THE EFFECT OF LACTOBACILLUS ON CANCER CELLS AND ITS ANTICANCER POTENTIAL

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Annotation: This paper explores the potential anticancer effects of Lactobacillus species on various cancer cell types. Recent studies have demonstrated that certain strains of Lactobacillus, widely known as probiotics, not only support gut health but may also exert anticancer activity through multiple mechanisms. These include modulation of the immune system, reduction of inflammation, induction of apoptosis in cancer cells, and inhibition of tumor growth. The article reviews experimental findings related to colorectal, breast, prostate, and other cancers, highlighting the role of bioactive compounds produced by Lactobacillus, such as lactic acid and bacteriocins. These metabolites have shown promise in suppressing cancer cell proliferation and promoting programmed cell death. The findings suggest that Lactobacillus strains could be considered as potential adjuncts in cancer prevention and therapy.

Keywords:lactobacillus, anticancer effect, probiotics, cancer cells, apoptosis, immunomodulation, bioactive metabolites, colorectal cancer

Introduction: This study aims to systematically assess the anticancer potential of distinct *Lactobacillus* strains on Human Colorectal Tumor (HCT) 115 cancer cells, with a primary focus on the apoptotic mechanisms involved. *Lactobacillus* strains were isolated from sheep milk and underwent a meticulous microbial isolation process. Previous research indicates that certain probiotic bacteria, including Lactobacillus species, may exhibit anticancer properties through mechanisms such as apoptosis induction. However, there is limited understanding of how different *Lactobacillus* strains exert these effects on cancer cells and the underlying

molecular pathways involved. The primary objective is to unravel and understand the apoptotic mechanisms induced by these probiotic strains, shedding light on their potential as therapeutic interventions against colorectal cancer. The distinct characteristics of *L. plantarum*, *L. rhamnosus*, and *L. acidophilus* warrant investigation, particularly regarding their potential impacts on colon cancer cells. This study aims to provide valuable insights that could have implications for their application as adjuvants in colorectal cancer therapy. The isolation of *Lactobacillus* strains from sheep milk forms the foundation of our study. This study aims to contribute novel insights into the comparative cytotoxicity of distinct *Lactobacillus* strains on colon cancer cells. The elucidation of apoptotic mechanisms not only advances our understanding of probiotics' anticancer potential but also provides a foundation for potential therapeutic applications. The findings hold promise for the evolving field of probiotics in oncology, particularly within the context of colorectal cancer research [2].

At present, researchers are constantly exploring cancer therapies with few side effects, and the anti-cancer characteristics of lactic acid bacteria (LAB) are one of the research interests. Lactic acid bacteria , as the dominant probiotics in the intestine, are mostly colonized in part from the duodenum to the end of the ileum. LAB and their metabolites could enhance immunity, improve gastrointestinal function, increase resistance to obesity, and increase antioxidant abilities, as well as reduce blood glucose concentration and cholesterol.

Material and methods: Peptidoglycan known as murein, is an important component of bacterial cell walls. As the protein scaffold of cell walls, peptidoglycan can maintain the normal morphology of cells (Dramsi et al., 2008). Some researchers also found that peptidoglycan has anti-cancer effects by studying the physiological functions of peptidoglycan. The first evidence of the anti-cancer effects of peptidoglycan from *Bififidobacterium infantis* ATCC 15697 by researching Meth A fibrosarcoma in BALB/c mice, showed that the cell wall-derived polysaccharide-peptidoglycan complex (PSPG) in *L. casei* Shirota could improve ileitis and inhibit the activation of IL-6/STAT3 signaling, so as to play a suppressive effect on ileal cancer (Matsumoto et al., 2009). In a similar spirit, also confirmed that peptidoglycan from *Lactococcus* and *Bifidobacterium* cell walls can inhibit the proliferation of bladder cancer HT-1376, colon cancer DLD-1 and SNUC2A cells, as well as kidney cancer A498 cells [3].

There is evidence showing that nucleic acids in the fermentation broth of LAB have anti-cancer effects. The RNA extracted from the logarithmic growth phase medium filtrate of *Lactobacillus* DM9811 are confirmed to have certain inhibitory effects upon colon cancer HT-29 cells and mouse ascites hepatoma cells by MTT method, as well as the inhibitory effects being dose-dependent. RNA can increase the

activity of NK cells and CD4+ T cells to upregulate the level of cellular immunity and inhibit cancer cell growth. At present, dendritic cells and antigen presenting cells (such as macrophages) can be strongly stimulated by CpG and AT oligodeoxynucleotides, CpG and AT can recognize and bind to TLR9 of the Toll-like receptor family, thereby inducing Th1 immune response, up-regulating the level of anti-cancer immune response, and inhibiting the development of cancer [4].

