

Potential anticarcinogenic effects of Probiotics on human Colo-rectal cancer cells

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Abstract

Colorectal cancer (CRC) is one of the most common cancers globally, associated with high morbidity and mortality rates. Although advances in medical treatments such as surgery, chemotherapy, and radiation have improved survival rates, new approaches to prevention and therapy are crucial for managing CRC. Recent studies have suggested that probiotics, live microorganisms that provide health benefits when administered in adequate amounts, may possess anticarcinogenic properties that could be harnessed for CRC prevention and treatment. This review explores the potential anticarcinogenic effects of probiotics on human colorectal cancer cells, focusing on mechanisms, preclinical and clinical findings, and the challenges and prospects for future research.

Introduction

Colorectal cancer (CRC) is a leading cause of cancer-related deaths worldwide, with a growing incidence in both developed and developing countries. The pathogenesis of CRC is complex and involves a combination of genetic, environmental, and lifestyle factors (Hossain et al., 2022). Although traditional treatments such as surgery, chemotherapy, and radiation have significantly improved survival rates, prevention remains the most effective strategy in reducing the burden of CRC. Recent studies suggest that probiotics, which are live microorganisms, may play a pivotal role in cancer prevention, including CRC (McCabe, 2022).

Probiotics, when consumed in adequate amounts, can promote beneficial effects on the host's health by modulating the gut microbiota, strengthening the intestinal barrier, enhancing immune function, and producing bioactive compounds with potential anticancer properties (Wong , 2006). This review delves into the current literature on the potential anticarcinogenic effects of probiotics on human colorectal cancer cells, investigating their mechanisms, experimental evidence, and implications for future therapies.

The Gut Microbiota and Colorectal Cancer

The human gastrointestinal tract hosts a complex and diverse microbial ecosystem, which plays a significant role in maintaining health and modulating disease processes. An imbalance in the gut microbiota, known as dysbiosis, has been implicated in the development of CRC. Dysbiosis can lead to inflammation, increased production of carcinogenic metabolites, and disruption of the intestinal epithelial integrity, all of which contribute to carcinogenesis (Sidhu et al., 2023).

Probiotics are thought to exert their beneficial effects by promoting a healthy gut microbiota. They achieve this by outcompeting harmful bacteria, producing antimicrobial compounds, enhancing the intestinal mucosal barrier, and modulating immune responses. Probiotic bacteria, such as *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces boulardii*, have been shown to influence key pathways involved in colorectal carcinogenesis, including cell proliferation, apoptosis, inflammation, and DNA damage repair. The ability of probiotics to modulate the gut microbiota composition and impact these cellular processes is central to their potential as a preventive and therapeutic tool for CRC (Molska & Regula, 2019).

Mechanisms of Probiotics in Colorectal Cancer Prevention

Several mechanisms have been proposed to explain the potential anticancer effects of probiotics on CRC:

Modulation of the Gut Microbiota

Probiotics can alter the composition of the gut microbiota,

promoting the growth of beneficial bacteria while inhibiting the proliferation of harmful microbes. This balance may reduce the production of pro-carcinogenic metabolites, such as bile acids and nitric oxide, which have been shown to promote colorectal carcinogenesis. By restoring microbial homeostasis, probiotics may contribute to the prevention of CRC.

Reduction of Inflammation

Chronic inflammation is a well-established risk factor for the development of CRC. Probiotics have been shown to exert anti-inflammatory effects by promoting the production of anti-inflammatory cytokines such as interleukin-10 (IL-10) and suppressing the production of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6). Probiotic-mediated modulation of the immune system can reduce gut inflammation, thereby lowering the risk of CRC development.

Strengthening the Intestinal Barrier

The integrity of the intestinal epithelial barrier is crucial for preventing the translocation of harmful microorganisms and inflammatory mediators into the bloodstream. Probiotics have been shown to enhance the function of tight junctions between intestinal epithelial cells, reducing intestinal permeability (leaky gut). This strengthens the barrier against pathogenic bacteria and toxins that could otherwise promote cancerous transformations in the colorectal epithelium.

Modulation of Cell Proliferation and Apoptosis

Probiotics have been found to influence the balance between cell proliferation and apoptosis, key processes in the development of cancer. In human CRC cell lines, probiotics such as *Lactobacillus* and *Bifidobacterium* have been shown to inhibit the proliferation of cancer cells and induce apoptosis. Probiotics may exert these effects by modulating various signaling pathways, including the Wnt/ β -catenin pathway, which is frequently dysregulated in CRC.

Furthermore, some probiotics have been shown to enhance the expression of tumor suppressor genes, such as p53, and

inhibit the activity of oncogenes, such as c-Myc, which further contribute to the regulation of cell cycle and apoptosis.

