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ANTI-CANCER DIET: REVIEWING THE ROLE OF NUTRITION IN CANCER PREVENTION

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ABSTRACT: Nutritional factors have been found to account for about 30 percent of cancers in western countries. The contribution of diet to cancer risk in developing countries has been considered to be lower, around 20 percent, when poor diet is included the incidences is much higher. 30 to 40 percent cancers can be prevented by appropriate diets, physical activities, and maintenance of appropriate body weight. The link between diet, nutrition and cancer is now fully appreciated and a new paradigm for diet, nutrition and cancer prevention can be developed as we have good epidemiological evidences that some foods prevent and cause cancer. New concepts for diet and cancer prevention include the nutritional modulation of the carcinogenesis pathway by nutrients, micronutrients and phytochemicals. Factors like over consumption of energy, obesity, alcohol drinking, high fat, low fibre diet, less vegetables and fruits, preserved food, tobacco, exposure to aflatoxin, less physical activity are linked to increase risk of one or another type of cancer. Dietary factors like more fibre, more fruits and vegetables in diet, along with micronutrients, phytochemicals and probiotics have been proved to have anti-caner effect. Unravelling the effects of diet on cancer risk is, therefore, of great public health importance.

KEY WORDS: Antioxidants, Cancer, Diet, Micronutrients, Nutrition, and Probiotics

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INTRODUCTION

Cancer cells are the result of multiple genetic defects resulting from exposure to environment, dietary and infectious agents. Nutritional factors have been found to account for about 30 percent of cancers in western countries (Doll and Peto, 1981). The contribution of diet to cancer risk in developing countries has been considered to be lower, around 20 percent (Timothy, *et al*. 2004), making diet second only to tobacco as a preventable cause of cancer. Tobacco use is directly related to at least 30 percent of cancers (ACS, 2007), when poor diet is included the incidences is much higher. Unravelling the effects of diet on cancer risk is, therefore, of great public health importance. Epidemiological studies have consistently shown that a high dietary intake of fruits and vegetable as well as whole grain is strongly associated with reduced risk of developing chronic diseases, such as cancer and cardiovascular disease, which are top two causes of deaths in the developed as well as to some extent in developing countries (Temple, 2000 and Willett, 2002). It has been estimated by American Institute of Cancer Research (AICR) and World Cancer Research Fund (WCRF) that 30-40 percent cancers can be prevented by appropriate diets, physical activities, and maintenance of appropriate body weight (WCRF/AICR, 1997). It can be higher for some individual cancers. In last three decades research on carcinogenesis has yielded sound knowledge base on cancer. Nutrients can help in reducing cancer by antioxidant activity, reducing free radicals, regulation of gene expression, stimulation of the immune system etc. (Vay *et al*. 2001). The field of investigation of the role of nutrition in the cancer process is very broad, and it is becoming clear as research continues that nutrition plays a major role in cancer. Some diets are the major risk factor for colon cancer. Mutations are likely to occur in the cell lining of the colon and rectum because stool usually stays in the large intestine or colon for 24 to 36 hours, allowing the carcinogen to make their effects. The link between diet, nutrition and cancer is now fully appreciated and a new paradigm for diet, nutrition and cancer prevention can be developed as we have good epidemiological evidences that some foods prevent and cause cancer.

CANCER AND FACTS

Cancer is caused by a variety of identified and unidentified factors. The most important established cause of cancer is tobacco smoking. Other important determinants of cancer risk include diet, alcohol and physical activity, infections, hormonal factors

and radiation. The relative importance of cancers as a cause of death is increasing, mostly because of the increasing proportion of people who are old, and also in part because of reductions in mortality from some other causes, especially infectious diseases. The incidence of cancers of the lung, colon and rectum, breast and prostate generally increases in parallel with economic development, while the incidence of stomach cancer usually declines with development (WHO, 2003 and ACS, 2007).

Cancer is now a major cause of mortality throughout the world and, in the developed world, is generally exceeded only by cardiovascular diseases. An estimated 10 million new cases and over 6 million deaths from cancer occurred in year 2000 (Parkin, 2001). As developing countries become urbanized, patterns of cancer, including those most strongly associated with diet, tend to shift towards those of economically developed countries. Between 2000 and 2020, the total number of cases of cancer in the developing world is predicted to increase by 73% and, in the developed world, to increase by 29% (Parkin, 2001).

DIETARY FACTORS WHICH INCREASES CANCER RISK

1. Over Consumption of Energy (Obesity)

Eating too much food is one of the main risk factors for cancers. Overweight/ obesity, a reflection of excessive energy intake, can result from both over consumption of energy from food or low expenditure of energy as physical activity; the relative importance of these two factors can vary between individual and populations. It is estimated in a recent study, from a prospective cancer prevention cohort, that overweight and obesity accounted for 14 percent of all cancer deaths in men and 20 percent of those in women (Calle *et al.* 2003). Significant positive association is found between obesity and higher deaths rates for the following cancers: oesophagus, colon and rectum, liver, gallbladder, pancreas, kidney, stomach, prostate, breast, uterus, cervix and ovary. Calle *et al.* (2003) estimated that over 90, 000 cancer deaths per year could be avoided if the adult population all maintained a normal weight (BMI<25.0). Clearly, obesity is a major risk factor for cancer. Although these figures/ percentages can be lower in some developing countries where virally related cancers are more important, the rapid increase in overweight/ obesity in developing countries means that cancers due to it will become increasingly important (Timothy, *et al.* 2004).

The large increase in endogenous estrogen levels caused by excess body fat among postmenopausal women probably explains the higher risk of postmenopausal breast and endometrial cancer. For other cancers mechanism is less clear, but it has been suggested that hyperinsulinaemia may increase the risk of colon cancer (Giovannucci, 1995).

The glycemic index is an indication of the blood sugar response of the body to a standardized amount of carbohydrate in food/diet. The glycemic load takes into account the amount of food eaten. Case-control studies and prospective population studies have tested the hypothesis that there is an association between a diet with a high glycemic load and cancer. The case control studies have found consistent increased risk of a high glycemic load with gastric (Augustin, *et al.* 2004), upper digestive tract, endometrial, ovarian, colon or colorectal cancers (Franceschi *et al.* 2001). The prospective studies results have been mixed. Some studies showed increased risk of cancer in the whole cohort with high glycemic load (Frazier, *et al.* 2004 and Higginbotham, *et al.* 2004); some studies found only increased risk among subgroups such as sedentary, overweight subjects (Michaud, *et al.* 2002); other studies concluded that there was no increased risk (Holmes, *et al.* 2004), but there is still strong link between diabetes and cancer (Hu, *et al.* 1999).

