



Ayurvedic Approach to Describe Probiotics and Their Therapeutic Implication for Cancer Therapy

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ABSTRACT

Ayurveda is one of the oldest medicinal system originated in India, and it has mentioned the crucial role of food in not only maintaining wellness but also for curing various disorders. Afterward many known personalities highlighted this notion, and modern science and technology justified it via discovering various factors influencing the impact. Recently, the researchers introduced the term functional food, which was initially regarded as the diet rich in components like calcium, and vitamins because of their well-known health promoting qualities, but now refers majorly to probiotics. These probiotics are the microbes, which promotes the health of an individual, inhaling them. Probiotics shows a direct impact on microbes inhabiting inside our gut, known as gut microbiota. Gut microbiota is responsible for proper functioning of several physiological processes. Hence, the enhancement in growth of good microbes in our gut via consumption of probiotics rich diet or supplements can eventually cure numerous disorders. There are various proofs with super quality, scientific trials that probiotics implementation can cure different kinds of diarrheal diseases; can alter the immune function, and other chronic gastrointestinal inflammatory disorders. Not only these disorders but also can cure several types of cancer as well. Hence, the potential of probiotics to eliminate or cure cancer holds a firm interest.

Keywords- Ayurveda, Probiotics, Indian diet, Therapeutic implication, Action mechanism, Cancer therapy.

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INTRODUCTION

The assumption of "food as medicine" has been around for millennia. In traditional cultures such as Native American, Indian, African, Chinese, Japanese, and various other food and medicine are firmly interlocked.

Ayurveda or the science of life is a conventional long established Indian System of Medicine, which has been in execution for more than 3000 years[1]. Ayurvedic treatments are ample, personalized and include diet, exercise and way of life prescriptions concurrently with drugs. According to Ayurveda "health" is recognized as not the mere non-appearance of disease but a condition of absolute homeostasis between the three humors (*doshas*), seven tissues (*dhatu*), three types of waste matter (*mala*), digestion and metabolism, satisfying senses, mind, and soul. This time-tested life science emphasizes the importance of the right kind of food for the formation and sustenance of body. Caraka, says that the human body is the result of food and humans acquires health and disease as the ultimate outcome of wholesomeness (complete/proper) and unwholesomeness (incomplete/improper) of the diet. An anuvakya in Caraka Samhita summarizes the importance given to *pathya* (suitable or special diet recommended during unhealthiness), "with accomplishment of proper diet, medicines are fruitless and with proper diet medicines are uninvited". Not only Ayurveda but other outstanding icons also recognized the importance of food as medicine and marked it. Thousands of years ago, Greek philosopher and Father of Medicine, Hippocrates, recognized that food influences a person's health, body, and mind to thwart illness and keep up wellness. He once mentioned "let food be thy medicine and let Medicine be thy food".

The cardinal role of diet is to serve enough nutrients to meet metabolic requirements while satisfying the hunger and maintaining well-being. However, recent studies reflect that food may be responsible for the regulation of various biological functioning and play a calamitous or favorable role against several diseases. Lately, the notion of “functional food” is getting enormous attention, which mainly claims to be efficaciously functionally (e.g. obviate the oxidative stress; antioxidants) and curtailment in disease rate. These functional foods can contain probiotics or prebiotics and some functional food should be a part of an individual’s life since growing years.

Initially, our studies focused on the lethal microorganisms found associated with the human body, whilst in recent years studies have explored the beneficial impact of inhabitant microbes in the human gut microbiome. The host and gut microbiota have co-evolved together for thousands of years and shows the symbiotic relationship. Gut microbiota contributes to prevention against infection, differentiation of host immune system, production of the certain nutrients (e.g. vitamins, short-chain fatty acid, and other low molecular weight molecules), and various other beneficiary effects. Several factors contribute to the foundation of gut microbiota during infancy and the configuration of an individual’s gut microbiota varies from childhood to adulthood[2]. Diet is one of the major factors that shape the gut microbiota across the lifespan. Hence, the introduction of functional food was resonating. Initially, functional foods were rich in the components like calcium, vitamins due to their know contribution towards good health. Latterly attentions relocated toward the components that can directly influence the gut composition, and this draws the enormous concentration towards probiotics and prebiotics.

