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Role Of Live Microorganisms In Colon Cancer- A Review On Probiotic Effect

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Abstract

The gut microflora plays important role in maintaining homeostasis in the human body. An unwanted disturbance in the gut microbiome can lead to pro-inflammatory immune responses and the initiation of disease processes, including cancer. Literature has recently highlighted the enormous scientific interest on the relationship between the gut microbiota and colon cancer, and how the use of some selected probiotics can have a future impact on the adverse events which occur during this disease. Studies prove that some strains of probiotics can be used for by modulating intestinal microbiota and immune response and can be an alternative healthy way to prevent for cancer or/and as adjuvant treatment during anticancer chemotherapy. This review presents the latest advances in research into the effectiveness of probiotics in the prevention and treatment support of cancer. The described issues concern to the anticancer activity of probiotic microorganisms and their metabolites. In addition, we described the potential mechanisms of probiotic, how they can contribute in cancer prevention. The aim of this review was to summarize the knowledge about the effect of probiotic microorganisms in well-balanced way to prevent colon cancer and the adverse effects caused by related therapies.

Keywords: gut microflora, colon cancer, probiotics, anticancer activity, effect, worldwide

INTRODUCTION

Probiotics are live microorganisms which if ingested in adequate amount can cause benefit to the host. Studies on the use of probiotics as an alternative therapy to prevent and cure human disease is in practice now a days globally. A variety of mechanisms have been identified that is followed by probiotic bacteria which include enhancement of immune system, immunomodulation, regulation of gut microflora, production of anticancer compound etc. (Marta Molska et al. 2019). As in recent days Cancer is a devastating disease that affects millions of people worldwide and there have been significant advances in cancer treatment, such as chemotherapy and radiation therapy. But these treatments can make the cancer patients immunocompromised or they may have other adverse side effects. As a result, there has been growing interest in using probiotics as an alternative or a

parallel therapy for cancer.In this review we will discuss the potential mechanisms by which probiotics may prevent or treat cancer, as well as the evidence from animal and human studies. Finally, we will discuss the potential clinical applications of probiotics in cancer treatment specifically on colon cancer (Wang Z et al. 2022).

METHODOLOGY

In PubMed, PubMed Central, Google Scholar, frontier, NCBI the published research works on probiotics and its effect of cancer specially in colorectal cases in the form of original studies and review article from around the world were searched for bringing out the proper information in this review article. only published data was taken into account, and ambiguous description of exposure were ruled out. the inclusion criteria include information gathered from reliable sources of publication on the subject. languages other than English were excluded from the study.

DISCUSSION

Probiotics in Practice:

FAO (Food and agricultural organisation) and WHO (world health organisation) have developed a joint guideline on probiotics, which can be used as a global standard to evaluate probiotics in food –

1. Strain definition
2. Functional characterisation of strain(s) for safety and probiotic properties.
3. Conformation of health benefits in human studies.
4. Honest, non-misleading efficacy claims and ingredientlabelling for the entire shelf life.

Keeping these standards in mind most of the globally used probiotics belongs to genus *Lactobacillus* and *Bifidobacteria.* Some of the *Streptococcus* strains and *Saccharomyces* are also used as probiotics.

The Mechanism of Action of Probiotics on Cancer:

The probiotics can maintain the gut health and support a healthy immune system by both the specific and non-specific physiological effects:

1. **Modulating the gut microbiome**: Probiotics can alter the composition of the gut microbiome, which has been linked to the development of cancer (S. Singh et al. 2022).
2. **Enhancing the immune system and immunomodulation**: Probiotics have been shown to stimulate the immune system by activating immune cells such as natural killer cells, macrophages, and dendritic cells, which can recognize and destroy cancer cells. (Wierzbicka et al. 2021; Cervantes-Barragan et al 2017)
3. **Modifying metabolic activities of intestinal microbiota:**

LAB produce hydrogen peroxide and bacteriocins (Rountree 2002). It can also cause cell lysis and interfering or inhibiting the synthesis of DNA, RNA and proteins (act as DNAase or RNAase) (Nazir et al. 2018). Some of the bacteriocins produced by probiotics e.g., bifidocin B produced by *Bifidobacterium bifidum,* is from *Lactococcus lactis* and lactacin B from *Lactobacillus acidophilus.*