2. Preserved meat and Red meat

The diet of human contains mutagenic material from numerous sources. The most prevalent source is fried or broiled protein rich food such as meat and fish. Amino acids and hexoses react to form hetero aromatic moieties and then condense with creatinine to form the imidazo moieties of heterocyclic amines. Role of intestinal bacteria in mutagenic activation was demonstrated by Overvik *et al.*, (1990), who found that the mutagenic content of urine and faeces were significantly higher in conventional rats than in germ free rats fed a fried meat diet. Red meat has been implicated in colon and rectal cancer. Slattery *et al.* (1998) reported a significant positive relationship between red meat and colon or colorectal cancer. A recent meta-analysis also found red meat, and processed meat, to be significantly associated with colorectal cancer (Norat *et al.* 2002). In many studies, high intakes of preserved meat or red meat have been associated with increased risk of colorectal cancer, whereas the total fat content of the diet does not appear to be related to risk. Sesink *et al.*, (1999) demonstrated that dietary heme induced faecal cytotoxicity and hyper proliferation of colonic mucosa in rats. Consumption of red meat but not of white meat is associated with a high risk of colon cancer because the heme content of red meat is ten fold higher than that of white meat. Meat, and the heterocyclic amines formed in cooking, has been correlated to breast cancer also.

Chao *et al.*, 2005 reported that consumption of red and processed meat had been associated with colorectal cancer in many but not all epidemiological studies; few studies had examined risk in relation to long-term meat intake or the association of meat with colon and rectal cancer. In their study they picked a cohort of 148610 adults aged 50 to 74 years (median, 63 years), residing in 21 states with population-based cancer registries, which provided information on meat consumption in 1982 and again in 1992/ 1993 when enrolled in the Cancer Prevention Study II (CPS II) Nutrition Cohort. Follow-up from time of enrollment in 1992/ 1993 through August 31, 2001, identified 1667 incident colorectal cancers. Participants contributed person-years at risk until death or a diagnosis of colon or rectal cancer. High intake of red and processed meat reported in 1992/1993 was associated with higher risk of colon cancer after adjusting for age and energy intake but not after further adjustment for body mass index, cigarette smoking, and other covariates. When long-term consumption was considered, persons in the highest tertile of consumption in both 1982 and 1992/1993 had higher risk of distal colon cancer associated with processed meat (RR, 1.50; 95% confidence interval [CI], 1.04-2.17), and ratio of red meat to poultry and fish (RR, 1.53; 95% CI, 1.08-2.18) relative to those persons in the lowest

tertile at both time points. Long-term consumption of poultry and fish was inversely associated with risk of both proximal and distal colon cancer. High consumption of red meat reported in 1992/1993 was associated with higher risk of rectal cancer (RR, 1.71; 95% CI, 1.15-2.52; *P*=. 007 for trend), as was high consumption reported in 1982 and 1992/1993 (RR, 1.43; 95% CI, 1.00-2.05). Their results demonstrated the potential value of examining long-term meat consumption in assessing cancer risk and strengthen the evidence that prolonged high consumption of red and processed meat may increase the risk of cancer in the distal portion of the large intestine.

3. Fat

As with meat, international correlation studies show a strong association between per capita consumption of fat and colorectal cancer mortality (Armstrong and Doll, 1975). The hypothesis postulated that a high fat diet enhanced the formation and degradation of bile acids and neutral sterols exerting promoting effects in colon carcinogenesis. It had been found that dietary fats increased the fecal concentration of bile acids. The primary bile acids cholic acid and chenodeoxycholic acid are dehydroxylated and converted to secondary bile acids, deoxycholic acid and lithocholic acid respectively.

Secondary bile acids can act as tumor promoters in animal experimentation, which are ideally performed in rodents, using azoxymethane as carcinogen (Nagangast *et al*., 1988). The various effects of secondary bile acids were reported as follows:

1. Bile acids can disrupt the integrity of the cell membrane of colonic mucosal cells (Rafter,1986)
2. It can release prostaglandin E_2 from colonic tissues, bile salts can enhance the release of arachidonate from colonocytes and subsequently the synthesis of PGE_2, which could be another explanation of the link between cell proliferation and bile acids (DeRubertis,1984)
3. Protein kinase C appears to play a critical role in tumor promotion and in the action of growth factors. Bile acids might have a direct stimulatory effect on subclasses of these enzymes (Craven et al., 1987)

The enhanced expression of Protein kinase C activates the specific isoform of cyclooxygenase i.e. Cox- 2, which plays an important role in colon carcinogenesis. The relationship of Cox- 2 and carcinogenesis may involve several pathways, including conversion of procarcinogen to active carcinogens, inhibition of apoptosis and increase in tumor cell invasiveness and promotion of angiogenesis. The over expression of Cox-2 in rat intestinal epithelial cells had been shown to increase the protooncogene *Bcl-2* and leads to inhibition of apoptosis (Tsujii *et al.,* 1995).

Bile acids increased the activity of PKC, in part, by inducing the translocation of selected isoform from cytosol to membrane fraction (Guillen, 1987). Zang et al., (1997) reported that dihydroxy bile acids are more effective in activating PKC than mono and tri hydroxy bile acids.

Some other studies reported over expression of inducible nitric oxide synthase (iNOS) in colonic tumors of human and also in rats treated with a colon carcinogenesis. Other isoforms like neural and endothelial nitric oxide synthase are different from inducible nitric oxide synthase in respect that these have constitutive but low gene expression. Rao *et al.,* (1999) demonstrated that administration of iNOS specific inhibitor, PBIT (S, S'-1, 4-phenylene-*bis*(1,2- ethanediyl)*bis*- isothiourea), significantly suppressed AOM induced colonic ACF formation in rats and that PBIT selectively suppressed the carcinogen induced colonic mucosal iNOS and Cox-2 activities. It was proposed that nitric oxide; a product of iNOS gene enhanced the activity and expression of Cox-2 in a variety of cell types.

