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Critical Review on Probiotics and its Effect on Cancer

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ABSTRACT

Probiotics are defined as live microbial food ingredients that produce several beneficial effects to human health . The effects of probiotics may be classified in three modes of action. (i) Probiotics might be able to modulate the host's defenses. (ii) Probiotics can also have a direct effect on other microorganisms, commensal and/or pathogenic ones. (iii) Finally, probiotic effects may be based on actions affecting microbial products like toxins, host products e.g. bile salts and food ingredients. All three modes of probiotic action are in all likelihood involved in infection defense, prevention of cancer and in stabilizing or reconstituting the physiological balance between the intestinal microbiota and its host. Numerous bacteria in and on its external parts protect the human body from harmful threats. Several animal studies have shown that supplementation with specific strains of lactic acid bacteria (probiotics) could prevent the establishment, growth, and metastasis of transplantable and chemically induced tumors. An inverse relationship between the consumption of fermented dairy products, containing lactobacilli or bifidobacteria (are the main probiotic groups) Pediococcus, Lactococcus, Bacillus, Shirota, Caseii, Lactis, Rhamnosus, Plantarum and yeasts and the incidence of colon, gastric cancer and breast cancer has also been reported in epidemiological and population based case-control studies. The effectiveness in the treatment of cancers is based on the restoration of the sensitivity of transformed cells to apoptotic signals. The anticancer activity through induction of apoptosis of cancer cells seems to be promising approach for use of some probiotic strains as a support therapy or disease prevention. A wealth of data implicates that special receptors have essential roles in tumor development. A wealth of evidence emerging from laboratory studies indicates anticancer activity of probiotics.

Keywords: Probiotic, Anticancer Effect, Bifidbacterium, *Lactobacillus*, Receptor

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One hundred years ago, we ate beneficial bacteria all the time but pasteurization, sterilization and irradiation of food have ended much of that. The concept of probiotics evolved at the turn of the twentieth century from a hypothesis first proposed by Nobel Prize-winning Russian scientist Elie Metchnikoff, who propounded that the long and healthy life of Bulgarian people resulted from their consumption of fermented milk products (1). Probiotic food can be defined as "food containing live microorganisms believed to actively enhance health by improving the balance of microflora in the gut". A number of health benefits have been claimed for probiotic bacteria such as Lactobacillus acidophilus, Bifidobacterium spp., and Lactobacillus casei. Because of the potential health benefits, these organisms are increasingly incorporated into dairy foods (2).

Molecular study

Increasingly, the microbiological scientific community is relying on molecular biology to define the complexity of the gut flora and to distinguish one organism from the next. Current techniques,

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Figure 1. The most commonly used species of lactic acid bacteria in probiotic preparations (3).

Lactobacillus sp.	*Bifidobacterium* sp.	*Enterococcus* sp.	*Streptococcus* sp.
L. acidophilus	*B. bifidum*	*Ent. faecalis*	*S. cremoris*
L. casei	*B. adolescentis*	*Ent. faecium*	*S. salivarius*
L. delbrueckii ssp. (*bulgaricus*)	*B. animalis*		*S. diacetylactis*
L. cellobiosus	*B. infantis*		*S. intermedius*
L. curvatus	*B. thermophilum*		
L. fermentum	*B. longum*		
L. lactis			
L. plantarum			
L. reuteri			
L. brevis			

including genetic fingerprinting, gene sequencing, oligonucleotide probes and specific primer selection, discriminate closely related bacteria with varying degrees of success. Additional molecular methods being employed to determine the constituents of complex microbiota in this area of research are community analysis, denaturing gradient gel electrophoresis (DGGE)/temperature gradient gel electrophoresis (TGGE), fluorescent in situ hybridisation (FISH) and probe grids (4).

Cancer

Cancer is a serious global public health problem. There are several epidemiological evidences that support a protective role of probiotics against cancer. A wealth of data implicates that ErbB receptors have essential roles in tumor development. Probiotic bacteria are known to exert an anticancer activity in animal studies(5).

Lactic acid bacteria and their probioactive cellular substances exert many beneficial effects in the gastrointestinal tract, and also release various enzymes into the intestinal lumen and exert potential synergistic (LAB) effects on digestion and alleviate symptoms of intestinal malabsorption (6). A carcinogen is any substance, radionuclide, or radiation that is an agent directly involved in causing cancer. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes.

