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Correspondence

Probiotic as anti-colorectal cancer agents: Challenges and further perspective

Dear Editor;

In recent years, colorectal cancer (CRC) has become one the main diseases associated with gastrointestinal disorders; Epidemiologic studies show that about 9% of fatal cancers are specific to this cancer [1]. According to the literature, several intestinal enzymes of both prokaryotic and eukaryotic sources such as β-glucosidase, β-glucuronidase, nitrate reductase, azoreductase, and 7-α-dehydroxylase have a pivotal role in inducing CRC; by converting aromatic hydrocarbons and amines to potential carcinogenic compounds such as aglycones, phenols, cresols, ammonia, as well as *N*-nitroso compounds (NOC), these enzymes contribute in the development of CRC [2].

According to studies, reactive oxygen species (ROS) are free radicals that play multiple roles in cells, at moderate levels, ROS damage cells and ultimately lead to cancer, while at high levels, they play an anticancer role [3]. Many studies have confirmed that pathogenic bacteria (*Bacteroides fragilis*, *Fusobacterium nucleatum*, *Helicobacter hepaticus*, *Streptococcus bovis,* and enterotoxigenic *Escherichia coli*) and diet containing red meat, high-fat, and low-fiber predispose people to CRC [4]. Most of probiotic bacteria belong to the genera Lactobacillus and Bifidobacterium as the main lactic acid-producing bacteria (LAB) [5].

Interestingly, consumption of certain probiotics can reduce the incidence of CRC; some anti-CRC mechanisms of probiotics contain: competitive colonization, induction of apoptosis, production of short-chain fatty acids, alteration of intestinal microflora enzyme activity, reduction of DNA damage, reduction of deoxycholate, binding heterocyclic amines (a carcinogen and mutagen compound), and anti-inflammatory responses [6,7]. Based on studies, the intervention of probiotics reduces the frequency of some colorectal cancer-associated pathogenic bacteria such as *Fusobacterium* and *Peptostreptococcus* [8]. ESP116 and Nisin are considered as two main anti-colorectal cancer molecules which are secreted by *Lactobacillus plantarum* NCU116 (*L. plantarum* NCU116) and *L. lactis*, respectively [9]. Studies have shown than a combination therapy with probiotics (*L. rhamnosus* GG or *L. acidophilus*) and celecoxib reduces the colorectal cancer cells in animal model by upregulating pro-apoptotic BAX and downregulating anti-apoptotic BCL-2 proteins [10].

In a meta-analysis conducted by Liu et al., they found that probiotic supplementation in patients undergoing colorectal resection is a significant strategy to protect the physical and biological barrier of the gastrointestinal mucosa [11]. Since Radiation-induced diarrhea (RID) occurs (ranging from 20% to 70%) during the third week of treatment, in a study fulfilled by Devaraj et al., they observed a significant improvement in RID patients receiving probiotic therapy using probiotics such as *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* [12]. Capecitabine is a prodrug that enzymatically converted to 5-fluorouracil (5-FU), a drug that inhibits DNA synthesis in tumor cells.

In a prospective study by Ghidini et al., they found that *Lactobacillus kefiri* LKF01 (Kefibios) is a safe and protective probiotic species in the prevention of severe diarrhea (a major side effect in patients with colorectal cancer) in patients receiving 5-FU [13]. In a systematic review of randomized controlled trials (RCTs) conducted by Redman et al., it was concluded that the consumption of probiotics in cancer patients significantly improved diarrhea with CTC grade $\geq$2 as well as CTC grade $\geq$3 [14].

According to a meta-analysis by Wang et al., although probiotics may rarely cause adverse events (AEs), these microorganisms are effect in preventing diarrhea caused during chemoradiotherapy period [15]. Based on examinations on the mouse model by Urbanska et al. and Chen et al., *Lactobacillus acidophilus* and *Saccharomyces boulardii* have an inhibitory role against CRC [16,17]. It seems that one of the most important challenges of probiotic therapy is long-term consumption of probiotics; for example in a trial study by Ishikawa et al. on men and women aged 40–65 years who had at least 2 colorectal tumors removed, they demonstrated that the full preventive role of *L. casei* required consumption of this bacterium for 4 years [18].

In conclusion, the consumption of probiotics can be considered as a useful strategy in the prevention as well as treatment of severe gastrointestinal diseases such as CRC. In the present study, we briefly mentioned the review studies about the benefits of probiotics on CRC. In the studies, Lactobacillus genus was the most widely used probiotic in the prevention or treatment of CRC. As mentioned, long-term probiotic consumption seems to be the main challenge in probiotics administration protocol.

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Declaration of competing interest

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