Beresford et al., 2006 evaluated the effects of a low-fat eating pattern on risk of colorectal cancer in postmenopausal women. The Women's Health Initiative Dietary Modification Trial, a randomized controlled trial conducted in 48 835 postmenopausal women aged 50 to 79 years recruited between 1993 and 1998 from 40 clinical centers throughout the United States. Participants were randomly assigned to the dietary modification intervention (n=19 541; 40%) or the comparison group (n=29 294; 60%).The intensive behavioral modification program aimed to motivate and support reductions in dietary fat, to increase consumption of vegetables and fruits, and to increase grain servings by using group sessions, self-monitoring techniques, and other tailored and targeted strategies. Women in the comparison group continued their usual eating pattern. A total of 480 incident cases of invasive colorectal cancer occurred during a mean follow-up of 8.1 (SD, 1.7) years. Intervention group participants significantly reduced their percentage of energy from fat by 10.7% more than did the comparison group at 1 year, and this difference between groups was mostly maintained (8.1% at year 6). Statistically significant increases in vegetable, fruit, and grain servings were also made. Despite these dietary changes, there was no evidence that the intervention reduced the risk of invasive colorectal cancer during the follow-up period. There were 201 women with invasive colorectal cancer (0.13% per year) in the intervention group and 279 (0.12% per year) in the comparison group (hazard ratio, 1.08; 95% confidence interval, 0.90-1.29). Secondary analyses suggested potential interactions with baseline aspirin use and combined estrogen-progestin use status (*P*=.01 for each). Colorectal examination rates, although not protocol defined, were comparable between the intervention and comparison groups. Similar results were seen in analyses adjusting for adherence to the intervention. In this study, a low-fat dietary pattern intervention did not reduce the risk of colorectal cancer in postmenopausal women during 8.1 years of follow-up.

4. Low Fiber diet

Unrefined plant foods typically have an abundance of fiber. Dairy products, eggs, and meat all have this in common – they contain no fiber. Refined grain products also have most of the dietary fiber removed from them. So, a diet high in animal products and refined grains is low in fiber. In prospective health studies low fiber was not found to be a risk for breast cancer (Holmes, *et al.* 2004). It is possible that fiber measurements are just a surrogate measure for unrefined plant food intake. Slattery *et al.* (2004) found an inverse correlation between vegetable, fruit and whole

grain intake plant food intake and rectal cancer, while refined grains were associated with increased risk of rectal cancer. A threshold of about 5 daily servings of vegetables was needed to reduce cancer risk and the effect was stronger among older subjects. Many other nutrients are co-variants with fiber, including folic acid.

5. Omega 3:6 Fatty Acids Ratio

Omega 3 fatty acids (alpha-linolenic acid, EPA, DHA) have been shown in animal studies to be protect from cancer, while omega 6 fatty acids (linoleic acid, arachidonic acid) have been found to be cancer promoting fats (Michael, *et al*. 2004). Studies found an association between a higher ratio of N-3 to N-6 fats and reduced risk of breast cancer (London *et al*. 1993). Long chain N-3 and N-6 fats have a different effect on the breast tumour suppressor genes BRCA1 and BRCA2 (Bernard *et al*. 2002). Treatment of breast cell cultures with N-3 fats (EPA or DHA) results in increased expression of these genes while arachadonic acid had no effect (Bernard *et al*. 2002).

6. Alcoholic Beverages

Another aspect of diet clearly related to cancer incidence is consumption of alcoholic beverages, which convincingly increases the risk of cancers of the oral cavity, pharynx, larynx, oesophagus, liver, breast and colorectum. (IARC, 1988). The increase in risk appears to be primarily due to alcohol per se rather than specific alcoholic beverages. Whereas most of the excess risks occur with high alcohol consumption, a small (about 7%) increase in risk of breast cancer has been observed with approximately one drink per day. Recent studies suggest that the excess risk of breast and colon cancer associated with alcohol consumption may be concentrated in persons with low folate intake (Timothy, *et al*. 2004). Liver cancer is also very prominent with alcohol consumption.

7. Aflatoxin

Food contaminated with aflatoxin convincingly increases the risk of liver cancer. Yeh, *et al*. (1989) evaluated the roles of HBV (hepatitis B virus) and AFB1 (aflatoxin B1) in the development of liver cancer. Aflatoxins, especially aflatoxin B1, are potent carcinogens in some animals; there is interest in the effects of long-term exposure to low levels of these important mycotoxins on humans. In 1988, the IARC placed aflatoxin B1 on the list of human carcinogens. This is supported by a number of epidemiological studies that have demonstrated a positive association between dietary aflatoxins and Liver Cell Cancer (LCC). However, this contamination occurs mainly in areas where hepatitis viruses are a major cause of liver cancer, and the importance of aflatoxin in the absence of hepatitis virus infections (for example, after immunisation) is not clear (Timothy, et al. 2004).

8. Salt preserved foods and Salt

High intakes of salt-preserved foods and of salt probably increase the risk of stomach cancer. Many, but not all, the results of case control studies have shown a positive association between gastric cancer and the intake of high salt foods such as salted fish, cured meat, and salted vegetables, or the use of table salt (Kono and Hirohata, 1996). Salt is not carcinogenic by itself, but in experimental animals, hypertonic sodium chloride solutions which produce increased DNA synthesis, (Furihata, *et al*. 1984) i.e. more cellular growth in the gastric mucosa, resulting ultimately in atrophic gastritis (Kodama, *et al*. 1984), become co-carcinogenic when given with nitrosamides, and promoting when administered after the carcinogen (Takahashi and Hasegawa, 1986). A high intragastric salt concentration destroys the mucosal barrier, and leads to inflammation and damage such as diffuse erosion and degeneration. The induced proliferous change might enhance the effect of food-derived carcinogens (Tsugane, 2005).

9. Very hot drinks and foods

Consumption of very hot drinks and foods typically consumed in some cultures probably increases risk of cancers of the oral cavity, pharynx and oesophagus. There is a possibility that drinking very hot drinks such as tea, coffee or soup (Ji *et al*., 1998) may increase risk. Studies have reported up to 3 times the risk in people who regularly drink hot drinks when they are burning hot, rather than warm. Hot drinks may damage the lining of the esophagus; even thermal irritation may have a role in gastric carcinogenesis (Vecchia, *et al*., 1990). The most important factors involved in esophageal cancer are the habit by which tea and foods are consumed. In most studies, the rapid ingestion of hot food and tea has been shown to be risk factor (.Cook-Mozaffari *et al*., 1979). Drinking hot coffee or other types of hot drinks is associated with esophagitis, which is probably a pre-neoplastic condition.

DIETARY FACTORS WHICH PROBABLY REDUCE RISK

1. Fruits and Vegetables

Most important idea of modern nutrition research is that a diet rich in fruits and vegetables protects against cancer. The same diet also protects against almost all other diseases, including cardiovascular disease and diabetes. For most cancers, people (1/4th of the population) who ate the least amount of fruits and vegetables had about twice the risk of cancer compared to those who ate the most fruits and vegetables. Even in lung cancer, after accounting for smoking, increasing fruits and vegetables reduces lung cancer; an additional 20 to 33 percent reduction in lung cancers is estimated (WCRF/AICR, 1997).

