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The beneficial role of probiotics in colorectal cancer development and their prospects for application

Kecheng Liu

University of Delaware,26 E MAIN ST, E111ott Hal1. Newark, America, DE 19716

Cosonliu@udel.edu

Abstract. Colorectal cancer (CRC) constitutes a significant global health concern, with its development closely associated with factors like diet, lifestyle, and imbalances in the gut microbiome. Probiotics, defined as beneficial microorganisms, have garnered substantial attention as a potential strategy for preventing and treating colorectal cancer. This paper explores the multifaceted role of probiotics in maintaining gut microbiota balance, regulating metabolites, and influencing the development of colorectal cancer. Probiotics function by competitively inhibiting harmful bacteria, producing cancer-fighting metabolites, such as short-chain fatty acids, and engaging in immunomodulatory mechanisms. While evidence from animal models and preliminary human studies suggests their potential in reducing the risk of colorectal cancer, further research is necessary to ascertain the optimal strains, dosages, and mechanisms in clinical trials. Simultaneously, probiotics are expected to serve as adjuvant therapies to enhance the effectiveness of colorectal cancer treatment. This paper sheds light on the evolving prospects of probiotics in colorectal cancer prevention and treatment, introducing new possibilities in the battle against this malignancy.

Keywords: Colorectal cancer, Probiotics, Gut microbiota, Mechanisms

1. Introduction

Colorectal cancer (CRC) poses a significant global health challenge, with a high prevalence in industrialized nations. Various factors, including dietary and lifestyle changes, contribute to its development. Emerging as a growing concern are imbalances in gut microbiota. Human health is intricately tied to the complex and diverse microbial ecosystem within the gut. In recent years, probiotics have garnered substantial interest as a potential means of preventing and treating colorectal cancer [1].

Probiotics are defined as a category of active microorganisms that confer health benefits to the host. They exert essential regulatory functions within the gut microbiota, influencing the host's metabolism, immune system, and intestinal barrier function through a multitude of mechanisms. Studies suggest that probiotics may play a crucial role in safeguarding against colorectal cancer, as well as other gastrointestinal disorders [2,3].

However, despite the abundant evidence from animal models and human studies supporting probiotic usage, further research is imperative to gain a comprehensive understanding of their mechanisms, optimal strains, and suitable dosages. Furthermore, epidemiological evidence concerning the connection between probiotics and colorectal cancer remains inconclusive. Therefore, it is imperative that human trials are conducted to validate this relationship without delay. This review aims to systematically assess

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the potential role and mechanisms of probiotics in colorectal cancer prevention. This undertaking will critically evaluate existing animal experiments and human research on probiotics to shed light on their efficacy in preventing colorectal cancer and enhancing their clinical application. Special attention will be given to their combined use with prebiotics to bolster their protective effects and broaden their applicability across diverse populations [4,5].

In this review, we explore the potential role of probiotics in preventing the development of colorectal cancer and examine their mechanisms of action. To elucidate the promise of probiotics in preventing and treating colorectal cancer, we will conduct a comprehensive review of existing animal experiments and human research. Moreover, we will explore the potential to enhance the protective effects of prebiotics and probiotics through their combined use.

2. Literature Review

2.1. Functions of Gut Microbiota and Probiotics

The gut microbiota, numbering in the trillions, comprise a diverse community of microorganisms inhabiting the human gastrointestinal tract. This microbial assembly serves a pivotal role in a wide range of physiological processes, orchestrated by bacteria, viruses, fungi, and other microorganisms. Beyond their involvement in food digestion and nutrient absorption, the gut microbiota regulate the immune system, metabolic processes, pathogen resistance, and the production of bioactive substances. Among the constituents of the gut microbiota, probiotics stand out as a category of beneficial microorganisms. Probiotics, when consumed in sufficient quantities, generate advantageous physiological effects [3]. They are commonly present in dairy products, fermented foods, and dietary supplements. Probiotics contribute to improved microbial community balance and not only uphold the integrity of the intestinal mucosa but also oversee immune regulation, microbial growth inhibition, food digestion promotion, and the generation of beneficial metabolic byproducts, such as short-chain fatty acids[6].