Probiotics: History and definition

An attractive surveillance convey that the systematized ayurvedic text, written 2000 years ago describes the Wholesome (*pathya*) and unwholesome (*apathya*) diet (food and drinks) for a disease or disorder at the end of the chapter dealing with that particular illness. *Pathya* include milk, milk products (buttermilk, curd, whey, cottage cheese, butter, ghee), old red rice, horse gram, turmeric, bitter gourd, barley, cardamom, clove, ginger, pepper, pomegranate, lemon, Indian gooseberry, honey, meats of animals and birds such as deer and pigeon etc. Metaphysical philosophy of *Ayurveda* explains a corporeal component/process called "*agni*", is accountable for assimilation of food components and metabolism of tissues. Particular fermented milk products were pinpoint to normalize "*agni*" (metabolism). Comprehensive effects and manipulation of fermented mil products with their respective precautions have been reported in traditional Ayurvedic literature.

The emergence of the science of modern probiotics lean back in year 1908 when Elie Metchinkoff reported that the long life of Bulgarian peasants is the outcome of the consumption of fermented milk. He later introduced sour milk in his diet, fermented by "*Bulgarian bacillus*" later named as "*Lactobacillus delbrueckii subsp.*" and observed the positive impact of it on his health. Later Lilly and Stillwell, coined the term "probiotic" meaning "for life" in year 1965.

Probiotics are basically the feasible microorganisms that after digestion have an advantageous effect in the prohibition and cure of specific clinical conditions[3]. The FAO/WHO defines probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host". The prominent strains consists of *Lactobacillus*, *Streptococcus*, and *Bifidobacterium* with other organisms such as enterococci and yeasts[4].

Since the efficiency of specific probiotics cannot be determined by any single strain[5]. Hence accurate strain identification is of utmost importance. For species identification 16S rRNA gene sequence analysis and DNA-DNA hybridization techniques can be conducted. In addition, Strain identification can be performed by various reproducible molecular methods (e.g. pulsed-field gel electrophoresis and randomly amplified polymorphic DNA) or using idiosyncratic phenotypic traits (involves the determining the presence of extrachromosomal genetic elements, range of the sugar undergoing fermentation, and detection of final fermentation products obtained from glucose utilization) . The beneficiary impact will be visible in the *in-vivo* studies only, still, the *in-vitro* mode can be used in order to understand the action mechanism, safety determination, and for conveying the other awareness regarding the individual strain[6]. Benchmarks for any microbe to be regarded as probiotics are;1. Ability to withstand low pH and encounter bile while passing through the GI tract, 2. Gluing to intestinal epithelial cells, 3. The steadiness of intestinal microflora, 4. Non-pathogenicity, 5.Endurance in foodstuffs and likelihood for production of pharmacopeia lyophilized preparations, 6.Rapid multiplication, with either persistent or non-persistent colonization of the gastrointestinal tract, 7.Generic specificity of probiotics[7–9].

THERAPEUTIC IMPLICATION OF PROBIOTICS FOR CANCER

Cancer is a lethal disorder, which act as a mainstream for enormous illness and death rates [10]. According to a survey, cancer is the second cause of mortality globally contributing to approximately 9.6 million deaths, in 2018[11]. The cancer rate has been increasing enormously in several region of globes

especially in developing countries, with 18.1 million new cases of 2018 and 29.4 million in 2040 [12]. One of the common type of cancer for men is prostate cancer with others such as tracheal, bronchus, and lung cancer. For women, the most common cancer was breast cancer. Scarcity of DNA repair or mutation during replication leads to cancer. Hazardous environmental elements (infectious agents, poisonous substances and UV radiation), lifestyle as well as genetic makeup of an individual plays a crucial role as a risk factor for cancer [13,14].