Steinmetz and Potter (1996) reviewed the relationship between fruits, vegetables, and cancer in human epidemiologic and animal studies and found "the evidence for a protective effect of greater vegetable and fruit consumption is consistent for cancers of the stomach, esophagus, lung, oral cavity, pharynx, endometrium, pancreas, and colon". Vegetables, particularly raw vegetables, were found to be protective; 85 percent of the studies that queried raw vegetable consumption found a protective effect. Allium vegetables, carrots, green vegetables, cruciferous vegetables, and tomatoes also had a fairly consistent protective effect (Steinmetz and Potter 1996). Allium vegetables (garlic, onion, leeks, and scallions) are particularly potent and have separately been found to be protective for stomach and colorectal cancers and prostate cancer.

There are many substances that are protective in fruits and vegetables, so that the entire effect is not very likely to be due to any single nutrient or phytochemical. Steinmetz and Potter (1996) list possible protective elements: dithiolthiones, isothiocyanates, indole-32-carbinol, allium compounds, isoflavones, protease inhibitors, saponins, phytosterols, inositol hexaphosphate, vitamin C, D, limonene, lutein, folic acid, beta carotene (and other carotenoids), lycopene, selenium, vitamin E, flavonoids, and dietary fiber. A joint report by the World Cancer Research Fund and the American Institute for Cancer Research found convincing evidence that a high fruit and vegetable diet would reduce cancers of the mouth, pharynx, esophagus, lung, stomach, colon and rectum; evidence of probable risk reduction was found for cancers of the larynx, pancreas, breast, and bladder.

Some recent prospective studies have not supported important protective effects for cancers of the lung and breast, and have suggested that the reduction in risk for colorectal cancer may be modest. These conflicting results, which add to concerns about the potential for bias in case-control studies, also suggest the need for some caution regarding diet, nutrition and cancer conclusions about intake of fruits and vegetables and the risks of oral, esophageal and stomach cancers, which have not been adequately examined in large prospective studies. Although support for a broad and strong protective effect of higher fruit and vegetable intake against cancer incidence has weakened with the results from recent studies, modest benefits of increasing fruit and vegetable intake have not been excluded and probably do exist. The issue of dose–response is important, and some evidence suggests that a very low intake of fruits and vegetables, e.g. less than 2 servings or 200 g/d, is related to increases in risk compared with higher intakes, but that there may be little additional benefit for intakes higher than about 400 g/d (Terray *et al*., 2001 and Smith, *et al*. 2001). Also, fruits and vegetables are extremely heterogeneous, and it is possible that only specific foods are related to risk for specific cancers.

Since, fruit and vegetable intakes have been associated with a reduced risk of colon cancer; however, in more recent studies associations have been less consistent (Kaushik *et al*., 2007) and it has been concluded that fruit and vegetable intakes were not strongly associated with colon cancer risk overall but may be associated with a lower risk of distal colon cancer. Hung *et al., 2004*, evaluated the relationship between fruit and vegetable intake and the incidence of cardiovascular disease and cancer and of deaths from other causes in two prospective cohorts. A total of 71 910 female participants in the Nurses' Health study and 37 725 male participants in the Health Professionals' Follow-up Study who were free of major chronic disease completed baseline semi quantitative food-frequency questionnaires in 1984 and 1986, respectively. Dietary information was updated in 1986, 1990, and 1994 for women and in 1990 and 1994 for men. Participants were followed up for incidence of cardiovascular disease, cancer, or death through May 1998 (women) and January 1998 (men). Multivariable-adjusted relative risks were calculated with Cox proportional hazards analysis. *Results:* We ascertained 9329 events (1964 cardiovascular, 6584 cancer, and 781 other deaths) in women and 4957 events (1670 cardiovascular diseases, 2500 cancers, and 787 other deaths) in men during follow-up. For men and women combined, participants in the highest quintile of total fruit and vegetable intake had a relative risk for major chronic disease of 0.95 (95% confidence interval [CI] 0.89 to 1.01) times that of those in the lowest. Total fruit and vegetable intake was inversely associated with risk of cardiovascular disease but not with overall cancer incidence, with relative risk for an increment of five servings daily of 0.88 (95% CI -0.81 to 0.95) for cardiovascular disease and 1.00 (95% CI - 0.95 to 1.05) for cancer. Of the food groups analyzed, green leafy vegetable intake showed the strongest inverse association with major chronic disease and cardiovascular disease. For an increment of one serving per day of green leafy vegetables, relative risks were 0.95 (95% CI- 0.92 to 0.99) for major chronic disease and 0.89 (95% CI -0.83 to 0.96) for cardiovascular disease. They concluded that increased fruit and vegetable consumption was associated with a modest although not statistically significant reduction in the development of major chronic disease. The benefits appeared to be primarily for cardiovascular disease and not for cancer.

2. Cruciferous Vegetables

Cruciferous vegetables such as cauliflower, cabbage, broccoli sprouts contain sulforophane, which has anti-cancer properties. In a study in China found that intake of cruciferous vegetables, measured by urinary secretion of isothiocyanates, was inversely related to the risk of breast cancer; the quartile with the highest intake only had 50% of the risk of the lowest intake group (Fowke, *et al*., 2003). In another study a high intake of cruciferous vegetables (5 or more servings/week vs. less than two servings/week) was associated with a 33% lower risk (Zhang, *et al*., 2000). Three or more servings per week, compared to less than one serving of cruciferous vegetables per week resulted in a statistically significant 41% decrease in prostate cancer risk (Cohen, *et al*., 2000). Similar protective effects of cruciferous vegetables were seen in a multi-ethnic case-control study (Kolonel, *et al*., 2000). Broccoli sprouts have a very high concentration of sulforophane since this compound originates in the seed and is not made in the plant as it grows (Fahey, *et al*., 1997). One sprout contains all of the sulforophane that is present in a full grown broccoli plant. So, if sulforophane is especially cancer-protective, it would seem reasonable to include some cruciferous vegetables in an anti-cancer diet.