4. **Producing anti-cancer compounds**: Probiotics can produce compounds such as short-chain fatty acids, which have been shown to have anti-cancer properties. These compounds can inhibit the growth of cancer cells and promote their apoptosis (programmed cell death). (Cervantes-Barragan 2017, Aindelis et al. 2020).
5. **Improvement of the Intestinal Barrier:** Research shows that some probiotics are able to reduce intestinal permeability by modifying the components of the intestinal barrier, such as intracolonic pH, or by the production of mucins and the cellular junction proteins. (Madsen et al. 2012)
6. **Binding and degradation of carcinogenic compounds present in the intestinal lumen:** Probiotic bacteria there are cationic exchange between the carcinogenic compounds and the peptidoglycan layer of the cell walls of some probiotic microorganisms. The carcinogenic compounds get eliminated together with the bacteria through the faeces (Burns et al. 2004)
7. **Influence on Other Mutagenic and Carcinogenic Factors:** Probiotics can increase the expression of GST(Glutathione S-transferase) thus increasing its activity through the action of butyrate, which could change the status of histone acetylation, thus increasing the expression of GST (Verma et al 2017).
8. **Induction of apoptosis:** The apoptosis signalling pathways can be activated by probiotic bacteria such as lactic acid bacteria via a mitochondria-dependent (intrinsic) and a death receptor–dependent, mitochondria-independent (extrinsic) pathway (Zhong et al 2014)

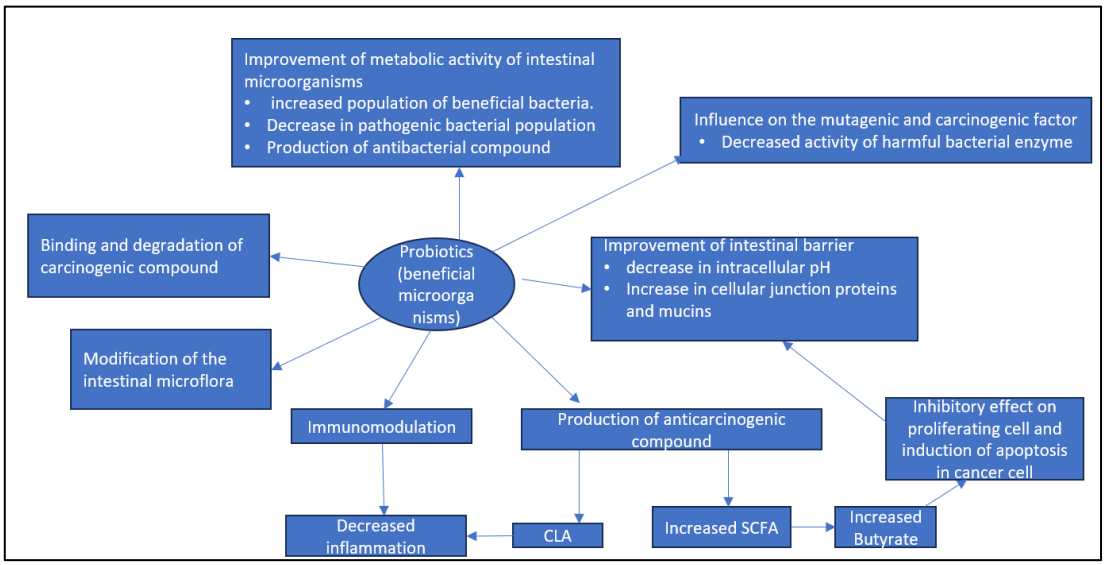

Fig.2 Proposed mechanisms of action of probiotics on cancer

Colorectal cancer and probiotics:

"CANCER TODAY (WHO)" shows that the data collected worldwide implies that colorectal cancer is the third most diagnosed cancer type, almost 10% of the total cancer cases (reported in 2020)and the global number of new CRC cases is predicted to reach 3.2 million by 2040.According to Globocan, 2018 data, incidence of colorectal cancer in India is lower than that in the western countries, and it is the seventh leading cancer in India while in U.S.A Colorectal cancer (CRC) is the second most common cause of cancer death. This is due to consumption of diet with high animal fat, red meat that increases secretion of N-nitroso compounds, which are carcinogenic. As western lifestyle involves red meat as a large part of their diet habits, is one of the major causes of the occurrence of CRC. The regulatory factors that cause CRC, lack of exercise, the diet, and lifestyle. So, to prevent the occurrence of colon cancer it is suggested include a healthy change in lifestyle, include more vegetable and fibre-in diets and switching to functional foods. Probiotics supplementation in patients with CRC enhanced gut microbiota diversity, inhibited pro-inflammatory cytokine production, reduced postoperative infection complications, and improved their quality of life it also reduced the side effects of chemotherapy, decreased the risk of death, shortened the duration of hospital stays, and improved the outcomes of surgery.