When probiotics are introduced, they exert several mechanisms that influence the gut microbiota. First, they competitively colonize ecological niches in the gut, limiting the growth opportunities for harmful microorganisms and thus preserving a healthy microbial equilibrium[7]. Second, probiotics contribute to the synthesis of short-chain fatty acids (SCFAs), which foster intestinal mucosal health, mitigate inflammation, and supply energy to the intestinal epithelium. Moreover, probiotics enhance the host's immune function, fortifying its ability to combat infections and diseases. Consequently, probiotics play a substantial role in supporting gut health, bolstering intestinal well-being, and maintaining microbiota balance [8].

2.2. Research Progress in the Prevention and Treatment of CRC

Colorectal cancer (CRC) is anticipated to give rise to approximately 1.9 million new cases in 2020, rendering it a paramount global public health concern. In most instances of CRC, the adenoma-carcinoma sequence unfolds gradually. Recent research underscores the pivotal role of the gut microbiota in the development of CRC, emphasizing the importance of early identification of microbiota alterations for disease detection and prevention. Various bacteria have been associated with CRC, including Streptococcus gallolyticus, Clostridium species, and Porphyromonas species. These microorganisms contribute to CRC by producing genotoxins, inciting inflammation, and influencing host cell signaling. Large-scale studies in Japan have uncovered distinctive microbiota characteristics linked to various stages of CRC. For example, Streptococcus gallolyticus exhibits a progressive increase from early adenomas to advanced-stage CRC, while other bacteria display diverse trends in abundance across different disease stages [9,10]..

Furthermore, metabolomic analysis has pinpointed biomarkers for early CRC lesions, such as elevated levels of bile acids and specific amino acids like deoxycholic acid. These microbiota and metabolite changes hold promise for the early detection of CRC, and dietary interventions that impact the microbiota provide potential avenues for CRC prevention [11].

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In summary, an in-depth exploration of the CRC microbiota unveils stage-specific biomarkers, offering insights into novel diagnostic, preventive, and treatment strategies. Research on gut microbiota not only advances our comprehension of CRC mechanisms but also opens up new prospects for enhancing CRC prevention and treatment through strategies like dietary modifications, prebiotics, probiotics, selective antibiotics, and fecal microbiota transplantation. Nonetheless, additional clinical research is imperative to ascertain the most effective microbiota modulation strategies.

3. The Mechanism and Therapeutic Prospects of Anti-Tumor (CRC) Effects of Probiotics

3.1. Probiotics Regulate the Microbiome and Influence Metabolites in CRC Development

Probiotics, acknowledged as live microorganisms that bestow health benefits when consumed in adequate quantities, wield a multifaceted influence on the gut microbiome, metabolites, and the development of colorectal cancer (CRC). They function by promoting equilibrium within the gut microbial community, suppressing the proliferation of harmful bacteria, and nurturing beneficial counterparts. This microbial balance is of paramount significance, given the established correlation between microbiome dysbiosis and the onset of CRC.

Furthermore, probiotics impact the metabolites generated in the gut environment. They work to diminish the presence of deleterious metabolites, often produced by bacteria with carcinogenic potential. Simultaneously, probiotics bolster the production of beneficial metabolites, such as short-chain fatty acids (SCFAs), renowned for their cancer-preventive properties [12]. This dual role in microbiome regulation and metabolite modulation underpins their potential in CRC prevention. Probiotics contribute to creating an intestinal milieu that promotes a healthier microbial balance while curtailing the presence of metabolites associated with carcinogenesis. In summary, probiotics emerge as influential actors in the realm of CRC prevention, orchestrating a balanced gut microbiome, inhibiting the growth of harmful bacteria, modifying metabolite profiles, and cultivating an environment within the colon that deters carcinogenesis.

