Critical Review of Literature of the Role of Beans (*Phaseolus vulgaris*) in Cancer Treatment and Prevention.

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Research is continuously expanding in the field of the beneficial effects of bean consumption. This research contains evidence on and for such chronic disorders as for obesity, diabetes, cardiovascular diseases, and cancer as well as their treatment and prevention.[1] Some of this research shows that when beans are consumed as part of a regular diet they can play an important role in cancer prevention, specifically colon cancer. Although these studies are encouraging, further studies into the role of beans in cancer prevention should be considered to achieve the full magnitude of their usefulness and the mechanisms of the preventative actions. With further studies the benefits of beans should be advertised to the public to increase awareness of the anticancer properties of *Phaseolus vulgaris.*

Beans have many properties which are now considered beneficial including dietary fiber, proteins, flavonoids, and phenolics. There are several potential anti-carcinogenic components in beans. Flavonoids are antioxidants which consume free radicals. Free radicals are those molecules that can damage the DNA, tissues, and other beneficial chemicals and chemical pathways in the body. Black beans contain about 2.37 grams of anthocyanin flavonoids in 1000 grams of seed coat material. It has also been shown that red kidney beans, pinto beans, and navy beans have the highest levels of antioxidant capacity and the highest levels of total phenolics of all fruits and vegetables tested. Phenolics are identified as a major proportion of the antioxidant capacity of many plants.[1] Phytochemicals regulates hormone metabolism, antioxidant effects, increase apoptosis (cell death), lower cellular proliferation, and decrease angiogenesis (blood vessel growth). Bean starch contains high levels of amylose which is known to have a low glycemic index. As well cooked beans contain 14 grams per cup of dietary fiber which is fermentable into butyrate. Beans have been shown to have anti-inflammatory properties. Beans also moves things through the intestinal tracts more quickly.[2]

Hughes et al. did a study using rats to collect experimental data on the inhibition of colon carcinogenesis by dry beans. In the study rats were put into three groups; a control group, a casein group, and a bean group. The casein and bean diet groups were injected with azoxymethane, whereas the control was not. Rats on the bean diet had significantly fewer colon adinocarcinomas than the rats on the casein diets (5 vs. 22). The number of rats with colonic tumors had similar results (24 vs. 50%). Those rats fed the bean diet also had lower tumor multiplicity than the rats on the casein diet (1.0 vs. 2.6 tumors per cancer-bearing rats). These results significantly indicate that dry beans contain anticarcinogenic components that inhibit colon cancer in rats that has been azoxymethane induced. This study did not look into which bean components were responsible for the inhibition of colon cancer. The study did suggest however that further research is needed to determine which chemical components are responsible for the anticarcinogenic effects of beans.[3]

A study by Kiss, et al. considered lectins from 5 different plants including *Phaseolus vulgaris*. The study was designed to observe if the lectins influence human colonic epithelial cell proliferation on three colorectal cancer cell lines. The cells were cultured in 4 lectin concentrations (0.1, 1.0, 10, and 100μg/ml) then the growth was assessed at days 2, 3, 5, and 7. The *Phaseolus vulgaris* samples showed a modest and uniform stimulatory effect over the three

colorectal cancer cell lines. The study concluded that the lectins in *Phaseolus vulgaris* have the potential to suppress colonic cancer growth in vitro.[4]

A study by Mitchell about the binding patterns of *Phaseolus vulgaris* leucoagglutinin (PHA-L) versus the binding patterns of *Helix pomatia* agglutinin (HPA) on metastasizing human breast and colon cancers was done. For colon cancers, the non-metastatic cell lines were unlabelled, meaning they did not show staining patterns, by neither HPA nor PHA-L. In the metastatic cell line cytoplasmic or membranous reaction occurred with the HPA and a variable reaction with the PHA-L, which was sometimes quite strong. The second metastatic cell line was variably positive with PHA-L, but negative with HPA. The study found that the two lectins gave different staining patterns and the HPA more often was associated with the metastasis compared to the PHA-L. Positive staining occurs when a dark reaction is observed. Positive staining indicates that there is binding of the lectin to the cancerous cells. This study found that PHA-L was not a reliable marker for breast cancer as it sometimes bound to the non-metastatic cancer cell lines. For colon cancer the study found that there was a wide range of staining intensities for colorectal cell lines. The authors of this study concluded that if PHA-L is to be used as metastasis indicator further studies would need to be preformed.[5]

