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REVIEW ARTICLE

THE APPLICATION OF PROBIOTICS IN DECREASE CANCER

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ABSTRACT

Cancer is one of the most important deaths causing in the world and many factors as chemicals, rays, viruses and genetic factors may influence it. Probiotics, live cells with different beneficiary characteristics, have been extensivelly studied and explored commercially in many different products in the world. A number of *Lactobacillus* species, *Bifidobacterium* spp., *Saccharomyces boulardii,* and some other microbes have been proposed as and are used as probiotic strains, i.e. Probiotic bacteria are used to treat or prevent a broad range of human diseases. They can decrease gut infection, colon cancer, cholesterol level, also they stimulate immune system. The aim of this review is to consider the current evidence on the effects of probiotics on human health and decrease cancer.

KEY WORDS: probiotics, intestinal microflora, *Bifidobacterium*, *Lactobacillus*, Cancer, Human Health

INTRODUCTION:

Probiotic is a relatively new word meaning 'for life', which is used to name microorganisms that are associated with the benefical effects for humans and animals. These microorganisms contribute to intestinal microbial balance and play a role in maintaining health [1]. The term probiotics was first coined by Lilly and Stillwell in 1965 in reference to substances produced by protozoa, which stimulated the growth of other organisms [2, 3]. A probiotic organism should be nonpathogenic and non-toxic, and also resistant to low pH and to bile salts to improve its chances of survival in the gastrointestinal tract. Probiotics have been used to treat a wide range of diseases, ailments, and conditions that affect humans and animals [4]. *Lactobacillus* and *Bifidobacterium* spp., which are normal inhabitants of the healthy intestine, are common species of probiotics. The major consumption of probiotics by humans is in the form of dairy-based foods containing intestinal species of *Lactobacilli* and *Bifidobacteria* [5]. In the scientific literature, populations of 10^6-10^7 CFU/g in the final product are established as therapeutic quantities of probiotic cultures in processed foods [6]. Interest in probiotics has been spurred by the growing abundance of modern disorders such as neoplasms, atherosclerosis, cardiac diseases, hypertension and HIV infection. Probiotic consumption is reported to exert a myriad of beneficial effects including: enhanced immune response, balancing of colonic microbiota, vaccine adjuvant effects, reduction of fecal enzymes implicated in cancer initiation, treatment of diarrhea associated with travel and antibiotic therapy, control of rotavirus and *Clostridium difficile*-induced colitis and prevention of ulcers related to *Helicobacter pylori* [7, 8]. Cancer is one of the most important deaths causing in the world. Cancer can take over 200 distinct forms, including lung, prostate, breast, ovarian, hematologic, skin, and colon cancer and leukemia, and both environmental factors (tobacco smoke, alcohol, radiation, and chemicals) and genetic factors (inherited mutations and autoimmune dysfunction) are associated with an increased risk of developing cancer. Bacterial and viral infections are also strongly associated with some types of cancer (stomach cancers and cervical cancer, respectively). The metabolic activities of the gut microflora can have wide ranging implications for the health of the host, resulting in both beneficial and detrimental effects [9].

LACTIC ACID BACTERIA:

Lactic Acid Bacteria are gram-positive, non-sporeforming cocci, coccobacilli or rods with a DNA base composition of less than 35mol% G+C. They ferment glucose primarily to lactic acid, or to lactic acid, CO_2 and ethanol. All LAB grow anaerobically, but unlike most anaerobes, they grow in the presence of O_2 as aerotolerant anaerobes. Although many genera of bacteria produce lactic acid as a primary or secondary end-product of fermentation, the term LAB is conventionally reserved for genera in the order *Lactobacillales*, which includes *Lactobacillus, Leuconostoc, Pediococcus, Lactococcus* and *Streptococcus,* in addition to *Carnobacterium, Enterococcus, Oenococcus, Tetragenococcus, Vagococcus,* and *Weisella. Other genera are: Aerococcus,*

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Microbacterium, Propionibacterium and Bifidobacterium. LAB are among the most important groups of microorganisms used in food fermentations [10, 11, 12]. The selection criteria for probiotic LAB include: human origin, safety, viability/activity in delivery vehicles, resistance to acid and bile, adherence to gut epithelial tissue ability to colonise the gastro intestinal tract, production of antimicrobial substances, ability to stimulate a host immune response and the ability to influence metabolic activities such as vitamin production, cholesterol assimulation and lactose activity [13]. The genus Lactobacillus belongs to the Phylum Firmicutes, Class Bacilli, Order Lactobacillales, Family Lactobacillaceae and its closest relatives, being grouped within the same Family, are the genera Paralactobacillus and Pediococcus. Some Lactobacillus cultures used as probiotic are *Lactobacillus acidophilus, L. casei, L. delbrueckii, L. plantarum, L. rhamnosus*. The genus Bifidobacterium, even if traditionally listed among LAB, is only poorly phylogenetically related to genuine LAB: it belongs to the Phylum Actinobacteria, Class Actinobacteria, Order Bifidobacteriales, Family Bifidobacteriaceae, its neighbor genera being Aeriscardovia, Gardnerella, Parascardovia, and Scardovia. The genus includes, at present, 30 species [14]. Bifidobacteria are normal inhabitants of the human and animal gastrointestinal tract and is not surprising to find them in mouth and feces. The intestinal tracts of newborns are colonized with Bifidobacterium within days after birth and the population is influenced by age, diet, antibiotics, and stress. The optimum pH for the growth of Bifidobacteria is 6–7 and virtually no growth at below of 4.5 or above of 8.5. The optimum temperatures of growth are 37–41°C, the minimum are 25–28°C, and the maximum are 43–45°C. Some Bifidobacterium cultures used as probiotic are *B. adolescentis*, *B. longum*, *B. infantis*, *B. bifidum* and *B. breve* [10].