Following are some probiotics strains used in treatment of colorectal cancer:

Human studies:

Probiotic Bacteria	Subject	Effects	References
Formula of: 2 mg *Enterococcus faecalis* 10 mg *Bacillus mesentericus* 10 mg*Clostridium butyricum*	156 patients undergoingcolorectal cancer surgery	Taking probiotics for 3-15 days prior to surgery reduce the post operative surgery site infection.	Aisu et al. 2015
Formula of: *Bifidobacteriumlongum*($1*10^7$cfu/gm) *Lactobacillus acidophilas*($1*10^7$cfu/gm) *Enterococcus faecalis*($1*10^7$cfu/gm)	60 patients undergoing colorectal cancer surgery	Perioperative administration of probiotic (5 days before ,7 days after surgery) induce faster bowel function recovery	Yang et al.(2016)

Animal studies:

Probiotic bacteria	Subject	Effects	References
Lactobacillus acidophilas, lactobacillus rhamnosus, Bifidobacterium bifidum	AOM/DSS tumorigenic mice C57BL/6 mice model	Reduced inflammatory index of gut Reduced expression of TNF α Increased expression of IL-10	Maria Carolina S Mendes(1995)
Lactobacillus plantarum	AOM/DSS tumorigenic mice C57BL/6 mice model	Reduced expression of pro inflammatory cytokines Increased expression of IL-10 Elimination of pathogenic bacteria from gut	Fenglian Maet al. (2022)

Studies showing probiotics found in traditional fermented food(global) and their efects against colo-rectal cancer:

FERMENTED FOOD	BACTERIA FOUND	EFFECTIVE ON CANCER TYPE	RSEARCH TYPE	REFERNCES
Kimchi	*Lactobacillus plantarum*DGK 17	Colon cancer	In vitro	Imran Khan et.al (2017)
Fermented cucumber	*Pedicoccuspentosaceus*CRAG 3	Colon cancer	In vitro	Shukla et al. (2013)
Fermented barley	*Lactobacillus plantarum dy-1*	Colon cancer	In vitro	Fang Yao et. Al (2017)
Koumiss	*Lactobacillus helveticus* NS8	Colorectal cancer	In vitro	Ronget.al(2019)

Indian traditional fermneted food and probiotics:

In 2021 researchers from IISER – BHOPAL (a team of scientist under Dr.Vineet Kumar Sharma) conducted a study where they showed that this low occurrence of colorectal cancer in Indian population is their diet which is mostly a plant-based diet rich in complex polysaccharides that support the growth environments for the good gut bacteria i.e the probiotics which probably in turn show an inhibitory effect to the cancer cell growth.

Indian fermented food	Probiotic strains found in them.
Cheese	*Lactococcus sp., Leuconostoc sp., Lactobacillus sp., Entrococcus sp., Debaryomyces sp., Penicillium sp.*
Dosa	*Leuconostoc sp., Enterococcus sp., Candida sp.*
Sauerkraut	*Lactobacillus sp., Leuconostoc sp.*

CONCLUSION

Probiotics have shown promise as a potential therapy for cancer. Animal and human studies have demonstrated that probiotics can modulate the gut microbiome, enhance the immune system, and produce anti-cancer compounds. Although the evidence is still limited, there is growing interest in using probiotics as an adjunct therapy for cancer. Probiotics may be used to prevent the development of cancer in healthy individuals, as well as to prevent the recurrence of cancer in survivors. Probiotics may also be used to reduce the side effects of cancer treatments such as chemotherapy and radiation therapy. However, more research is needed to determine the optimal dose, duration, and strain of probiotics for cancer prevention and treatment. In conclusion, probiotics offer a promising avenue for the prevention and treatment of cancer, and further research in this area is warranted. With the growing interest in natural and alternative therapies for cancer, probiotics may offer a safe and effective option for patients seeking to improve their quality of life and reduce the risk of cancer.

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