A Novel *Lactobacillus gasseri* MF1 Strain: Mechanism of Probiotic Actions in the Prevention of Colorectal Cancer

Nannu Shafakatullah*
Department of Bio-Sciences, Mangalore University, Mangalagangothri-574199, Karnataka
*E-mail: shafakhath@yahoo.com

ABSTRACT

The environment harbours beneficial bacteria which can protect human from harmful threats when identified and utilized them accurately. In the present study a probiotic bacterial strain was isolated from marine fish and identified through 16S rRNA sequencing. Results of 16S rRNA sequence disclosed that the organism was related to the *Lactobacillus gasseri* species. The isolate exhibited good probiotic properties. The anti-colorectal cancer properties of the strain on N, N'-Dimethylhydrazine dihydrochloride (DMH) induced mice were investigated. The study discusses and presents findings about the formulation of novel probiotic *Lactobacillus gasseri* MF1 strain for colorectal cancer (CRC) treatment. The mechanisms are based on bacterial activity on CRC induced mice model. The results of this investigation indicated the potential role of probiotic treatment in the overall change of gut microbial actions, their inhibition potentials in colorectal cancer and improve overall gut health.

Keywords: Colorectal cancer, gut health, *Lactobacillus gasseri* MF1, Probiotics.

INTRODUCTION

Colorectal cancer is the most common cancers of the gastrointestinal tract. It is more common in industrialized countries due to their life style and dietary habits than in the developing countries. It is known to be a type of cancer that is preventable by changes in diet and life style. Mounting evidences are supporting the role of gut microbiome in the etiology of CRC and emphasize on the potential of probiotics as bio-therapeutics in the prevention and management of CRC. The probiotic bacteria, their metabolic activities in the intestinal tract have a preventive role on colorectal cancer. The beneficial effects of probiotics are also depending upon the strain and dose intake. *Lactobacilli* were suggested to balance pathogenic and oncogenic microbial community in the colon and produce anti-tumorigenic and anti-inflammatory effects in healthy individuals at risk and CRC patients. There is a requirement to find out potential probiotic bacteria with anti-colorectal cancer properties. DMH has been generally used as a model to study the effect of anti-colorectal cancer agents on physiological and biochemical changes that occur during different stages of carcinogenesis (Rajeshkumar N.V., Kuttan R. 2003; Asha, and Devaraja Gayathri. 2012).

OBJECTIVES

1. To study the protective role of *Lactobacillus gasseri* strain MF1 on DMH induced colorectal cancer in mice.
2. To study the possible mechanism of the action of *Lactobacillus gasseri* strain MF1 and its products on prevention and cure of colorectal cancer.

METHODOLOGY

The animal experiments were conducted based on the guidelines from the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India after permitted by the Institutional Animal Ethics Committee (IAEC) of Mangalore University (MU/AZ/99/2013-14/IAEC). The study was conducted on Twenty-Five male Swiss albino mice (Mus musculus) aged around 6 weeks. Husk

lined polypropylene cages were used to house the experimental animals. The husk was renewed every 24 hours. The animals were fed with standard diet pellets and water ad libitum. They were maintained under 12:12 hours of dark and light cycles. The temperature of the animal house was maintained around 22℃ throughout the experimental period. Mice were injected subcutaneously (s. c) every week with N, N'-Dimethylhydrazine dihydrochloride (DMH) (Sigma-Aldrich, USA) at 20 mg/kg body weight. They were fed with probiotic *Lactobacillus gasseri* strain MF1 at a concentration of $2X10^8$ CFU suspended in milk by gavages twice a week throughout the experiment. The general health status of experimental mice, food intake, body growth and survival study, tumour assessment, histopathology, faecal microbial count, Glutathione-S-transferase (GST), Superoxide dismutase (SOD) and Reduced Glutathione (GSH) activity, β-glucosidase activity and β-glucuronidase activities were analysed following the standard protocols.

RESULTS AND CONCLUSION

Treatment of colorectal cancer induced mice with the probiotic *Lactobacillus gasseri* strain MF1 resulted in significant decrease in the proliferation of cancerous growth. The antioxidant study results showed that there is significant increase ($P < 0.001$) in GST activity, SOD level ($P<0.001$) and GSH concentration ($P<0.001$) in the treatment groups. Mutagens, toxic and carcinogenic compounds of the body will be detoxicated by the action of these enzymes (Benson, A M *et al*. 1979). Bacterial enzyme study results revealed that the faecal β-glucosidase and β-glucuronidase activity significantly ($P<0.001$) reduced compared to positive control groups. Significant ($P<0.001$) reduction in the harmful coliforms in the intestinal tract and significant ($P<0.001$) increase in the *Lactobacillus* count was observed. Specific strains of probiotic bacteria have a potential effect on inhibiting growth of cancer-causing bacteria in the GI tract, they have role in neutralizing free radicals and enzymes involved in cancer formation, and also to destroy the cancer cells and tissues in GI tract. Probiotics and synbiotics provided protective effects on colorectal cancer induced rats (Sivieri *et al*., 2008). The anti-microbial agents secreted by the probiotic bacteria play an important role in eliminating pathogenic bacteria from the GI tract and intern confer anti- carcinogenic effects. Their metabolites also activate host immune system. The scientific findings from this study support that *Lactobacillus gasseri* strain MF1 can act as potent bacteria against colorectal cancer. The isolate has exhibited promising potentiality in eradicating DMH induced tumours in experimental animal models. However, the successful use of this strain will depend upon the clinical trial outcomes. Therefore, this isolate must be subjected to the other advanced tests to prove its potency for therapeutic application. Many *lactobacilli*, such as *L. acidophilus* and *L. casei* have shown to possess anti-cancer properties by halting the multiplication of tumour cells (Lee *et al*., 2004).

REFERENCES

1. Asha, and Devaraja Gayathri. "Synergistic impact of *Lactobacillus fermentum*, *Lactobacillus plantarum* and vincristine on 1,2-dimethylhydrazine-induced colorectal carcinogenesis in mice." *Experimental and therapeutic medicine*. vol. 3,6 (2012): 1049-1054. doi:10.3892/etm.2012.536.
2. Benson, A M *et al*. "Elevation of extrahepatic glutathione S-transferase and epoxide hydratase activities by 2(3)-tert-butyl-4-hydroxyanisole." *Cancer research* vol. 39,8 (1979): 2971-7.
3. Lee, Jung-Woo *et al*. "Immunomodulatory and antitumor effects in vivo by the cytoplasmic fraction of *Lactobacillus casei* and *Bifidobacterium longum*." *Journal of veterinary science* vol. 5,1 (2004): 41-8.
4. Rajeshkumar, N V, and Ramadasan Kuttan. "Modulation of carcinogenic response and antioxidant enzymes of rats administered with 1,2-dimethylhydrazine by Picroliv." *Cancer letters* vol. 191,2 (2003): 137-43. doi:10.1016/s0304-3835(02)00203-3.
5. Sivieri, K., Spinardi-Barbisan, A.L.T., Barbisan, L.F. *et al*. "Probiotic *Enterococcus faecium* CRL 183 inhibit chemically induced colon cancer in male Wistar rats." *European food research and technology* vol. 228(2008): 231–7 https://doi.org/10.1007/s00217-008-0927-6.