Currently the clinical administration of standard drugs plays a major role in a treatment for cancer. However, the persistent use of these drugs as well as synthetic agents in terms of safety and strength for the cancer therapy are precarious as these agents not only terminate the cancerous cells but also harm the healthy cells, evolve drug resistance, and several life threatening side effects even worse than malignancy. Even after the administration of these hazardous chemotherapeutic agents no acceptable remedy or treatment of cancer until date. Scientists are examining the clinical administration with least side effects and maximum effectiveness[15]. One of the promising cure can be probiotics and several studies have proven the same (table 1) [16-19].

Action mechanism

Various mechanistic action have been proposed, significantly showing anti-carcinogenic activity of probiotics, with the experimental study and evidences to prove. Probably several probiotic strains can influence different stages of carcinogenesis. A number of potential mechanisms are summarized in Figure 1.

Indian fermented food and probiotics

The significance of probiotics is well known in the form of habit of acquiring foods gained via fermentation, developed in households or in small industry via simple tools and techniques. Fermentation is one of oldest as well as economical technique developed by humankind in order to preserve as well as avert the spoilage of food products. Fermentation add other benefits to food such as improvement of flavors, enhanced digestibility, better nutritional and pharmacological standards[20]. Indian subcontinent is rich with fermented foods (table 2) [21-25]. Use of local good crops and various biological resources are further motivated.

DISCUSSION

Our understanding for gut microbiota composition is still underdeveloped and has a long way to cover. We need to discover more in order to understand the structure and fundamentals of healthy gut microbiome. Even though the administration of probiotics for medical purposes has increased enormously in recent years, because of the discovered correlation between probiotics and gut microbiota, the therapeutic implication remains in repressed stage.

Several strains of *Lactobacillus* and *Bifidobacterium* has been found to be associated with the reduction in the possibility of developing malignancy. Moreover, strains of *Lactobacillus*, *Bifidobacterium*, and *Bacteroides* are found to be involved in several immune as well as cytotoxic therapies. Majority of these results were observed in animal models. However, most of the data on human research, specially the clinical approaches has depicted the miscellaneous results for administration of probiotics, prebiotics as well as synbiotics. The formulations are also crucial. No specific formulations is found to be favored over another. Even though the knowledge for administration of probiotic strains translated into clinical applications, more questions will arise as would there be any chance of overcoming the deficiency of specific probiotic strain. As the microbes are well known for interacting among themselves and may ultimately results in increased susceptibility of any individual to any pathogenic strain. Although multiple strains formulation is used more nowadays as it is considered more efficient but at the same time reverse can be true as well.

Additionally, few patients or individuals may experience ill effects after the ingestion of probiotics as probiotics is involve with the death of the pathogens that will lead to release of toxic cell products in the near surrounding, "die-off reaction". In such cases, that particular individual must keep going with the use of probiotics, as it will eventually show the improvement in symptoms. Some other showed the increase in gas production, abdominal discomfort and even, in few cases, diarrhea, which eases spontaneously by time. Hence, more researches should be done in order to depict promising microbiome related therapy via probiotic regimens with particular strains and doses that are actually efficient. Even then, more research need to be focused on the synergistic impact between probiotics and anti- cancer drugs that will lead us to enhanced development with increased survival and cure.