3.2. Antioxidant, Anti-inflammatory, and Immunomodulatory Effects of Probiotics

Probiotics have exhibited significant potential in utilizing their antioxidant, anti-inflammatory, and immunomodulatory mechanisms to enhance intestinal health. Numerous studies have consistently unveiled promising results across various contexts, providing clinical evidence for their efficacy. Probiotics play a pivotal role in regulating intestinal inflammation by fostering a balanced immune response and mitigating oxidative stress. Their capacity to modulate cell signaling, particularly by promoting anti-inflammatory cytokines and inhibiting proinflammatory mediators, underscores their profound anti-inflammatory effects. Furthermore, research indicates that probiotics bolster immune responses by stimulating the production of immunoglobulin A (IgA) antibodies, enhancing pathogen clearance, and fortifying the integrity of the epithelial barrier[13]. Clinical investigations have yielded positive outcomes, demonstrating that probiotics can ameliorate symptoms and biomarkers in inflammatory conditions, such as irritable bowel disease, celiac disease, and obesity. While further exploration is warranted to fully comprehend the mechanisms underlying these effects, probiotics are considered promising candidates in the domain of immunomodulation and inflammation management. Their potential role in the prevention and treatment of colorectal cancer (CRC) is particularly intriguing, as they could form integral components of future strategies aimed at reducing CRC incidence and enhancing therapeutic interventions [13,14].

3.3. Effects of Probiotics on CRC in Animal Models and Clinical Trials

Probiotics have demonstrated substantial potential in enhancing intestinal health through their antioxidant, anti-inflammatory, and immunomodulatory mechanisms in animal models. Numerous studies have provided clinical evidence showcasing encouraging outcomes in diverse settings. Probiotics play a central role in regulating intestinal inflammation by promoting a balanced immune response and mitigating oxidative stress. Their capacity to modulate cell signaling, especially by

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promoting anti-inflammatory cytokines and inhibiting proinflammatory mediators, highlights their profound anti-inflammatory effects. Additionally, probiotics have been reported to bolster immune responses by stimulating the production of immunoglobulin A (IgA) antibodies, enhancing pathogen clearance, and fortifying the integrity of the epithelial barrier. Clinical investigations have revealed positive results, demonstrating that probiotics can alleviate symptoms and biomarkers in inflammatory conditions such as irritable bowel disease, celiac disease, and obesity. Although further research is necessary to elucidate the mechanisms underlying these effects, probiotics are regarded as promising contenders in the field of immunomodulation and inflammation management. Their potential role in the prevention and treatment of colorectal cancer (CRC) is particularly captivating, as they could constitute integral components of future strategies geared towards reducing CRC incidence and refining therapeutic interventions [7,15].

4. Conclusion

In summary, the expanding body of research underscores the significant promise of probiotics in the context of colorectal cancer (CRC) prevention and treatment. CRC represents a global health concern, with lifestyle factors, including diet and microbiota composition, implicated in its pathogenesis.

Probiotics offer multifaceted mechanisms through which they impact CRC development. Their potential influence encompasses the regulation of the gut microbiome, modulation of metabolites, anti-genotoxic effects, fortification of the immune system, and enhancement of epithelial barrier function. Probiotics exhibit strain-specific actions, with lactobacilli and bifidobacteria emerging as prominent candidates for CRC prevention. While human clinical evidence is still evolving, initial studies suggest that probiotics can reduce CRC risk biomarkers, further confirming their potential application in the comprehensive strategy against CRC. Moreover, probiotics may hold promise as adjuncts to optimize CRC treatment outcomes, particularly by affecting chemotherapy metabolism and enhancing immunotherapy efficacy.

However, while the landscape of probiotics in CRC prevention and treatment appears promising, further research is essential to elucidate optimal strains, dosages, and precise mechanisms. These findings emphasize the potential of probiotics as integral components of treatment aimed at reducing CRC incidence and improving therapeutic interventions, heralding a new frontier in the fight against this prevalent and challenging malignancy.

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