A study by Hangen and Bennink was done to determine if there is a relationship between black and navy beans in a diet and the incidence of colon cancer. Rats were fed diets including black beans, navy beans or a control diet. The rats were injected twice with a known colon carcinogen. After 31 weeks the incidence of colon cancer in the rats on the black bean diet was 9% lower than the control rats, and the rats on the navy bean diet had a colon cancer incidence which was 14% lower than the control rats. The multiplicity of the tumors was also lower in the rats on the black bean (1.1) and navy bean (1.0) diets compared to the control diet (2.2). It was determined that there was a significantly lower incidence and multiplicity of colon cancer in rats on black and navy bean diets compared to the control group diet.[6]

Moss gathered some interesting information about beans and cancers. He posed questions about the benefits of beans including if eating beans as a staple in a diet can reduce risks of cancers. He then went on to discuss the dietary habits of different nationalities and concluded that nations that consume a large amount of dark-coloured beans had a lower incidence of colon cancer deaths. In fact, 30% lower than the United States, a country generally not known for high bean consumption.[7]

A study was done on white kidney, red pinto, Swedish brown, and black kidney beans to determine the phenolic content and antiradical activities of the beans and hull fractions. Total phenolic content of bean hulls and whole seed extracts ranged from 6.7 to 270 and 4.9 to 93.6 mg/g extract as catechin equivalents, respectively. Trolox equivalent antioxidant capacity (TEAC) assay, based on scavenging of 2, 2, 9-azinobis-(3-ethylbenzothiazoline-6-sulfonate) radical anion, revealed that the antioxidant capacity of red, brown, and black whole seed extracts was in the same order of magnitude with little variation. TEAC values of red and brown whole seed extracts were superior to that of black whole seed extract. On the basis of the total phenolic content and TEAC values, it can be deduced that colored beans possess superior antioxidative activity compared with white beans. The hydrogen peroxide scavenging capacity of different bean extracts ranged from 58% to 67% at 50 ppm and 65% to 76% at 100 ppm. The

corresponding superoxide radical scavenging capacity was 24% to 29% at 50 ppm and 53% to 60% at 100 ppm. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging capacity of black bean whole seed extracts was 22% at 50 ppm, whereas the other extracts showed 100% scavenging of this radical at both 50 and 100 ppm levels. The hydroxyl radical scavenging capacities of the bean extracts at 50 and 100 ppm were 12% to 29% and 32% to 49%, respectively. All extracts used prevented human low-density lipoprotein (LDL) cholesterol oxidation by 61.4% to 99.9% at 2 to 50 ppm level as catechin equivalents. The study postulates that the antiradicals found in these bean types may be effective in reducing the occurrence of cancers.[8]

In 2005 Heinrich et al. did a study looking into the toxicity of lectins in cancerous and non-cancerous colon cells. This study found that at 12 and 24 hours, both the cancer and noncancerous cell lines were affected by *Phaeolus vulgaris* agglutinin in a similar way, suggesting that incubation time, the amount of time after the cells have been introduce to the agglutinin and before further study, is an important factor in differential lectin effects. For incubations with *Phaseolus vulgaris* agglutinin at the 48 and 72 h time points, the 1 mg/ml concentration resulted in the non-cancer line having almost the same cell proliferation as the control (104% and 98.6%, respectively) while the cancer cell line had a significant decrease in proliferation (62.3% of control at 48 h, $p<0.00001$ and 65.8% at 72 h, $p<0.00001$). Using this as a starting point there should be further studies to look at the optimum incubation time and agglutinin concentration. With the right combination of lectin concentration and incubation time, it may be possible to selectively target cancer cells for death.[9]

