diseases. *Ann. Med.* 29:95-120.[Medline]
13. Martin PM, Horwitz KB, Ryan DS, McGuire WL. Phytoestrogen interaction with estrogen receptors in human breast cancer cells. *Endocrinology* 1978;103:1860-7.[Abstract]
14. Markiewicz L, Garey J, Adlercreutz H, Gurdip E. In vitro bioassays of non-steroidal phytoestrogens. *J Steroid Biochem Mol Biol* 1993;45:399-405.[Medline]
15. Crandall DL, Busler DE, Novak TJ, et al. Identification of estrogen receptor beta RNA in human breast and abdominal subcutaneous adipose tissue. *Biochem Biophys Res Commun* 1998;248:523-6.[Medline]
16. Kuiper GGJM, Lemmen JG, Carlsson B, et al. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor β . *Endocrinology* 1998;139:4252-63.[Abstract/Free Full Text]
17. Akiyama T, Ishida J, Nakagawa S, et al. Genistein, a specific inhibitor of tyrosine-specific protein kinases. *J Biol Chem* 1987;262:5592-5.[Abstract/Free Full Text]
18. Okura A, Arakawa H, Oka H, et al. Effect of genistein on topoisomerase activity and on the growth of [Val 12] Ha-ras-transformed NIH 3T3 cells. *Biochem Biophys Res Commun* 1988;157:183-9.[Medline]
19. Markovits J, Linassier C, Fosse P, et al. Inhibitory effects of the tyrosine kinase inhibitor genistein on mammalian DNA topoisomerase II. *Cancer Res* 1989;49:5111-7.[Medline]
20. Linassier C, Pierre M, LePecq J-B, Pierre J. Mechanisms of action in NIH-3T3 cells of genistein, an inhibitor of EGF receptor tyrosine kinase activity. *Biochem Pharmacol* 1990;39:187-93.[Medline]
21. *Am J Epidemiol.* 2001 Sep 1;154(5):434-41. Horn-Ross PL, John EM, Lee M, Stewart SL, Koo J, Sakoda LC, Shiau AC, Goldstein J, Davis P, Perez-Stable EJ.
22. *I J Natl Cancer inst.* 2003 Aug 6;95(15):1158-64. Horn-Ross PL, John EM, Canchola AJ, Stewart SL, Lee MM
23. *Cancer Epidemiol Biomarkers Prev.* 2002 Jan;11(1):43-9 Horn-Ross PL, Hoggatt KJ, Lee MM
24. Peterson and Barnes 1993 Peterson G., Barnes S. Genistein and biochanin-A inhibit the growth of human prostate cancer cells but not epidermal growth factor receptor tyrosine autophosphorylation. *Prostate* 1993;22:335-345[Medline].
25. Adlercreutz 1990 Adlercreutz H. Western diet and Western diseases: some hormonal and biochemical mechanisms and associations. *Scand. J. Clin. Lab. Investig.* 1990;50(suppl. 20):13-23
26. *Cas Lek Cesk.* 2000 Dec;139 Suppl 1:31-3.
27. Dietary Phytoestrogen Intake Is Associated with Reduced Colorectal Cancer Risk. *J Nutr.* 2006 Dec;136(12):3046-3053.)
28. Isoflavones in menopause women *Med Clin (Barc).* 2006 Sep 9;127(9):352-6. Spanish. PMID: 16987456
29. Fraser GE, Sabate J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of coronary heart disease. The Adventist Health Study. *Arch Intern Med* 1992;152:1416-24.[Abstract]
30. Raicht RF, Cohen BI, Fazzini EP, Sarwal AN, Takahashi M. Protective effect of plant sterols against chemically induced colon tumors in rats. *Cancer Res* 1980;40:403-5.[Medline]
31. Onyeneho SN, Hettiarachchy NS. Antioxidant activity of durum wheat bran. *J Agric Food Chem* 1992;40:1496-1500.
32. *Journal of the American College of Nutrition, Vol. 19,*

- No. 90003, 312S-319S (2000). Harold E. Miller, PhD, Fred Rigelhof, Leonard Marquart, PhD, RD, Aruna Prakash, PhD and Mitch Kanter, PhD.
