

# Probiotics as Human Health Promoters

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## ABSTRACT

Probiotics (Pro-life live entities) provide the health and well being with multitude of beneficial effects on humans and animals (and relief against varied disorders). Probiotics may manage lactose intolerance, elevate immune profile, prevent colorectal cancers, reduce cholesterol and triglyceride profile, lowering blood pressure and inflammatory process. They also prevent osteoporosis, allergic reactions and help suppress *H. pylori* infections and other pathological manifestations.

Microbial metabolites (even in the absence of live entities) may exert (analogous) effects on signal pathways and barrier functions. Such substances are referred as 'Postbiotics' (the plain metabolic byproduct of probiotics, bioactive manifestations in the host). Generally, postbiotics include secondary metabolites such as bacteriocins, organic acids, ethanol, acetaldehyde, reactive oxygen species (ROS). Such metabolites are inhibitory against pathogenic strains of different broad spectrum drug resistant microbial groups (MDR, XDR etc). Postbiotics are safe, apathogenic which may resist hydrolysis by enzymes of mammalian origin. It has been described that micro-RNA profile of human milk may exert the inhibitory effects of probiotics.

Our research group has been investigating the merits of mammalian milk as a viable source of probiotics that secrete bioactive peptides against MDR/biofilm producing strains (ref. *Streptococcus thermophilus* and *Enterococcus faecalis*, a GIT probiont). These peptides are in the range of 10-16KDa molecular mass (sensitive to proteolytic enzymes as well). Genes coding for these peptides are plasmid associated. Mode of action of these peptides is bacteriostatic. Molecular identification of these Probiotic strains is being followed. This, on the whole marks an emphasis on biological operation of novel strains of Probiotic and their applications in medico-clinical areas to improve the human health and wellness.

### Keywords

Probiotics, postbiotics, bioactivity, MDR, biofilm.

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## INTRODUCTION

Probiotics constitute live microorganisms that are laced with medical and health advantages. Human gut is a unique reservoir for such microbes. Despite the fact that microorganisms are frequently considered as destructive "germs", numerous microorganisms enable our body to work legitimately. For instance, microbes that are typically present in our digestive tract (GIT) help in digestion of food, repulse infection causing microorganisms, and

deliver vitamins. Substantial quantities of microorganisms live on and in our bodies. Actually, microorganisms in the human body out number human cells by 10:1. Probiotics play a vital role in digestive tract and maintain healthy balance between normal flora of gut and in turn healthy digestive tract filters out toxins, chemicals, pathogens and waste products <sup>1</sup>. The probiotics help boost immune system. They protect body against pathogens (Fig. 1).

Otherwise, allergic manifestations, autoimmunity processes (e.g. colon ulcer, IBD) and infection based diarrheas, dermatitis and vagino-urinary clinical indications may ensue<sup>2,3</sup>.

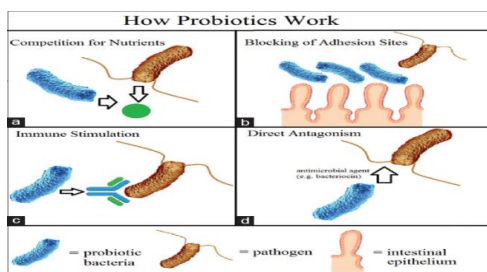


Fig. 1: Mode of action of probiotics.

In 1908 a Russian Noble Laureate, **Ellie Metchnikoff**, revealed the useful effects of probiotics on human wellbeing. He proposed that natives of Bulgaria feel comfortable and enjoy longevity as they consume probiotic processed milk products (courtesy LAB strains). The term probiotic was first coined by **Parker** as microorganisms and metabolites that establish GIT microbiome equilibrium. The updated statement regarding probiotics was referred by **Havenaar** and **Huisint Veld** as live single or consortia of bacterial strains that (after application) do benefit the host by boosting the merited characteristics of resident microbiome (Fig. 2). Some of the common probiotic bacterial genera include *Lactobacillus* (LAB), *Bifidobacterium*, *Enterococcus*, *Streptococcus*, *Bacillus*, *Pediococcus* and *Saccharomyces*<sup>4,5</sup>.