3. Phytochemicals in the prevention of cancer

Evidence suggests that dietary phytochemicals/antioxidants can reduce cancer risk. Block *et al*. (1992) established this in an epidemiologic review of 200 studies that examined the relationship between fruit and vegetable intake and cancers. In 128 of 156 dietary studies, the consumption of fruit and vegetables was found to have a significant protective effect. The risk of cancer for most cancer sites was twice as high in persons whose intake of fruit and vegetables was low compared with those with high intake. A prospective study showed an inverse association between the intake of flavonoids and the incidence of all sites of cancer combined (Knekt, *et al*. 1997). The risk of lung cancer was reduced to 50%

in the high flavonol intake. Consumption of quercetin in onions and apples was found to be inversely associated with lung cancer risk (Le, *et al.* 2000). The effect of onions was particularly strong against squamous cell carcinoma. Boyle, *et al.* (2000) showed that increased plasma levels of quercetin following a meal of onions were accompanied by increased resistance to strand breakage by lymphocyte DNA and decreased levels of some oxidative metabolites in the urine.

Surh *et al.* (1998) reviewed evidence from animal studies to support the anti-carcinogenic and anti-mutagenic effects of capsaicin, the pungent ingredient present in red pepper and ginger. As evaluated by several biomarkers in tumor tissue, soy products decreased angiogenesis, increased apoptosis and slightly decreased proliferation of MB49 bladder carcinoma cells injected into mice (Kubena, and McMurray, 1996; and Zhou, *et al.* 1998). Genistein (5, 7, 4'-trihydroxyisofavone) is one of the major isofavonoids in soy. In human breast cancer cells in culture, genistein has anti-proliferative effects on mitogen-stimulated growth. Soy isofavonoid conjugates have chemopreventive activity in carcinogen induced rat models of breast cancer (Barnes, 1997). In rats, the mechanism of the preventive action is in part dependent on its estrogenic activity, which causes rapid differentiation of cells of the mammary gland. As it is important to remember that food phytochemicals are not consumed in isolated, purified form, but in combination with other Phytochemicals and food components, this type of approach should apply to studies of the health benefit effects of all food phytochemicals.

Oxidative damage is linked to formation of tumors through several mechanisms. Oxidative stresses induced by free radicals cause DNA damage, which, when left unrepaired, can lead to base mutation, single and double strand breaks, DNA cross-linking, and chromosomal breakage and rearrangement(Ames, *et al.* 1993 and Liu, 2004). This potentially cancer-inducing oxidative damage might be prevented or limited by dietary phytochemicals found in fruit and vegetables. Studies to date have demonstrated that phytochemicals in common fruit and vegetables can have complementary and overlapping mechanisms of action, including modulation of detoxification enzymes, scavenging of oxidative agents, stimulation of the immune system, regulation of gene expression in cell proliferation and apoptosis, hormone metabolism, antibacterial and antiviral effects (Dragsted, *et al.* 1993 and Waladkhani, and Clemens, 1998).

4. Probiotics

The Bogdanovet *et al.,* (1962) reported that *Lactobacillus bulgaricus* produced substances which were active against tumor development. The anti carcinogenic properties of lactobacilli fall in to three categories

1. Inhibition of tumor cells (Reddy *et al.,* 1973)
2. Suppression of bacteria which produced enzymes such as β -glucuronidase, nitroreductase and azoreductase, responsible for the release of carcinogens (goldin and gorbach, 1977)
3. Destruction of carcinogens such as nitrosamines (Rowland and Grasso, 1975).

Intake of fermented or culture containing dairy foods have been reported to reduce the risk of colon cancer (Miller *et al.,* 2000). Although these findings are not entirely consistent and may depend in part on such factors as the strain of bacteria used in dairy foods. It was reported that consuming yogurt as infrequently as one to three times a month was associated with protection against colon cancer (Peters *et al.*, 1992). Consumption of products containing viable lactic acid bacteria may lower risk of colon cancer by reducing pro carcinogenic substances or by reducing the level of enzymes (β- glucuronidase, β- glucosidase, azoreductase and nitroreductase) that convert pro carcinogen into carcinogens in the intestine.

Most of the research of probiotics and cancer has been done in animals. Studies have looked at markers of tumor growth or at animals with chemically induced tumors. Goldin and Gorbach (1980) noted that rats challenged with DMH and fed grain diet for 36 weeks had an incidence of colon cancer of only 31% versus 83% in rats fed beef diets. Rats given *Lb. acidophilus* supplements and beef had a cancer incidence of 73%. Rats examined at 20 weeks had a 77% incidence of colon cancer when fed beef, but only 40% with beef supplemented with *Lb. acidophilus*. The marked increased in induction time for DMH induced colon cancer with *Lb. acidophilus* supplements would be of great importance if the data could be extrapolated to colon cancer in humans. Mitsuka (1981) also noted that the presence of *Lb. acidophilus* and *Bifidobacterium bifidum* in the intestine suppressed the formation of gut tumors by other intestinal organisms in the mice. Takano *et al.*, (1985) also found that feeding acidophilus milk reduced the proliferation of colon tumors in rats injected with DMH. Another strain of *Lactobacillus GG,* had been demonstrated to decrease colon tumors incidence in DMH treated laboratory rats. It appeared that this *Lactobacillus* species interfere with the initiation of early promotional stages of chemically induced carcinogenesis. Its effect was more pronounced in animal fed a high fat (20% corn oil) diet than a low fat (5% corn oil) diet (Goldin *et al.*, 1996).

In human, *Lb. acidophilus* supplements have been demonstrated to decrease activities of fecal bacterial β-glucuronidase, nitroreductase and enzymes that may convert procarcinogen to proximate carcinogen (Goldin *et al.*, 1980; Goldin and Gorbach, 1984). These enzymes returned to base line in 30 days after intake of *Lb. acidophilus* supplements ceased. Similar results were reported by investigators in Finland (Ling *et al.*, 1994) with women volunteers. Supplementation of normal omnivorous diet with yogurt (containing viable cell of *Lactobacillus GG)* for four weeks, decreased the fecal β-glycocholic acid hydrolase activities, and these activities returned to base line level during 2 weeks follow up period after the *Lactobacillus GG* treatment was discontinued. Feeding of viable cultures of *Lb. acidophilus* significantly lowered the activities of fecal β- glucuronidase, nitroreductase and azoreductase in rats consuming grain diet (Goldin and Gorbach, 1977). Reddy and Wynder (1973) found that Americans consuming a mixed "western diet" had a higher level of fecal β- glucuronidase than did American vegetarians.