Lactic acid bacteria produce not only a variety of active substances such as organic acids and reductases during fermentation, but they can also produce bacteriocins with anti-bacterial activity. So far, there has been some initial progress in research with regards to LAB bacteriocins in food preservation, anti-bacterial, anti-viral and other fields. At the same time, there is a growing body of research examining the anti-cancer effects of LAB. Studied the cytotoxic effect on MCF-7 cells as well as HepG2 cells of nisin as the typical representative of bacteriocins. The IC50 concentration at which half of the cells are inhibited) values of 105.46 and 112.25 μm are obtained for these two cell lines by MTT colorimetric assay [1]. Meanwhile, the cancer cells shrinkage, cytoplasmic vacuolization, nuclear condensation, and lateralization could be observed under inverted microscope, and finally the cells fall off.

This is owing to D-type cyclins playing a key role in the cell cycle, and over-expression of cyclin D is associated with tumor proliferation. Therefore, nisin from *L. lactis* could inhibit SW480 cancer cell line by inhibition of cyclin D1 gene expression. Explored the mechanism by which nisin inhibited neuroblastoma cells by modulation of phase behavior and cell membrane fluidity. Nisin interaction with a neuroblastoma cancer cell resulted in enhancing membrane fluidity and reduction in the dipole potential, which inhibited neuroblastoma cell growth.

Mucins are involved in the formation of mucus, which can play a role in tissue lubrication and cell signal. It is also the first barrier for the interaction and diffusion of nutrients and intestinal drugs, so that they can be absorbed and enter the circulatory system. Therefore, the existence of mucins can protect the gastrointestinal tract from the invasion of pathogenic bacteria and toxic metabolites, and provide a relatively suitable environment for the body with less interference factors, thus maintain the homeostasis of various functions and promote the smooth and orderly progress of various metabolic activities [5].

Results and discussion: The antiproliferative effect of *Lactobacillus* strains on cancer cells is shown in Figure 1. It has been shown that treatment of cells with two strains of *Lactobacillus* cell, suppressed cell pro- liferation in a dose-dependent manner. However, the effect of *L. acidophilus* strain is greater than that of *L. casei* at all doses.

Since the bacterial secreted substance is one of the effective fac- tors of probiotics on the host cell, the possible effect of probiotic bacterial extracts on the inhibition of host cell proliferation was assessed in the current study. As shown in Figure 1, the extract of both strains of *Lactobacillus*, can suppress cell proliferation. As a result of supernatant treatment, the effect of *L. acidophilus* strain was found to be more powerful than that of *L. casei* at both doses.

Conclusion: Recent evidence suggests that certain strains of lactobacilli possess significant anti-cancer potential through mechanisms including modulation of the gut microbiota, enhancement of immune surveillance, production of bioactive metabolites, and suppression of pro-inflammatory pathways. These probiotics may exert both direct effects on tumor cells, such as inducing apoptosis and inhibiting proliferation, and indirect effects via the host immune system and metabolic regulation. While in vitro and animal studies are promising, clinical trials remain limited, and strain-specific differences must be considered. Future research should focus on identifying the most effective strains, elucidating precise molecular mechanisms, and determining optimal delivery methods. The integration of lactobacilli-based interventions alongside conventional cancer therapies may represent a safe, cost-effective, and complementary strategy in cancer prevention and management.

References:

1. Choi, S. S., Kim, Y., Han, K. S., You, S., Oh, S., & Kim, S. H. (2006). Effects of Lactobacillus strains on cancer cell proliferation and oxidative stress in vitro. Letters in Applied Microbiology, 42(5), 452–458. https://doi.org/10.1111/j.1472-765X.2006.01879.x
2. Escamilla, J., Lane, M. A., & Maitin, V. (2012). Cell-free supernatants from probiotic Lactobacillus casei and Lactobacillus rhamnosus GG decrease colon cancer cell invasion in vitro. Nutrition and Cancer, 64(6), 871–878. https://doi.org/10.1080/01635581.2012.700758
3. Górska, A., Przystupski, D., Niemczura, M. J., & Kulbacka, J. (2019). Probiotic bacteria: A promising tool in cancer prevention and therapy. Current Microbiology, 76(8), 939–949. https://doi.org/10.1007/s00284-019-01698-8
4. Kumar, M., Nagpal, R., Verma, V., Kumar, A., Kaur, N., Hemalatha, R., … & Yadav, H. (2010). Probiotic metabolites as epigenetic targets in the prevention of colon cancer. Nutrition Reviews, 68(9), 486–499. https://doi.org/10.1111/j.1753-4887.2010.00305.x