Postbiotics are non-viable, non-toxic and non-pathogenic bacterial secondary metabolites of probiotics which exhibit bioactivity within the host. They constitute bacteriocins, ethanol, hydrogen peroxide, acetaldehyde, diacetyl and organic acids. Researchers have revealed that these metabolic byproducts carry broad spectrum bioactivity against pathogenic microorganisms and hence, may be used as an alternative to antibiotics. Bacteriocins constitute the most appealing research topic of recent era. Antibiotic resistance has led to loss of efficacy of conventional antimicrobials. In that case bacteriocins can be used to target MDR, EDR, XDR strains and biofilm formers. Probiotics possess important aspects that can fulfill our daily nutritional requirements and help our body combat different clinical conditions. A few prominent characteristics regarding probiotics include strategies that

may be applied to encounter cancers, pathogenicity, obesity, allergies and diabetes etc<sup>2,6</sup> (Fig. 3).

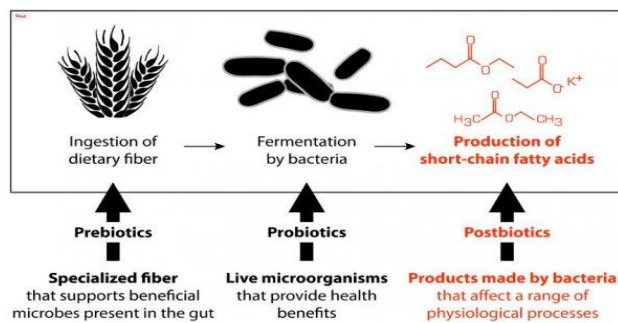


Fig. 2: Beneficial effects of 'biotics'.

### DEFERING THE CANCER ACTIVITY

Cancers are referred as the syndromes that affect people all over the world. Radiotherapy, chemotherapy and surgical interventions are used to treat different kinds of tumors and cancers, but they leave behind the side effects which outnumber the positive aspects. The natural products and sources with anti cancerous activity are of major value in recent era. Probiotics have attracted interest by medical researchers to develop effective drugs with anti-cancerous property and minimal side effects. *L. acidophilus* and *L. rhamnosus* are known for their anti-tumor activity. Moreover, *L. casai* and *L. acidophilus* have also shown anti-cancer property to encounter cancers of colon and rectum in vitro<sup>2,7</sup> (Fig. 3).

### ENCOUNTERING PATHOGENESIS

Apathogenesis is considered as an important function of the biotics. Tejero-Sarinena *et al.* revealed the pathogen inhibition by producing short chain fatty acids e.g. acids of butyrate, propionate, acetate and lactate. They assist in maintaining pH of the gut thereby, creating favorable environment for normal flora to flourish<sup>8</sup>.

Mohseni *et al.* concluded that *Lactobacillus acidophilus*, due to the production of the antimicrobial compounds, effects on bacteria and yeast pathogens of vagina. Obviously, it also helps in prevention and treatment of uro-genital infections<sup>2,9</sup>.

### ANTI-OBESITY ACTIVITY

Obesity or excessive weight gain is a well known side effect of modern life style and unhealthy food intake. It is

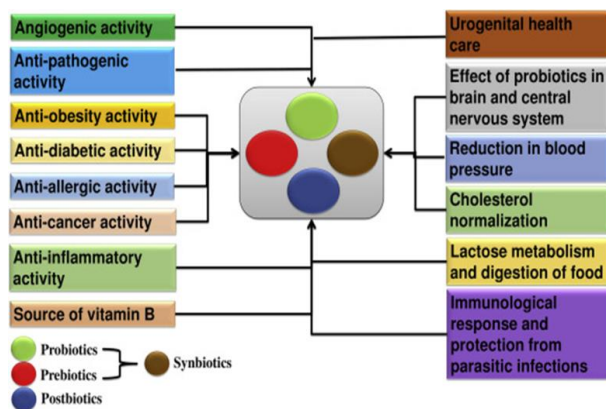
the cause of many other underlying medical conditions like hypertension, hypercholesteremia and diabetes. Probiotics possess physiological functions that facilitate weight loss by lipolytic and thermogenic response by regulating sympathetic nervous system. *L. gasseri* with its metabolites inhibits the enhancement in adipocyte tissues which principally produces leptin and adiponectin. Generally, strains of LAB and bifidobacteria have been recorded for hypocholesteremic state <sup>10</sup>.