The protective effect of *Bifidobacterium* was first suggested in

1899 and its therapeutic effects were made use of by the Japanese, who included it in their diets. *Bifidobacterium* are the predominant bacteria in human gut micro flora and have been considered to exert a beneficial effect on human health by maintaining the equilibrium of the colonic microflora (Ueda, 1986). *B. longum* also reduced carcinogen induced cell proliferation, the activity of colonic mucosal and tumor ornithine decarboxylase, and the expression of Ras- p21 oncoprotein in rats (Singh *et al.,* 1997). Increased activity of ornithine decarboxylase, a rate limiting enzyme in the metabolism of polyamines, had been observed in colon adenomas and carcinomas, reflecting colonic mucosa hyper proliferation.

In general species of *Bifidobacterium* and *Lactobacillus*, have low activities of enzymes involved in carcinogen formation and metabolism in comparison to other major anaerobes in the gut such as bacteroids, eubacteria and clostridia (Saito *et al.,* 1992). This suggests that increasing the proportion of LAB in the gut could modify, beneficially the level of xenobiotic metabolizing enzymes.

Other studies have shown that probiotics can inhibit the formation of aberrant crypt foci (Rowland, *et al*. 1998, Singh *et al.*, 2007), thought to be a pre-cancerous lesion in the colon. A probiotic mixture, given to rats fed azoxymethane reduced colon tumors compared to the control (50% vs. 90%), and also reduced the number of tumors per tumor-bearing rat (Marotta, *et al*. 2003). The research on probiotics and disease is still an emerging field. There is a high degree of variation of health benefits between different strains of bacteria. As new methods for selecting and screening probiotics become available, the field will be able to advance more rapidly.

5. Vitamin C

Vitamin C, most common supplement taken, has been studied in relation to health. Low blood levels of ascorbic acid are detrimental to health (Fletcher *et al*. 2003) and vitamin C is correlated with overall good health and cancer prevention (Lee, *et al*. 2003). At high concentrations ascorbate is preferentially toxic to cancer cells. There is some evidence that large doses of vitamin C, either in multiple divided oral doses or intravenously, have beneficial effects in cancer therapy (Riordan, *et al*. 1995). Oral doses, even in multiple divided doses, are not as effective as intravenous administration. Vitamin C at a dose of 1.25 g administered orally produced mean peak plasma concentrations of 135±21 ìmol/L compared with 885±201 µmol/L for intravenous administration (Padayatty, *et al*. 2004), thus intravenous Vit. C may be beneficial for prevention of cancer.

6. Vitamin B12

Vitamin B12 has not been proven to be an anti-cancer agent, but there is some evidence indicating that it could be beneficial. Some experimental cancer studies have been carried out with various forms of vitamin B12. Methylcobalamin inhibited tumor growth into mice (Nishizawa, *et al*. 1997), and caused mouse mammary tumor cells to undergo apoptosis, even when stimulated to grow by the presence of growth-inducing androgen. Methylcobalamin, but not cyanocobalamin, increased the survival time of mice bearing implanted leukemia tumor cells (Tsao, and Myashita, 1993). 5'-deoxyadenosylcobalamin and methylcobalamin, but not cyanocobalamin, were shown to be effective cytotoxic agents. Methylcobalamin also was able to increase survival time and reduce tumor growth in laboratory mice. Laboratory mechanistic evidence for the effects of vitamin B12 was seen in a laboratory study with vitamin B12 deficient rats. This evidence indicating that vitamin B12 is an important nutrient for genetic stability, DNA repair, carcinogenesis, and cancer therapy (Choi, *et al*. 2004). The form of administered vitamin B12 may be important.

7. Folic Acid

Folic acid has an integral role in DNA methylation and DNA synthesis. It works in conjunction with vitamin B6 and vitamin B12 in the single carbon methyl cycle. If insufficient folic acid is not available uracil is substituted for thymidine in DNA, which leads to DNA strand breakage. Many studies have found a significant reduction in colon, rectal, and breast cancer with higher intakes of folic acid and their related nutrients (vitamin B6 and B12) (Freudenheim, *et al.* 1991, Giovannucci, *et al*. 1995 and Slattery, *et al.* 1997). Alcohol is an antagonist of folate, so that drinking alcoholic beverages greatly magnifies the cancer risk of a low-folate diet Genetic polymorphisms in the methylene tetra hydrofolate reductase and the methionine synthase genes which increase the relative amount of folate available for DNA synthesis and repair also reduces the risk of colon cancer (Ma, *et al*. 1997 and Le, *et al*. 2002). Most of the breast cancer studies only found a protective effect of folate among women who consumed alcohol (Zhang, *et al*. 2003 and Sellers, *et al*. 2004). Studies showed that the risk of cancer due to family history can be modified by high folate intake, so a prudent anti-cancer diet would be high in dark green leafy vegetables.

8. Vitamin D

Active hormonal form of vitamin D has the potent anticancer properties (Michael, 2004). It has been discovered that various types of normal and cancerous tissues, including prostate cells (Schwartz, *et al*. 1998), colon tissue (Tangpricha, *et al*. 2001), breast, ovarian and cervical tissue (Friedrich, *et al*. 2003), pancreatic tissue and a lung cancer cell line (Mawer, *et al*. 1994) all have the ability to convert the major circulating form of vitamin D, 25(OH) D, into the active hormonal form, 1, 25 (OH) 2D. So, there is a local mechanism in many tissues of the body for converting the form of vitamin D in the body into a hormone that has anticancer activity. Indeed, 25(OH) D has been shown to inhibit growth of colonic epithelial cells, primary prostatic epithelial cells, and pancreatic cells (Holt, *et al*. 2002 and Schwartz, *et al*. 2004).

9. Carotene

α- and β-carotene and other carotenoids have been studied to see if these compounds can decrease cancer risk. Generally accepted that β-carotene is a cancer-protective agent (Michael, 2004). Beta-carotene may be a marker for intake of fruits and vegetables, but it does not have a powerful protective effect in isolated