Previously there existed limited evidence to suggest an inverse relationship between bean consumption and colon cancer among the Mexican population. The objective of a rat feeding study by González-Dávalos was to evaluate different cultivars, over colon cancer, of common beans, at the average per capita consumption existing in Mexico, over colon cancer in rats. Rats were fed a control diet or diets containing 2% colored beans (“Negro 8075”, “Ayocote Morado”, “Pinto Zapata”, and “Ayocote Negro”) and white-beige beans (“Flor de Mayo Anita”, “Blanco Tlaxcala”, and “Marcela”) for 4 wk before, during (8 wk) and 10 wk after having been treated with the carcinogen dimethylhydrazine. The colons were removed so that the tumor volume, incidence, multiplicity could be evaluated. The incidence of adenocarcinomas in the colon was lower in rats fed the “Negro 8075” (72%) , “Ayocote Morado” (90%), and “Pinto Zapata” bean (67 %) diets than those for rats fed the control diet and the other beans (100%). Total tumor multiplicity was also significantly lower in rats fed the “Negro 8075” bean (1.0), “Pinto Zapata” bean (0.8) and “Ayocote Morado” bean (1.1) diets compared to the rats fed the control diet (3.0). Similar results were observed for the tumor volume. The reduction in colon carcinogenesis in rats fed the colored beans might be attributed to the content of phenolic compounds, among other substances.[10]

González De Mejía and Prisecaru found that several lectins possess anticancer properties in vitro, in vivo, and in human case studies. It is postulated these lectins are used as therapeutic agents, preferentially binding to cancer cell membranes or their receptors, causing cytotoxicity, apoptosis, and inhibition of tumor growth. These compounds can become internalized into cells, causing cancer cell agglutination and/or aggregation. Ingestion of lectins also sequesters the available body pool of polyamines, thereby thwarting cancer cell growth. They also affect the

immune system by altering the production of various interleukins, or by activating certain protein kinases. Lectins can bind to ribosomes and inhibit protein synthesis. They also modify the cell cycle by inducing non-apoptotic G1-phase accumulation mechanisms, G2/M phase cell cycle arrest and apoptosis, and can activate the caspase cascade, which initiates apoptosis. Lectins can also downregulate telomerase (an enzyme which adds a specific repeating base pair sequence to the 3' end of DNA in the telomere region) activity as well as inhibiting angiogenesis. This means that the DNA will be shortened in each replication. The lectins discussed in this study came from many foods including kidney beans.[11]

A study by Wetly et al. considered lectins binding to cancerous cells versus their counterpart non-cancerous cells. This is important because the lectins need to bind to the cancer cells so that they will be internalized and their toxic effects can be exerted on the cell. It was observed that there was positive binding of cultured and fixed colon cancer cell (CCL-220) to an agarose bead derivatized with *Phaseolus vulgaris agglutinin* (PHA) in distilled water. There was negative binding of cultured and fixed colon non-cancer cell (CRL-1459) to an agarose bead derivatized with PHA in distilled water. There was negative binding of cultured and fixed colon cancer cells (CCL-220) to agarose beads derivatized with PHA and 0.2M D-glucosamine in distilled water. There was positive binding of cultured and fixed colon cancer cells (CCL-220) to agarose beads derivatized with PHA and 0.2M L-fucose in distilled water. Previous studies have shown that certain lectins bind better to human colon cancer cells than their counterparts using the bead binding assay. This study looked at expanding on this to another method. It looked at whether conventional fluorescent-lectin binding techniques would produce the same results as the bead binding assay method. The Fluorescent-lectin binding techniques is more sensitive than bead binding assays. This study was not looking directly at the role of *Phaseolus vulgaris* for its cancer preventative properties, instead it showed that there is a more precise method to look at the lectin binding of cancer cells, such as the lectins that would be found in *Phaseolus vulgaris*.[12]

A study by Lanza et al examined the association between fruits and vegetables and adenomatous polyp recurrence in the Polyp Prevention Trial (PPT). The PPT was a low-fat, high-fiber, high-fruit, and vegetable dietary intervention trial of adenoma recurrence, in which there were no differences in the rate of adenoma recurrence in participants in the intervention and control arms of the trial. In this analysis of the entire PPT trial–based cohort, multiple logistic regression analysis was used to estimate the odds ratio (OR) of advanced and nonadvanced adenoma recurrence within quartiles of baseline and change (baseline minus the mean over 3 y) in fruit and vegetable intake, after adjustment for age, total energy intake, use of nonsteroidal anti-inflammatory drugs, BMI, and gender. There were no significant associations between nonadvanced adenoma recurrence and overall change in fruit and vegetable consumption; however, those in the highest quartile of change in dry bean intake (greatest increase) compared with those in the lowest had a significantly reduced OR for advanced adenoma recurrence (OR = 0.35; 95% CI, 0.18–0.69; P for trend = 0.001). The median in the highest quartile of change in dry bean intake was 370% higher than the baseline intake. The PPT trial–based cohort provides evidence that the level of dry bean intake in the diet may be inversely associated with advanced adenoma recurrence.[13]