**ANTI-INFLAMMATORY ACTIVITY**

Inflammatory chronic disorders like IBS/IBD could be rescued by probiotic–postbiotic supplements. Malfunction of short chain fatty acids may result in IBD onset. SCFAs are involved in regulating homeostasis and also defer allergic reactions <sup>11</sup>. For this purpose, LAB, bifidobacteria and members of family Enterobacteriaceae carry due importance (e.g. *E. coli*) <sup>6</sup>.

**ANTI-DIABETIC ACTIVITY**

Diabetes is a non-communicable chronic condition associated with absence or insufficient production of insulin. There is no definitive cure for this condition and is managed by multiple medications (e.g. the use of synbiotics in curing the diabetic condition). Larsen *et al.* proposed that by increasing the number of probiotics, metabolic diseases like diabetes can be managed. Firmicutes dominate the gut microenvironment. Research shows that patients suffering from metabolic disorders have reduced numbers of these species (Fig. 3). In this aspect, probiotics could help in regulation of gut flora and managing the chronic conditions <sup>12,13</sup>.

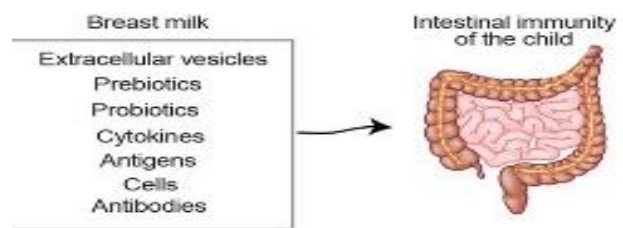


**Fig. 3:** Multiple role of the ‘biotics’.

**ANTAGONISM BY PROBIOTIC LACTIC ACID BACTERIA AND OTHERS**

*Lactobacillus reuterii* produces a small molecular mass metabolite “reuterin” (a class I bacteriocin with broad spectrum bioactivity) <sup>14</sup>. *E. faecalis* also synthesizes a class I bacteriocin against MDR strains. A class II protein antibiotic is produced by *L. plantarum*. *L. lactis* produces “Nisin”, an FDA approved food preservative/additive <sup>15</sup>. Bacteriocins such as lugdunin, streptococcin are also known for manifestation of bioactivity against MDR strains<sup>16</sup>.

Micro-RNAs are in abundance in milk of the mammals. It can mediate the inhibitory effects of probiotics. It helps in boosting the immunity process and gastrointestinal tract of the newborn, also prevents atopic dermatitis by probiotic intake in perinatal period <sup>17,18</sup> (Fig. 4).



**Fig. 4:** Valuable components of human milk.

We have been focusing on the significance of mammalian milk as a rich source of probiotics that possess peptides with bioactive potential against MDR and biofilm producer strains. The isolated producer strains include: *Streptococcus thermophilus* from goat (*Capra aegagrus hircus*) milk and *Enterococcus faecalis* (a gut probiont). These secondary metabolites are peptides (10KDa streptococcin and enterococcin of 16KDa. mass). Genes that code for these bioactive peptides are plasmid borne. Mode of action is bacteriostatic. Experiments on the molecular identification of these probiotic strains are underway. These studies are in accordance with the emphasis on natural activities of novel strains of probiotics and their application in the field of biomedico-clinical sciences for enhancing the human wellbeing <sup>5,6</sup>.

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