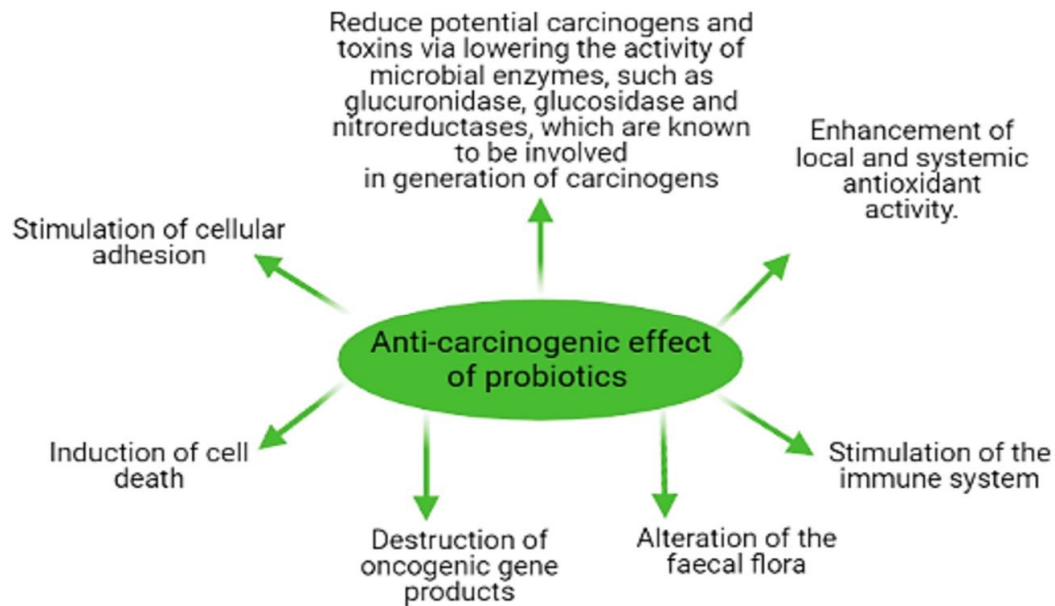


Figure 1: Diagrammatic representation of mechanistic action underlying the anti-carcinogenic effect of probiotics; via lowering the activity of microbial enzymes such as glucuronidase, glucosidase, and nitroreductase, which are well known cause of carcinogen generation; it also enhances the antioxidant activity; stimulate cellular activity; and various other effects such as induction of cell death, destruction of oncogenic gene products. Created with biorender.com

Table 1: Tabular representation of different probiotic strains with their respective biological effect onvarious cancer types

Probiotic Strain	Cancer Type	Biological impact
<i>Lactobacillus acidophilus</i> , <i>Lactobacillus plantarum</i>	Glioblastoma and breast cancer	Cytotoxic effects
<i>Lactobacillus lactis</i>	Breast cancer	Inhibition of cancer growth
<i>Lactobacillus acidophilus</i>	Lung cancer	Reduction in tumor size and survival rates increased
<i>Lactobacillus plantarum</i> and <i>L. rhamnosus</i>	Colon cancer	Reduction of tumor incidence, suppression of COX-2 expression
<i>Lactobacillus salivarius</i>	Colorectal cancer	Decreased cancer incidence
<i>Lactobacillus crispatus</i> and <i>L. rhamnosus</i>	Cervical and colon cancer	Cytotoxic effects
<i>Lactobacillus crispatus</i> and <i>L. rhamnosus</i>	Cervical cancer	Anti-proliferative effects
<i>Lactobacillus crispatus</i> and <i>L. rhamnosus</i>	Breast cancer	Cytotoxic effects
<i>Lactobacillus plantarum</i> LS/07	Breast cancer	Anti-proliferative and immunomodulatory
<i>Lactobacillus plantarum</i>	Sarcoma	Anti-proliferative and immunomodulatory
<i>Lactobacillus rhamnosus</i>	Colorectal cancer	Reduction of tumor incidence
<i>Lactobacillus casei</i>	Colon cancer	Apoptosis via JNK signaling pathway
<i>Lactococcus lactis</i> subsp. <i>lactis</i>	Stomach cancer	G0/G1 cell cycle arrest and apoptosis
<i>Lactococcus lactis</i> subsp. <i>lactis</i>	Colon, cervical, gastric, and breast cancer	Apoptosis
<i>Lactococcus lactis</i>	Lung, breast, and colon carcinoma	Decreased cell proliferation, Anti-proliferative
<i>Lactococcus lactis</i> subsp. <i>lactis</i>	Breast cancer	Antitumor
<i>Bifidobacterium lactis</i>	Colorectal cancer	Antibiotic proliferative
Recombinant <i>B. infantis</i>	Lung cancer	Antitumor effect and survival rates increased, Increased necrosis rate of tumor, survival rates increased
<i>Bifidobacterium</i> cocktail	Melanoma	Antitumor

Table 2: Tabular representation of different diet of the Indian subcontinent rich in respective probiotics