PROBIOTICS AND ANTIMUTAGENIC AND ANTICARCINOGENIC PROPERTIES:

Cancers in many organs almost are developed because of genetic mutation. Any action for removing, inhibiting and inactivating of mutagen substances is valuable. Many researchers suggested that use of Probiotics decrease the risk of cancer. Colon cancer inhibition by yoghurt containing live microorganisms was studied in an experimental model using BALB/c mice [15]. Hosono *et al*, were the first to report that milk fermented with *L. delbrueckii* subsp*. bulgaricus*, *Lactococcus lactis* subsp*. lactis* or *Enterococcus faecalis* exhibited an antimutagenic activity against NQO [16]. Matar et al, reported different roles and functions of biologically active peptides released from fermented milks. Peptide fractions liberated during milk fermentation with *Lactobacillus helveticus* R389 stimulated the immune system and inhibited the growth of an immunodependent fibrosarcoma in a mouse model [17]. Gonet-Surowka et al, suggested that only some species of lactobacilli were probiotic and that both live and heat-killed forms had strongly activated pan-caspases, resulting in colon cancer cell apoptosis. The action mode of both probiotic strains in our finding might trigger a mechanism in colon cancer cells, resulting in cell apoptosis [18]. Chalova *et al*, evaluated the ability of some probiotic bacterial supernatants to decrease the effects of two mutagenic substances benzo[a]pyrene and sodium azide in different growth phases and *Bifidobacterium adolecenti* ATCC 15703 had 48.7% inhibitory in Log phase duration, *L. plantarum* ATCC 8014 showed 59.37% inhibitory function on mutagenic substance benzo[a]pyrene and *L. plantarum* ATCC8014 had 54.64% inhibitory on mutagenic substance sodium azide in lag phase duration [19]. Pei-Ren *et al*, evaluated the ability of Several Probiotic Bifidobacteria against Benzo[a]pyrene and Cells of *Bifidobacterium lactis* Bb-12 and *B. longum* CCRC 14634 showed higher antimutagenic activities than their supernatants [20]. Lankaputhra and Shah, proved that *Lactobacillus* spp*.* has good activity in decreasing mutagenic substances [21]. Park and Rhee showed that, *L. plantarum* KLAB 21 was isolated from Kimchi can inhibit four mutagenic and carcinogenic agents effects; Aflatoxin B1, NQO, MNNG and NPD. He used two salmonella strains TA100 and TA98. Results showed that the bacterial culture supernatant inhibited mutagenic effects of MNNG (98.4%) in presence of TA100 and NQO (57.3%) in presence of TA98 [22]. Mechanisms of probiotics in decrease cancer: 1. Binding of Carcinogens. There are a large number of reports describing the adsorption or binding in vitro by LAB and other intestinal bacteria, of a variety of food-borne carcinogens including the heterocyclic amines formed during cooking of meat, the fungal toxin Aflatoxin B1, benzo(a)pyrene. In several of these studies, a concomitant decrease in mutagenicity was reported 2. Effects on Bacterial Enzymes. The ability of the colonic microflora to generate a wide variety of mutagens, carcinogens and tumour promoters from dietary and endogenously-produced precursors is well. For example, the enzyme ß-glucuronidase is involved in the release in the colon, from their conjugated form, of a number of dietary carcinogens, including polycyclic aromatic hydrocarbons. Species of Bifidobacterium and Lactobacillus, have low activities of these enzymes involved in carcinogen formation and metabolism by comparison to other major anaerobes in the gut such as bacteroides, eubacteria and clostridia. This suggests that increasing the proportion of LAB in the gut could modify, beneficially, the levels of xenobiotic

metabolising enzymes [23]. 3. Production of anti-tumorigenic or antimutagenic compounds. Lactic acid bacteria or a soluble compound produced by the bacteria may interact directly with tumour cells in culture and inhibit their growth. Lactic acid bacteria significantly reduced the growth and viability of the human colon cancer cell line HT-29 in culture, with a significant increase in dipeptidyl peptidase IV and brush border enzymes, suggesting that these cells might have entered a differentiation process. Milk fermented by *B. infantis*, *B. bifidum*, *B. animalis*, *L. acidophilus* and *L. paracasei* inhibited the growth of the MCF7 breast cancer cell line, the antiproliferative effect not being related to the presence of bacteria. These findings suggest the presence of an ex novo soluble compound produced by lactic acid bacteria during milk fermentation or the microbial transformation of some milk components in a biologically active form [24]. 4. Enhancement of the host's immune response. One explanation for tumour suppression by lactic acid bacteria may be that it is mediated via an immune response in the host. Sekine et al, suggested that *B. infantis* stimulates the host- mediated response, leading to tumour suppression or regression. In addition, there are studies to suggest that lactic acid bacteria play an important role and function in the host's immunoprotective system by increasing specific and non-specific mechanisms to exert an anti-tumour effect [24, 25].

CONCLUSION:

There is some evidence from animal and in vitro studies that yogurt, other fermented milks, and probiotics can reduce cancer risk; however, human studies to date provide little support for such a reduction in risk. Probiotic bacteria as gastrointestinal flora cause to decrease absorption of mutagenic and carcinogenic substance. At presence, with increasing of the antibiotic resistance and side effects of chemical drugs, it seems, we need to use alternative remedies.

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