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Probiotics: A New Popular Option for Cancer Inhibition*

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Abstract: Cancer is an important global public health problem. Cancer incidence and mortality have been steadily rising throughout the last century in most areas of the world. Recent epidemiological evidences support to protective effects of probiotic bacteria against to colorectal cancer. While numerous of healthful effects have been attributed to the probiotic lactic acid bacteria; perhaps the most suspicious remains that of anticancer effects. In recent years, there have been many studies using animal models, which have clearly demonstrated a protective effect of dietary supplements of lactic acid bacteria against colon tumour development. This study gives a short overview on the present state of recent knowledge of the effects of the probiotic bacteria on the colon cancer development.

Key words: Colon cancer, functional food, health, health-promoting bacteria

Introduction

Cancer is a disease where abnormal cells divide without control and form a lump (called a tumour) as their numbers increase. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic systems to other parts of the body. Cancer is an important global public health problem. Cancer incidence and mortality have been steadily rising throughout the last century in most areas of the world. One in every three men and one in every four women will be directly affected by cancer before the age of 75. Cancer occurs more commonly in males than females and the risk of cancer increases with age (Young and Leu, 2002). Colon cancer is the fourth most common cause of cancer-related mortality in the world (Gill and Rowland, 2003).

It is the aim of the food industry to continually offer innovative new products which satisfy the consumer needs. Functional foods containing probiotic microorganisms with scientifically supported health claims for improving ones state of well-being and helping reduce the risk of diseases already constitute a growing market (Vaughan and Mollet, 1999). Probiotic foods and supplements continue to gain in popularity with a worldwide market worth around US 6 billion a year (Hoesl and Altwein, 2005). Probiotics are usually defined as microbial food supplements with beneficial effects on the consumer. Most probiotics fall into the group of organisms known as lactic acid bacteria and are normally consumed in the form of yoghurt or fermented milks, although capsules of freeze dried organisms are on the market (Rowland, 1999). Probiotics are the subject of much current research. A possible role of dietary supplements of lactic acid bacteria in the prevention of cancer has received special attention.

Several studies have used colonic precancerous lesions, termed aberant crypt foci, as an index of cancer risk. These are focal lesions found in the colons of carcinogen-treated animals. The distribution of the aberrant crypts mirrors that of tumours (Gallaher and Kill, 1999). A number of studies in animal

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models demonstrate that consumption of probiotic bacteria can reduce the development of aberant crypts or colon cancer risk (Kulkarni and Reddy, 1994; Gallaher *et al*., 1996; Arimochi *et al*., 1997; Challa *et al*., 1997). Recent researches demonstrated that different lactobacillus strains have a protective effect against to heterocyclic amine-induced DNA damage in colon and liver of rats. Oral administration to rats of strains of Lactobacillus and Bifidobacterium has been shown to inhibit DNA damage induced by heterocyclic aromatic amines (HCAs) in the colon mucosa (Zsivkovits *et al*., 2003).

Arimochi *et al*. (1997) reported that the metabolites of *Lactobacillus acidophilus* inhibits the aberrant crypt foci formation in rats treated with azoxymethane and that the inhibitory effect of *L. acidophilus* is due to the enhanced removal O^6-meG from the colon mucosal DNA. Rowland *et al*. (1998) showed that consumption of *Bifidobacterium longum* or inulin was associated with potentially beneficial changes in caecal physiology and bacterial metabolic activity in relation to carcinogen-induced tumour risk and in the incidence of putative preneoplastic lesions in the colon. More recently, Balansky *et al*. (1999) reported the protective effect of a milk product fermented by two *Lactobacillus bulgaricus* strains towards the tumorogenic activity of 1, 2-dimethylhydrazine in rats and diethylnitrosamine in the Syrian golden hamster. The authors concluded that some fermented milk products might exert a significant chemoprevention of cancer in humans. In the most recent work by Haza *et al*. (2004), they reported that *Lactobacillus plantarum* showed a protective effect against three N-nitrosamines. In this research, the highest protective effect was observed at populations of 10^7 cfu mL^{-1}.