Colon Cancer

Colon cancer is the second to third most frequent type of cancer in Western industrialized countries. fiber diet, are of greater interest because they represent controllable risk factors. Within the complex gut microflora, which consists of >1 1011

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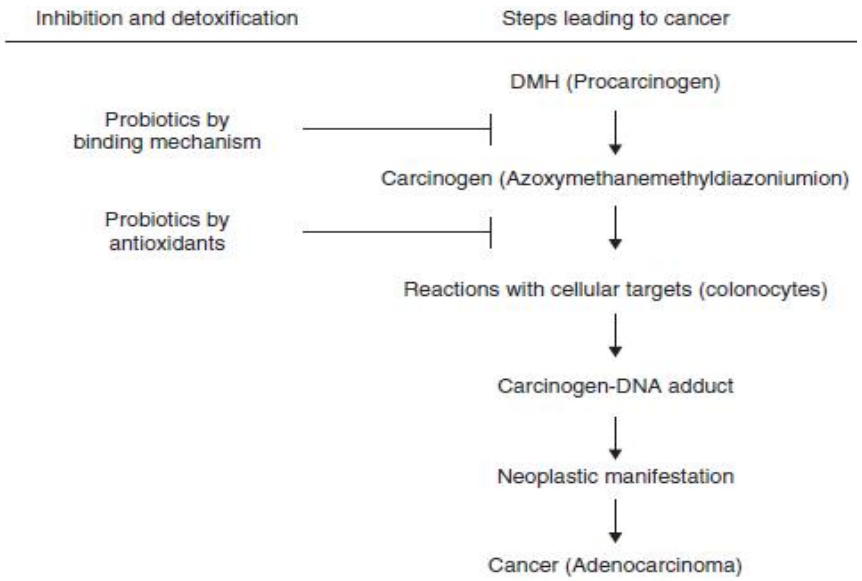
living bacteria/g colon content, LAB belong to those bacteria with such beneficial effects (7) investigated for possible use as probiotics and for colon cancer biological products. Five of these strains inhibited growth of eight food-borne pathogens including Helicobacter pylori, Escherichia coli and Salmonella typhimurium (8).

Figure 2. Mechanism of action of probiotics during colon cancer progression (6)



Several mechanisms have been proposed as to how LAB may inhibit colon cancer, including enhancing the host's immune response, altering the metabolic activity of the intestinal microbiota, binding and degrading carcinogens, producing antimutagenic compounds, and altering the physiochemical conditions in the colon (6) It appears that LAB can reduce the levels of colon enzymes that convert pro-carcinogens to carcinogens. Specifically, LAB can reduce levels of the enzymes β-glucuronides, nitro-reductase, and azo-reductase (Kampmanet al. 1994). Most animal and human studies do indicate that feeding certain LAB decreases fecal enzyme levels that may be involved in formation of carcinogens. Also, beneficial effects can be attributed to immune-potentiating effects by LAB strains. One specific effect was shown by heat-killed Lactobacillus plantarum L-137, which restored the inhibited IL-12 production in DBA/2 mice with tumors (9). The anti -tumor effects were found to be due to the activation of macrophage by LC9018 (10).

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Breast Cancer

Results of cross-cultural and regional correlation studies have shown that breast cancer mortality correlates positively with the consumption of milk products (11). Milk fermented by B. infant is, B. bifidum, B. animalis, L. acidophilus and L. paracasei inhibited the growth of the MCF7 breast cancer cell line, and the antiproliferative effect was not related to the presence of bacteria (12). Isoflavones are a class of phytoestrogens plant-derived compounds with estrogenic activity. Soybeans and soy products are the richest sources of isoflavones in the human diet (13) Soy phytoestrogens were suggested to reduce the risk of a number of diseases including breast cancer. Given that these compounds are metabolized by bacteria, alteration of intestinal bacteria and enzymes may affect phytoestrogen metabolism (14). Observational studies suggest that dietary isoflavones reduce breast cancer risk, and this may be caused in part by effects on endogenous hormone concentrations. Because intestinal bacteria metabolize isoflavones, it was hypothesized that consumption of probiotic bacteria would enhance the biologic effects of isoflavones, including effects on endogenous hormones (15).

Bladder Cancers

Few human clinical trials conducted, one showed that L. casei consumption (three times per day for 1 year) increased the recurrence free period among subjects with bladder cancer (16).

Daily intake of a viable L. casei strain postponed recurrence of bladder tumors in a randomized, controlled, multicenter study in 48 Japanese patients. Patients were enrolled within 2 week after removal of one or more bladder tumors (17). One hypothesis for the prevention or delay of tumor development by lactobacilli is that they might bind to mutagenic compounds in the intestine (18).

Liver cancer: Liver cancer is the sixth most commonly diagnosed cancer in the world, and the third most common cause of death from cancer, according to Cancer Research UK (19).

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Probiotics have also been shown to attenuate hepatotoxic effects of aflatoxin, a well known liver carcinogen, in rats (20) and to reduce biomarkers of liver cancer risk in a human intervention trial (20). probiotic bacteria could block the intestinal absorption of aflatoxin B1 and thereby lead to reduced urinary excretion of aflatoxin B1-N7-guanine (AFB-N7-guanine), a marker for a biologically effective dose of aflatoxin exposure. Elevated urinary excretion of this aflatoxin-DNA adduct is associated with an increased risk of liver cancer (19).

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Conclusion

The probiotic theory offers an intriguing approach to controlling negative metabolic or pathogenic activities of microbes to which we are exposed on a daily basis. results suggest that consumption of a high amount of fermented milk products may have a protective effect on the risk of cancer (3).