Region	Food	Probiotics found
Southern region	Koozhu, Pazhaiya soru, Idli, Dosa, Adai dosa, Kallappam, Mor kuzhaqmbhu	<i>W. paramesenteroides</i> , <i>L. fermentum</i> <i>E. faecalis</i> , <i>P. Acidilactici</i> <i>L. mesenteroides</i> , <i>E. faecalis</i> , <i>P. cerevisiae</i> <i>L. mesenteroides</i> , <i>E. faecalis</i> <i>Pediococcus</i> sp., <i>Streptococcus</i> sp., <i>Leuconostoc</i> <i>L. fermentum</i> , <i>L. plantarum</i>
Western region	Dhokla, khaman, Buttermilk, kadhi Rabdi, Bhatura	<i>L. fermentum</i> , <i>L. mesenteroides</i> , <i>E. faecalis</i> <i>Bacillus</i> sp., <i>Micrococcus</i> sp. <i>L. plantarum</i> , <i>L. acidophilus</i> , <i>L. mesenteroides</i>
Northern region	Dahi(lassi), bhatooru Jilebi	<i>S. cremoris</i> , <i>S. lactis</i> , <i>S. thermophilus</i> , <i>L. bulgaricus</i> , <i>L. acidophilus</i> , <i>L. helveticus</i> , <i>L. cremoris</i> , <i>P. pentosaceus</i> , <i>P. acidilactici</i> , <i>W. cibara</i> , <i>W. paramesenteroides</i> , <i>L. fermentum</i> , <i>L. plantarum</i> , <i>Lactobacillus delbrueckii</i> subsp. <i>indicus</i> <i>L. fermentum</i> , <i>S. lactis</i> , <i>L. buchneri</i> , <i>E. faecalis</i>
Eastern region	Chhurpi or durkha Chhu, Philu or Philuk, Shyow, Mohi, Somar	<i>L. plantarum</i> , <i>L. curvatus</i> , <i>L. fermentum</i> , <i>L. paracasei</i> subsp. <i>pseudoplantarum</i> , <i>L. alimentarius</i> , <i>L. kefir</i> , <i>L. hilgardii</i> , <i>E. faecium</i> and <i>L. mesenteroides</i> , <i>L. helveticus</i> <i>L. farciminis</i> , <i>L. brevis</i> , <i>L. alimentarius</i> , <i>L. lactis</i> subsp. <i>cremoris</i> <i>L. casei</i> , <i>L. bifermentans</i> and <i>E. faecium</i> <i>L. bifermentans</i> , <i>L. alimentarius</i> , <i>L. lactis</i> subsp. <i>cremoris</i> <i>L. paracasei</i> subsp. <i>pseudoplantarum</i>

CONCLUSION

The correlation between gut microbiota and their host is composite. Every person holds a specific composition of gut microbiota since the birth, and this intestinal microbiota develops and evolves with age, under the influence of diet and lifetime exposure to the heterogeneous environment. Since this balance is of utmost importance and very sensitive to changes. Nowadays, studies have revealed the growing attention towards the depiction of the gut microbiota composition. Genetics, along with various other functional studies, underlined the dual role played by the gut microbiome in cancer. As microbes can lead to dysbiosis eventually enhancing the carcinogenesis, via triggering the production of inflammatory and pro-carcinogenic surroundings. Other way various probiotics can defend the host, via resuming the healthy environment in an individual with dysbiosis, including cancer patients.

Proper precautions needs to be implemented as patients are mostly immune-compromised; therefore, it is necessary to check the side effects of administration of probiotics as therapeutic agents. In the upcoming future, the model of standard experimental studies can lead to the development of personalized-homogenized approach, considering the particular and pathological background of every patient to be treated, to maximize the positive results with minimized side effects. Even the dosages and administration regimes at different stages of cancer must be thoroughly examined. Hence, to overcome this disadvantage every individual must consume diet rich in probiotics. Various traditional diets holds a huge respect for fermented food and one of them is Indian diet that evolves around the thousands of years old medicinal system, the Ayurveda.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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