An epidemiologic study of pulses and cancer looked at stomach, prostate and colon cancers. This set of studies showed that over the 3 cohort studies all showed that higher pulse intakes

decreased the risk of stomach and prostate cancers, while one cohort study showed that increased pulse intake has no effect on colorectal cancer. There was some evidence of protective effects in case-control studies, but they were inconsistent. There were limitations to the applications of these studies because there were few randomized trials and most were case-controlled. The study was done in western countries where pulse intakes tends to be low, so the range was limited.[2]

A study done by Brick and Thompson using 300 rats in 10 groups was done to evaluate nine bean market classes for cancer inhibitory activity. The rats were injected with 1-methyl-1-nitrosurea (MNU) and azoxymethane (AOM) two carcinogens. A suppression of the carcinogenic process, which was not predicted, was observed in the colon of the control group in comparison to the responses observed in the feeding study. There were no differential effects of bean market classes on colon aberrant crypt foci numbers. The suppression of the carcinogenic response in the control group was in excess of 50% in the colon and therefore the results are potentially suspect. Therefore the study would need to be repeated.[14]

An investigation done by KGK Synergize Inc. looked at the effects of eight cultivars of dry beans on cancer cell proliferation. When tested in a supernatant, proliferation of all cell lines was significantly inhibited in the presence of all bean cultivar supernatants for 24, 48, and 72 hours. Black beans and pinto beans maintained higher levels of inhibition during all incubations. Lypohilization of the supernatant as well as dilution decreased the rates of cell inhibition in all cell lines after 24 hours. Decreased rates of cell inhibition were seen in two of the cell lines and an increase in cell inhibition was seen in the third cell line after 48 hours. After 72 hours the third cell line continued to increase in cell inhibition up to 60% inhibition in black beans, navy beans, and cranberry beans. When tested in re-suspended precipitate all bean cultivars inhibited cell proliferation with different bean cultivars being most effective towards the different cell lines.[15]

A study by Spanou et al. looked at different types of *Leguminosae* plant varieties including *Phaseolus vulgaris*. The study looked at the methanolic extract from each plant type at different dose levels (100, 200, 400, 800, and 1600μg/ml) and the effect it has on the % inhibition of hydroxyl radical-induced DNA strand scission. It was found that the percent inhibitions were 10±3, 10±3, 31±4, 37±4, and 38±2 respectively. These findings put *Phaseolus vulgaris* towards the centre of the percent inhibition of the plants tested.[16]

Bobe et al. looked into the protective effects of cooked dry bean consumption in a human intervention study, and evaluated which fraction of cooked dry beans is responsible for its cancer-preventive effects. Cooked navy beans (whole beans), the insoluble fraction (bean residue) or soluble fraction of the 60% (vol:vol) ethanol extract of cooked navy beans (bean extract), or a modified AIN-93G diet (16.6% fat including 12.9% lard) as control diet were fed to 160 male obese *ob/ob* mice after 2 azoxymethane injections. In comparison to control-fed mice, dysplasia, adenomas, or adenocarcinomas were detected in fewer mice on either bean fraction diet (percent reduction from control: whole beans 54%, $P = 0.10$; bean residue 81%, $P = 0.003$; bean extract 91%, $P = 0.007$), and any type of colon lesions, including focal hyperplasia, were found in fewer mice on each of the 3 bean diets percent reduction from control: whole bean 56%, $P=0.04$; bean residue 67%, $P=0.01$; bean extract 87%, $P = 0.0003$. These results suggest that

both the soluble and the insoluble fraction of the extract contribute to the cancer-protective effect ascribed to cooked navy beans.[17]

A study by Korus et al. recently considered the phenolic composition of dry beans and extrudates to evaluate the effect of extrusion process on their antioxidant activity. Myricetin, quercetin, kaempferol, cyanidin, chlorogenic acid, caffeic acid, ferulic acid and *p*-coumaric acid were identified in raw and processed bean seeds(extrudates). The effect of extrusion on the total phenolic content of beans depended on the cultivar – one variety showed a 14 % increase in the amount of phenolics in extrudates compared to raw beans, while the other two exhibited a decrease by 19 and 21 %. Extracts from bean extrudates showed a faster initial free radical scavenging activity than the extracts from raw beans; however, the final values were similar. The least active extrudates were obtained by using the initial moisture of 20 % and the temperature of 180 °C. Extrusion also decreased the antioxidant activity, compared to the raw material. Consequently there would be less of an impact on cancer prevention. Extrusion seems to negatively affect a component of the bean which has a cancer prevention effect.[18]