Production of Bioactive Compounds

Certain probiotic strains can produce bioactive compounds such as short-chain fatty acids (SCFAs), particularly butyrate, which have demonstrated anticarcinogenic properties. SCFAs play an important role in maintaining gut health by promoting apoptosis in cancer cells, inhibiting histone deacetylases, and modulating immune responses. Butyrate, in particular, has been found to reduce the proliferation of CRC cells and promote apoptosis in preclinical models. Other metabolites, such as bacteriocins and lactic acid, also have antimicrobial and anticancer properties.

Preclinical and Clinical Evidence

Preclinical Evidence

Numerous in vitro and animal studies have investigated the potential anticarcinogenic effects of probiotics on CRC. Studies using human CRC cell lines, such as Caco-2, HT-29, and HCT-116, have demonstrated that probiotics can inhibit cell growth, induce apoptosis, and suppress metastasis. For example, *Lactobacillus rhamnosus* and *Lactobacillus acidophilus* have been shown to reduce the proliferation of CRC cells and modulate key signaling pathways involved in cell survival and apoptosis (Ahn et al., 2015).

Animal studies have also provided strong evidence for the protective effects of probiotics against CRC. In a mouse model of colorectal carcinogenesis induced by chemical carcinogens such as azoxymethane (AOM), the administration of *Lactobacillus* species significantly reduced tumor formation and colonic inflammation (Zhou et al., 2016). These findings suggest that probiotics may have a protective role in CRC development by modulating inflammatory pathways and reducing tumor burden.

Clinical Evidence

The clinical evidence for the anticarcinogenic effects of probiotics in humans remains limited, though a number of

studies have reported promising results. Clinical trials have primarily focused on the use of probiotics to prevent colorectal adenoma recurrence, a precursor to CRC. A randomized controlled trial involving patients with a history of colorectal adenomas found that daily supplementation with *Lactobacillus* and *Bifidobacterium* species led to a reduction in adenoma recurrence compared to placebo (Gonzalez et al., 2016). Additionally, some studies have observed beneficial effects of probiotics in reducing CRC-associated inflammation, improving gut microbiota composition, and enhancing immune responses.

However, while these studies suggest a potential role for probiotics in CRC prevention, larger and more robust clinical trials are needed to confirm their efficacy and safety in human populations.

Challenges and Future Directions

Despite the promising preclinical data and early clinical findings, there are several challenges in translating the anticarcinogenic effects of probiotics into clinical practice:

- **Strain-Specific Effects:** The effects of probiotics are strain-specific, meaning that different strains may have varying effects on CRC prevention and treatment. Further research is needed to identify the most effective probiotic strains for CRC prevention and therapy.
- **Lack of Standardization:** There is considerable variability in the formulation, dosage, and administration of probiotics in clinical studies. Standardized protocols are needed to ensure consistency and reproducibility of results.
- **Safety Concerns:** While probiotics are generally considered safe for healthy individuals, their use in immunocompromised patients or those with severe gastrointestinal diseases may require caution.
- **Long-Term Efficacy:** Long-term clinical studies are necessary to evaluate the sustained benefits of probiotics in CRC prevention and treatment.

Future research should focus on conducting large-scale randomized controlled trials to confirm the anticarcinogenic effects of probiotics, elucidating the underlying mechanisms, and identifying the most effective strains and dosages. Additionally, studies on the synergistic effects of probiotics with other preventive strategies, such as diet and chemoprevention, could provide insights into integrated approaches for CRC prevention.

Conclusion

Probiotics represent a promising approach for the prevention and treatment of colorectal cancer. Through mechanisms such as modulation of the gut microbiota, reduction of inflammation, strengthening of the intestinal barrier, and production of bioactive compounds, probiotics have shown potential anticarcinogenic effects in both preclinical and clinical studies. However, further research is needed to optimize their use, determine the most effective probiotic strains, and establish standardized treatment protocols. With continued scientific exploration, probiotics could become an integral part of colorectal cancer prevention and management strategies in the future.

Reference

- Hossain, M. S., Karuniawati, H., Jairoun, A. A., Urbi, Z., Ooi, D. J., John, A., ... & Hadi, M. A. (2022). Colorectal cancer: a review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. *Cancers*, 14(7), 1732.
- McCabe, M. (2022). *Molecular Profiling of Colorectal Cancer within South Africa* (Doctoral dissertation, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg).
- Molska, M., & Reguła, J. (2019). Potential mechanisms of probiotics action in the prevention and treatment of colorectal cancer. *Nutrients*, 11(10), 2453.
- Sidhu, S., Deep, J. S., & Sobti, R. C. (2023). Role of Repair Gene Polymorphism and Hypermethylation of GSTP Gene in the Risk of Prostate Cancer. In *Biomedical Research, Medicine, and Disease* (pp. 231-253). CRC Press.

- Wong, H. L. (2006). *Colorectal cancer: Genomic variations in insulin-like growth factor-1 and-2*. University of Southern California.