33. Journal of the American College of Nutrition, Vol. 19, No. 90003, 312S-319S (2000)
34. Graf E, Eaton JW. Suppression of colon cancer by dietary phytic acid. *Nutr Cancer* 1993;19:11-9.[Medline]
35. *J Surg Res.* 2005 Jun 15;126(2):199-203. Somasundar P, Riggs DR, Jackson BJ, Cunningham C, Vona-Davis L, McFadden DW.
36. Prostate cancer and inositol hexaphosphate IP6 : efficacy and mechanisms. *Anticancer Res.* 2005 Jul-Aug;25(4):2891-903. Singh RP, Agarwal R. Department of Pharmaceutical Sciences, School of Pharmacy, University of Colorado Health Sciences Center, Denver, CO 80262, USA.
37. Novel anticancer function of inositol hexaphosphate IP6 : inhibition of human rhabdomyosarcoma in vitro and in vivo. *Anticancer Res.* 1998 May-Jun;18(3A):1377-84.
38. Anti-HIV-1 activity of myo-inositol hexaphosphoric acid (IP6 . and myo-inositol hexasulfate(IS6). *Anticancer Res.* 1999 Sep-Oct;19(5A):3723-6.
39. *Anticancer Res.* 1999 Sep-Oct;19(5A):3695-8. Laboratory of Nutritional Science, Faculty of Education, Hiroshima University, Japan.
40. PMID: 11366552 [PubMed - indexed for MEDLINE]
41. Agarwal C, Dhanalakshmi S, Singh RP, Agarwal R. PMID: 15548374 [PubMed - indexed for MEDLINE]
42. *Int J Oncol.* 2003 Nov;23(5):1413-8. Sharma G, Singh RP, Agarwal R.
43. *J Surg Res.* 2006 Jun 1;133(1):3-6. Epub 2006 Mar 23.
44. Collins FW: Oat phenolics: Structure, occurrence and function. In Webster F (ed): 'Oats: Chemistry and Technology.' St Paul, MN: Am Assoc Cereal Chem, pp 227-296, 1986.
45. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer. II. Mechanisms. *Cancer Causes Control* 1991;2:427-42.[Medline]
46. AsiaPacificJournalofClinicalNutrition Volume 9 Issue s1 Page S23 October 2000
47. Cummings J, Bingham S, Heaton K, Eastwood M. Fecal weight, colon cancer risk and dietary intake of nonstarch polysaccharide (dietary fiber). *Gastroenterology* 1992;103:1783-7.[Medline]
48. *Am J Clin Nutr.* 2002 May;75(5):848-55.
49. American heart association web site <http://www.americanheart.org/presenter.jhtml?identifier=3042737>
50. Chandaila et al..Chandaila M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. *N Engl J Med.*2000;342:1392-8.
51. Jenkins DJ, Wolever TM, Jenkins AL, et al. Low glycemic response to traditionally processed wheat and rye products: bulgur and pumpernickel bread. *Am J Clin Nutr* 1986;43:516-20.[Abstract]
52. McIntyre A, Gibson PR, Young GP. Butyrate production from dietary fiber and protection against large bowel cancer in a rat model. *Gut* 1993;34:386-91.[Abstract]
53. Jenkins DJ, Wesson V, Wolever TM, et al. Wholemeal versus wholegrain breads: proportion of whole or cracked grain and the glycaemic response. *BMJ* 1988;297:958-60.[Medline]
54. *Int J Cancer.* 2002 May 10;99(2):267-72. Kasum CM, Jacobs DR Jr, Nicodemus K, Folsom AR.
55. Gibson GR, Beatty ER, Wang X, Cummings JH. Selective stimulation of bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* 1995;108:975-82.[Medline]
56. Buddington RK, Williams CH, Chen SC, Witherly SA. Dietary supplement of neosugar alters the fecal flora and decreases activities of some reductive enzymes in human subjects. *Am J Clin Nutr* 1996;63:709-16.[Abstract]
57. *Am J Clin Nutr.* 2003 Nov;78(5):920-7. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G
58. Jacobs DR, Pereira MA, Meyer KA, Kushi LH. *J Am Coll Nutr.* 2000;19(3 Suppl):326S-330S.
59. *American Journal of Gastroenterology*
60. Benton D, Griffiths R, Haller J et al. Thiamine supplementation mood and cognitive functioning. *Psychopharmacology (Berl).* 1997;129:66-71.