pharmacological doses. α -carotene has been found to be a stronger protective agent (Michaud, *et al*. 2000 and Knekt, *et al*. 1999) than its well-known isomer β-carotene. Studies tend to agree that overall intake of carotenoids is more protective than a high intake of a single carotenoid (Stefani, *et al*. 1999). So, a variety of fruits and vegetables is still a better anti-cancer strategy than just using a single vegetable high in a specific carotenoid. Bjelakovic *et al*., 2007, tried to assess the effect of antioxidant supplements on mortality in randomized primary and secondary prevention trials. They searched electronic databases and bibliographies published by October 2005. All randomized trials involving adults comparing beta carotene, vitamin A, vitamin C (ascorbic acid), vitamin E, and selenium either singly or combined vs. placebo or vs. no intervention were included in their analysis. Randomization, blinding, and follow-up were considered markers of bias in the included trials. The effect of antioxidant supplements on all-cause mortality was analyzed with random-effects meta-analyses and reported as relative risk (RR) with 95% confidence intervals (CIs). Meta-regression was used to assess the effect of covariates across the trials and to know the effects of antioxidant supplements on prevention of several diseases. When all low- and high-bias risk trials of antioxidant supplements were pooled together there was no significant effect on mortality (RR, 1.02; 95% CI, 0.98-1.06). Multivariate meta-regression analyses showed that low-bias risk trials (RR, 1.16; 95% CI, 1.05-1.29) and selenium (RR, 0.998; 95% CI, 0.997-0.9995) were significantly associated with mortality. In 47 low-bias trials with 180 938 participants, the antioxidant supplements significantly increased mortality (RR, 1.05; 95% CI, 1.02- 1.08). In low-bias risk trials, after exclusion of selenium trials, beta carotene (RR, 1.07; 95% CI, 1.02-1.11), vitamin A (RR, 1.16; 95% CI, 1.10-1.24), and vitamin E (RR, 1.04; 95% CI, 1.01-1.07), singly or combined, significantly increased mortality. Vitamin C and selenium had no significant effect on mortality. And they concluded that treatment with beta carotene, vitamin A, and vitamin E might increase mortality. The potential roles of vitamin C and selenium on mortality need further study.

10. Selenium and Calcium

Selenium is a mineral with anti-cancer properties. Many studies in the last several years have shown that selenium is a potent protective nutrient for some forms of cancer (Duffield, *et al*. 2002 and Clark, *et al*. 1996). The selenium supplement was most effective in ex-smokers and for those who began the study with the lowest levels of serum selenium (Van, et al. 2003). Several prospective studies have also examined the role of selenium in cancer prevention, particularly for prostate cancer (Li, *et al*. 2004). If a person has low selenium levels and other antioxidant defences are also low the cancer risk is increased even further. Women do not appear to be as sensitive to selenium, as breast cancer has not been found to be influenced by selenium status in studies (Ghadirian, *et al*. 2000), although both men and women were found to be protected by higher levels of selenium from colon cancer and lung cancer (Reid, *et al*. 2002).

High intakes of calcium may reduce the risk for colorectal cancer, perhaps by forming complexes with secondary bile acids in the intestinal lumen (WCRF, 1997) or by inhibiting the hyperproliferative effects of dietary haem (Sesink, *et al*. 2001). Supplemental calcium may have a modest protective effect on the recurrence of colorectal adenomas (Bonithon, *et al*. 2000).

11. Conjugated Linolic Acid

CLA has shown to have positive effects on immune function and body composition. CLA in unusual among anticancer compounds because it reduces the incidences of cancer and also suppresses the growth of existing cancers. It has been suggested that CLA may act by antioxidant mechanisms, pro-oxidant cytotoxicity and reduction in cell proliferation activity. CLA has shown to inhibit the development of mouse epidermal tumors, mouse fore stomach cancer and rat mammary cancer. Feeding mice (Ha, *et al*. 1990) and rats (Ip, *et al*. 1991) a mixture of CLA isomers resulted in the preferential incorporation of the 9-cis, 11-trans isomer into membrane phospholipids, suggesting that the 9-cis, 11-trans CLA is the biologically active isomer. The fact that CLA is protective in the methylnitrosourea model suggests that it may have a direct modulating effect on susceptibility of the target organ to neoplastic transformation.

Kim, *et al*. (2002) provides the first evidence that the growth inhibitory effect of CLA on Caco-2 colon cancer cells is attributed to the action of the t10c12 isomer. Decrease in Caco-2 cell number by CLA may, at least in part, be mediated by decreasing IGF-II secretion that is an autocrine growth stimulator of Caco-2 cells. Ochoa, et al. (2004) shows an antiproliferative, anti-viability effect of conjugated linoleic acid on the androgen-independent human prostate cancer cell line PC-3. However, the anti-proliferative / anticancer effects of CLA mixtures and their constituent isomers on this cell line are not equivalent. These differences are apparently due to the different pathways modulated by the individual isomers. The trans-10, cis-12 CLA isomer appears to elicit the greatest effect and apparently works preferentially through modulation of genes involved in apoptosis and cell cycle control. CLA is prone to oxidation *in vitro*, and it has been suggested that increased lipid oxidation may contribute to the cytotoxic effects of this agent in cancer cell lines (Devery, *et al*. 2001).

12. Dietary fibres and prebiotics

Whole grains are important source of many nutrients including dietary fibers, resistant starches, oligosaccharides, trace minerals, vitamins and other compounds of interest in disease prevention, including phytoesterogens and antioxidants (Cummings *et al.,* 1992). The major grains include wheat, rice and corn whereas minor grains include oat, rye, barley and sorghum (potter, 1997). Grain is composed of endosperm, germ and bran. The endosperm comprises 80% of the whole grain, whereas the percentage accounted for germ and bran components vary among different grains. With the exception of rice, grains are high in dietary fibers, low in fats, have 10-15% protein and source of vitamin and minerals. Nutrients and phytochemicals are not evenly distributed throughout the grain, with higher concentration in the outer part of the grain, so refining results in reduced nutrient content.

The fermentation products of dietary fibers are H_2O, CO_2, CH_4, H_2 and short chain fatty acids (SCFA). Out of various SCFA, butyrate may have the inhibitory effect on colon carcinogenesis. The presence of butyrate in the distal colon is also believed to be important in the prevention of colon cancer, because majority of tumors in both humans and experimentally induced rodent cancer models occur in the distal colon. Butyrate is the primary fuel of colonocytes; it is utilized preferentially over glucose, glutamine and other short chain fatty acids (Roeidger, 1982).

Dietary fibers may be divided into two categories. One water soluble and another is water insoluble which soften stools and help to move it through the intestinal tract in less time. Water soluble fibers delay starch absorption, stabilizing the serum insulin level that might otherwise increase and promote the intestinal tumerogenesis. Wheat bran consists of insoluble dietary fibers, which ferment slowly, resulting in greater concentration of butyrate in the distal colon (Reddy *et al.,* 1975).

The effect of fiber on the action of bile acids may be attributable to the binding or diluting the bile acids. Fermentation of dietary fibers result in the formation of SCFA, which lowers the intestinal pH, this in turn inhibit the conversion of primary bile acids to secondary bile acids, also at low pH, the solubility of free bile acids is reduced, diminishing their availability for carcinogenic activity(McIntyre,1993).