Finley et al. carried out a study to determine if eating pinto beans on a daily basis instead of another protein source would be a preventative measure against colon cancer. Although there were other health benefits observed, i.e. lower cholesterol, the study was unable to clearly link the benefits of pinto beans to colon cancer prevention.[19]

Bile acid–binding potential is related to lowering the risk of heart disease as well as cancer prevention. Previously, it has been reported bile acid binding by several uncooked vegetables. However, most vegetables are consumed after cooking. This study looked at whether cooking would influence in vitro bile acid binding of various vegetables by investigating a mixture of bile acids secreted in human bile under physiologic conditions. Eight replicate incubations were conducted for each treatment simulating gastric and intestinal digestion, which included a substrate only, a bile acid mixture only, and 6 with a substrate and bile acid mixture. Cholestyramine (a cholesterol-lowering, bile acid–binding drug) was the positive control treatment, and cellulose was the negative control. Relative to cholestyramine, in vitro bile acid binding on a dry matter basis was, for beets, 18%; okra, 16%; eggplant, 14%; asparagus, 10%; carrots, 8%; green beans, 7%; cauliflower, 6%; and turnips, 1%. These results point to the significantly different ($P \leq .05$) health-promoting potential of these vegetables (from highest to lowest, beets, okra, eggplant, asparagus, carrots and green beans, cauliflower, turnips) as indicated by their bile acid binding on a dry matter basis. Steam cooking significantly improved in vitro bile acid binding of beets, eggplant, asparagus, carrots, green beans, and cauliflower compared with previously observed bile acid–binding values for these vegetables uncooked. Inclusion of steam-cooked beets, okra, eggplant, asparagus, carrots, green beans, and cauliflower in our daily diet as health-promoting vegetables should be encouraged.[20]

Phaseolus vulgaris α-amylase inhibitor isoform 1 (a-AI1) starch blockers is used as a remedy against obesity and diabetes. Consumption of the a-amylase inhibitor causes marginal intraluminal α -amylase activity facilitated by the inhibitor's appropriate structural, physico-chemical and functional properties. As a result there is decreased postprandial plasma hyperglycemia and insulin levels, increased resistance of starch to digestion and increased activity of colorectal bacteria. The efficacy and safety of the amylase inhibitor extracts,

however, depend on the processing and extraction techniques used; there are several techniques which include: supercritical carbon dioxide extraction, fractionation and heat treatment. The extracts are potential ingredients in foods for increased carbohydrate tolerance in diabetics, decreased energy intake for reducing obesity and for increased resistant starch. Research developments in the distribution and biosynthesis of the α -amylase inhibitor, relevant physico-chemical properties, the molecular starch-blocking mechanism, anti-obesity and anti-diabetes effects, safety of extracts and the need for research into their potential anti-colorectal cancer effect are needed.[21]

Other than weight control products the use of *Phaseolus vulgaris* maybe limited to being a functional food product. Although there are many products on the market that utilize beans as a weight loss supplement there are no current products that are marketed towards the other health benefits that come from regular bean consumption. Even as a weight loss product the FDA has not certified that any of the claims of weight loss by the products will come true and in fact that the advertisements by these products may be construed as misleading. With further research it would be important to market beans for the other health benefits. To effectively market beans to the general population, specific attributes such as : the bean's ability to mitigate and or 'fight' chronic diseases can only be done after further research.[1]

Overall there has been much research into *Phaseolus vulgaris* and its beneficial health effects. Over time opinions have changed but now the research seems to indicate that there is an association between diets with high bean intake and a lowered incidence of many types of chronic ailments coming into greater prominence in western societies, one in specific is colon cancer. The research seems to point to a few components of the bean which helps in colon cancer prevention. Further studies of phenolics, lectins, and α-amylase inhibitors should be done to confirm these previous results. Once proven these results should be used to increase public knowledge of the benefits of bean consumption.

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