Different types of probiotic preparations showed antitumour activities. Some glycoproteins isolated from *B. infantis* and Lactobacillus cultures have antitumour activities (Sekine *et al*., 1995; Manjunath and Ranganathan, 1989). In the most recent work, You *et al*. (2004) reported that whole cells or cytoplasm extracts of *Bifidobacterium bifidum* BGN4, isolated from human feces, inhibited the growth of several cancer lines. They extracted a novel polysaccharide fraction (BB-pol) from *B. bifidum*. According to their observations, BB-pol inhibits the growth of colon cancer cell lines *in vitro*.

Matsumoto and Benno (2004) investigated the effects of consumption of *Bifidobacterium lactis* LKM12 containing yoghurt (100 g/days) on fecal probiotic metabolites (polyamines, lactate and acetate) and mutagenicity in seven healthy adults. Interestingly, results of the study was suggested that increased gut spermidine level by *B. lactis* containing yoghurt was responsible for the reduction of mutagenicity in the gut of healthy adults. The authors was also suggested that spermidine produced by probiotic yoghurt consumption contributes to host health as a bioantimutagenic factor. Another study by Oberreuter-Moschner *et al*. (2004) reported that consumption by healthy volunteers of 300 g/day of yoghurt containing probiotic strains can modify the genotoxicity of faecal samples, in comparison with a non-probiotic yoghurt. This study clearly indicate that probiotic consumption may have a beneficial effect on events related to colon cancer in human subjects.

Consumption of probiotics may lower risk of colon cancer directly by reducing procarcinogenic substances such as ammonia and secondary bile acids or indirectly by reducing the level of enzymes such as β-glucuronidase, nitroreductase, choloylglycine hydrolase and azoreductase that convert procarcinogens to carcinogens in the intestine (Ling *et al*., 1994; Jain, 1998; Roos and Katan, 2000). Several researches showed an effect of consumption of probiotics on these enzymes activities, which are measured in feces (Ling *et al*., 1994; Ross and Katan, 2000). Ingestion of viable probiotics is associated with anticarcinogenic effecs, one mechanism of which is the detoxification of genotoxins in the gut. This mechanism was shown experimentally in animals with use of the rat colon carcinogen 1,2-dimethylhydrazine and by determining endpoints that range from tumorigenesis to induction of DNA damage. Because of the complexity of the cancer initiation, cancer progression and the exposure of cancer in the gut, many types of interactions may be envisaged (Wollowski *et al*., 1999; Wollowski *et al*., 2001).

As apparently, there have been many studies using animal models, which have clearly demonstrated a protective effect of dietary supplements of lactic acid bacteria against colon tumour development. However, the precise mechanisms are presently unknown (Wollowski *et al*., 2001;

Hirayama and Rafter, 2000; Lee and Lee, 2000; Yamazaki *et al*., 2000). Some possible mechanisms can explain below (Zsivkovits *et al*., 2003; Matsumoto and Benno, 2004; Wollowski *et al*., 2001; Hirayama and Rafter, 2000; Orrhage *et al*., 1994; Hirayama and Rafter, 1999; Knasmuller *et al*., 2001; Rafter, 2002).

- Alteration of the metabolic activities of intestinal flora
- Alteration of physico-chemical conditions in the colon
- Decreasing of DNA damage in colon cells (antigenotoxicity)
- Binding and degrading potential carcinogens such as heterocyclic aromatic amines
- Production of antitumourigenic or antimutagenic compounds
- Enhancing the host's immune response
- Increasing in gut spermidine level
- Effects on physiology of the host

From *in vitro* and *in vivo* data it is now evident, that different strains have diverse characteristics. Thus, further research should be aimed at the selection of *in vitro* and *in vivo* assessed, target and function of specific probiotics. Rowland (Rowlan, 2004) indicate that well-defined mechanisms need for targeted probiotics that can be evaluated for activity in human intervention trials. We think that administration of deliberately selected probiotic microorganisms could become a viable alternative option for preventing cancer.

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