Reddy *et al.,* (1973) found that even though residents of both New York City and Finland consumed high fat diets, the incidence of colon cancer was decreased in the finish people due to the consumption of high fiber diets.

McIntyre *et al.*, (1993) studied the effects of 3 types of dietary fibers on fermentative production of butyrate in the distal colon to their effects on tumor mass in a rat model of bowel cancer. Guar gum was chosen because of its known solubility and high fermentability in the rats, while WB was selected for its relatively low fermentability and oat bran as tropical interest of product due to its effect on cholesterol metabolism and because it is generally considered to be well fermented. They reported that wheat bran fed rats had the lowest tumor number and mass and did not have the falling caeco – fecal gradients in butyrate concentration as seen with the other diets. They also proposed that highly fermentable fibers could be completely broken down, leaving no substrate for fermentation in the distal colon.

Prebioticis is a nondigestible food ingredients that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon that have the potential to improve host health' (Gibson and Roberfroid, 1995). Consumption of non digestible carbohydrates can reduce the concentration of certain biomarkers of carcinogenesis. Combination of probiotics and probiotics can result in additive or synergistic effects on gastrointestinal function. Challa et al (1997) demonstrated a small reduction (22%) in total ACF in AOM treated F344 rats when the synthetic, non digestible disaccharides lactulose was incorporasted in the diet at 2%. Both challa et al (1997) and Rowland et al (1998) studied the effect of combined treatment of probiotic and probiotic on ACF numbers. The combination of *Bifidobacterium longum* and lactulose resulted in a 48% inhibition of colonic ACF, which was significantly greater than that achieved by either B. longum or lactulose alone (challa *et al*, 1997).

Park *et al*., 2005 evaluated the association between dietary fiber intake and risk of colorectal cancer. From 13 prospective cohort studies included in the Pooling Project of Prospective Studies of Diet and Cancer, 725 628 men and women were followed up for 6 to 20 years across studies. Study- and sex-specific relative risks (RRs) were estimated with the Cox proportional hazards model and were subsequently pooled using a random-effects model. During 6 to 20 years of follow-up across studies, 8081 colorectal cancer cases were identified. For comparison of the highest vs. lowest study- and sex-specific quintile of dietary fiber intake, a significant inverse association was found in the age adjusted model (pooled RR=0.84; 95% confidence interval [CI], 0.77 0.92). However, the association was attenuated and no longer statistically significant after adjusting for other risk factors (pooled multivariate RR=0.94; 95% CI, 0.86-1.03). In categorical analyses compared with dietary fiber intake of 10 to _15 g/d, the pooled multivariate RR was 1.18 (95% CI, 1.05-1.31) for less than 10 g/d (11% of the overall study population); and RR, 1.00 (95% CI, 0.85-1.17) for 30 or more g/d. Fiber intake from cereals, fruits, and vegetables was not associated with risk of colorectal cancer. The pooled multivariate RRs comparing the highest vs. lowest study- and sex-specific quintile of dietary fiber intake were 1.00 (95% CI, 0.90-1.11) for colon cancer and 0.85 (95% CI, 0.72-1.01) for rectal cancer (*P* for common effects by tumor site=.07). And they concluded that in this large pooled analysis, dietary fiber intake was inversely associated with risk of colorectal cancer in age-adjusted analyses. However, after accounting for other dietary risk factors, high dietary fiber intake was not associated with a reduced risk of colorectal cancer but a diet high in dietary fiber from whole plant foods can be advised because this has been related to lower risks of other chronic conditions such as heart disease and diabetes.

CONCLUSION

Our current acquaintance points to the idea that diet contains multiple biologically active compounds and nutrients and non-nutritive compounds that can affect gene expression and have different bioavailability profiles and can be converted into isomers and metabolites of different potency, which lead to complex beneficial interactions including cancer prevention. The knowledge we have gained of the carcinogenesis process and the role of dietary constituents on the effects of tumorigenesis processes, it is now a widely accepted concept that cancer is mostly a preventable disease. A new concept for diet and cancer prevention, research and strategy must be developed to include the nutrition modulation of the carcinogenesis pathway by nutrients, micronutrients and phytochemicals. This pathway includes nutrition modulation of DNA damage and repair mechanisms; DNA methylation pathways influencing gene expression and cellular phenotypes; antioxidant rearranging and oxidative stress modulation; target receptors and signaling pathways; cell cycle controls and check points; and antiangiogenic properties.

With new DNA chip technology and functional proteomics, complex nutrient-gene interactions can now be investigated.

Research on nutrient-gene interactions not only provides pathophysiologic mechanisms of cancer causation and prevention, but also improves the ability to conduct the cancer surveillance that is crucial in identifying at-risk populations. By combining chemoprevention approaches using single nutrients with multiple dietary constituents and functional foods, the scope of the future cancer prevention strategies will be broadened. Research on eating behaviour and changing dietary patterns as well as psychobiological approaches must be included in any cancer prevention strategy. New frameworks are to be developed logically, using multidisciplinary approaches that include lifestyle and environmental changes, dietary modifications and physical activity to reduce the burden of cancer for the general population as well as high risk individuals (Vay, *et al*. 2001, Michael, 2004 and Thorogood, *et al*. 2007).

CANCER-SPECIFIC RECOMMENDATIONS

The main recommendations (WHO, 2003) for reducing the risk of developing cancer are as follows:

1. Maintain weight (among adults) such that BMI is in the range of 18.5— 24.9 kg/m2 and avoid weight gain (>5 kg) during adult life (WHO, 2000).
2. Maintain regular physical activity. The primary goal should be to perform physical activity on most days of the week; 60 minutes per day of moderate-intensity activity, such as walking, may be needed to maintain healthy body weight in otherwise sedentary people. More vigorous activity, such as fast walking, may give some additional benefits for cancer prevention (IARC, 2002).
3. Consumption of alcoholic beverages is not recommended: if consumed, do not exceed two units1 per day.
4. Chinese-style fermented salted fish should only be consumed in moderation, especially during childhood. Overall consumption of salt preserved foods and salt should be moderate.
5. Minimize exposure to aflatoxin in foods.
6. Have a diet, which includes at least 400 g per day of total fruits and vegetables.
7. Those that are not vegetarian are advised to moderate consumption of preserved meat (e.g. sausages, salami, bacon, ham).
8. Do not consume foods or drinks when they are at a very hot (scalding hot) temperature.

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