61. Tang AM, Graham NHM, Kirby AJ, et al. Dietary micronutrient intake and risk of progression to acquired immunodeficiency syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected homosexual men. *Am J Epidemiol.* 1993;138:937-951.
62. Gold M, Hauser RA, Chen MF. Plasma thiamine deficiency associated with Alzheimer's disease but not Parkinson's disease. *Metab Brain Dis.* 1998;13:43-53.
63. Bettendorff L, Mastrogiacono F, Wins P, et al. Low thiamine diphosphate levels in brains of patients with frontal lobe degeneration of the non-Alzheimer's type. *J Neurochem.* 1997;69:2005-2010.
64. *American Journal of Clinical Nutrition*, Vol. 83, No. 6, 1395-1400, June 2006 Anwar T Merchant, Waranuch Pitiphat, Mary Franz and Kaumudi J Joshipura.
65. Steffen L., Jacobs DR Jr, Stevens J, Shahar E, Carithers T and Folsom AR. *Am J Clin Nutr.* 2003 Sept;78:383-390
66. Liu S, Sesso HD, Manson JE, Willett WC, Buring JE. *Am J Clin Nutr.* 2003Mar;77:594-9.
67. Liu SM, Stampfer MJ, Hu FB, Giovannucci E, Rimm E, Manson JE, Hennekens CH, Willett WC. *Am J Clin Nutr.* 1999;70:412-429.
68. Type 2 diabetes and the vegetarian diet Jenkins D, Kendall C, Marchie A , Jenkins A, Augustin L, Ludwig D, Barnard N and Anderson, J. *Am J Clin Nutr.* 2003 Sep;78(3):610S-616S.
69. Whole-grain intake and the risk of type 2 diabetes: a prospective study in men. Fung TT, Hu FB, Pereira MA, Liu S, Stampfer MJ, Colditz GA, Willett WC. *Am J Clin Nutr.* 2002 Sep;76(3):535-40.
70. Whole Grain Consumption and Risk of Ischemic Stroke in Women: A Prospective Study Liu S, Manson J, MD, Stampfer M, Rexrode K, Hu F, Rimm E, Willett W *JAMA.* 2000;284:1534-1540.
71. McKeown NM, Meigs JB, Liu S, Wilson PW, Jacques PF. *Am J Clin Nutr.* 2002 Aug;76(2):390-8.
72. A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women.Liu S, Manson JE, Stampfer MJ, Hu FB, Giovannucci E, Colditz GA, Hennekens CH, Willett WC. *Am J Public Health.* 2000 Sep;90(9):1409-15.
73. McKeown NM, Meigs JB, Liu S, Wilson PW, Jacques PF. *Am J Clin Nutr.* 2002 Aug;76(2):390-8.)
74. Slavin JL, Martini MC, Jacobs DR Jr, Marquart L. *Am J Clin Nutr.* 1999 Sep;70(3 Suppl):459S-463S. Review.
75. Refined and whole grain cereals and the risk of oral, oesophageal and laryngeal cancer.Levi F, Pasche C, Lucchini F, Chatenoud L, Jacobs DR Jr, La Vecchia C.Eu.
76. Jacobs DR, Meyer KA, Kushi LH, Folsom AR. *Am J Public Health.* 1999;89:322-329.
77. *Int J Cancer.* 1998 Jul 3;77(1):24-8. Chatenoud L, Tavani A, La Vecchia C, Jacobs DR Jr, Negri E, Levi F, Franceschi S. .
78. *Nutr Cancer.* 1995;24(3):221-9.

79. Nutr Cancer. 1998;30(2):85-96. Jacobs DR Jr, Marquart L, Slavin J, Kushi LH

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