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REVIEW ARTICLE OPEN ACCESS

Bifidobacterium sp as Probiotic Agent - Roles and Applications

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Abstract

Probiotics are live microorganisms (mostly bacteria) that colonize the gut and supply helpful benefits. Probiotics are completely different from other varieties of microorganism in that they are considered "good" microorganism or non-pathogenic in healthy individuals. Genus *Bifidobacterium* is the primary microbe that colonizes human channel, and it has positive health effects on its host. Because of the acknowledged health benefits, it is included in several purposeful foods. *Bifidobacteria* generally occur in extremely varied ecological niches. In order to survive in these explicit ecological niches, they should be highly adaptive. This review helps researchers incorporate the utmost criteria for an acceptable probiotic strain as in the case of *Bifidobacterium sp. Bifidobacteria* can be considered as a probiotic and it plays an important role in anticholesterolemic, lactose intolerance, anticancerogenic, immunomodulatory effects etc.

Keywords: Probiotics, *Bifidobacterium* species, Beneficial microorganisms, Functional foods.

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INTRODUCTION

Bifidobacterium consists of about 45 species and belongs to phylum Actinobacteria. They are indigenous components of human and animal gastrointestinal micro flora. They are gram +ve, non-sporing, non-motile, rod-shaped and catalase-negative anaerobes, which produce acetic acid and lactic acids from carbohydrates without the generation of carbon-dioxide[1]. Genus can be distinguished from other bacterial groups like *Lactobacilli*, *Actinomycetes* and anaerobic *Corynebacterium* by Fructose-6-phosphate phosphoketolase (F6PPK) assay[2,3].

Tissier isolated *Bifidobacterium* from healthy breastfed infants in the year 1899. It is also isolated from infant feces, breast milk, cow's milk, yogurts, sour cream, cheese desserts, ice cream and powdered milk[4]. *Bifidobacteria* species is predominant in the guts of breastfed infants[5,6,7].

Bifidobacteria turn out medicinal drug chemicals, enzymes, vitamins B and K and carboxylic acid which decreases the growth of fungus, also helps in digestion and facilitates absorption of nutrients[8,9]. Probiotics are "live microorganisms that, once consumed in sufficient quantity, offer health benefits to their host"[10] .

Selection criteria for probiotics

While choosing the probiotics strain for human purpose, it ought to be isolated from the microflora that probably stick to the human intestinal wall. The strain ought to be properly isolated and known before use[11,12,13,14] .

There are a variety of standards to be followed throughout while choosing microorganism for probiotics. Strains of eubacterium and *Bifidobacterium* are usually used. Members of alternative genus like *Bacillus licheniformis* have conjointly been investigated to be used as probiotics[7,15]. Selected strains should be non-pathogenic and non-toxic. *Bifidobacterium* is generally considered safe[16,7]. Before choosing alternative probiotics, toxicologic studies should be performed[17].

Commercially important probiotics

The world population have become alert to the relation between nutrition and physiological state. Probiotic cultures are exploited extensively by the dairy farm business as tools for the production of novel purposeful products. Historically probiotics are incorporated in dairy products, milk and cheese; besides milk-based probiotic products, attempts are being made to use and develop nonmilk probiotic products. A variety of carriers of probiotics have been examined recently together with edible spreads and meat. New product like cereals, fruits and vegetables are in the developmental stages[18] .

The Beneficial effects of probiotics

Probiotics offer familiar health benefits like prevention and amelioration of intestine diseases. They have hypocholesterolemic, anticancer and antioxidative effects. Probiotics are reported to be helpful in atopic dermatitis, wound and scar-healing, and possess skin-rejuvenating properties[19,20]. The major health attributes of probiotics are shown in Fig.1.

Bifidobacterium

Bifidobacterium species are one of the most abundant microbes in natural microflora of colon. The bacteria in 25% of adult feces and 80% of infant feces are *Bifidobacterium*[35,36]. Bifidobacterium species plays an important role in human health by prevention of intestinal infections, decreasing cholesterol, stimulating immune system therfor decreasing cancer risk[34]. The beneficial effects of *Bifidobacterium* sp (Table 1).

Health benefits of Bifidobacterium

Bifidobacteria in diarrhoea

Many studies have reported *Bifidobacteria* is used to treat various gasterointestinal disorders[21]. This is mainly due to the administration of *B*. *breve* and *B*. *longum*. A review containing 8,014 infants, children and adult with acute diarrhea were given probiotics which contains *Bifidobacterium* strains, the result were found to reduce the duration

Table 1. Beneficial effects of *Bifidobacterium* sp

Beneficial Effects	Reference
Production of vitamins: B1 (Thiamine), B7 (Biotin), B11 (Folic acid), B12 (Cobalamine) and Riboflavin biosynthesis.	8
Alleviation of lactose intolerance	60,61,62
Prevention and treatment of inflammatory bowel disease	63,64
Reduction of serum cholesterol	65
Prevention of acute diarrhea	66
Prevention of colorectal cancer	67,25,68

of diarrhea[22]. Antibiotic associated diarrhea in children and adult patients are also recommended to take probiotics along with antibiotics this have proven antibiotic donot interfere with the probiotics[23].

***Bifidobacteria* in colorectal cancer**

Probiotics supress the growth of bacteria which convert procarcinogens into carcinogens thereby reducing the amount of carcinogens in the intestine[17]. Many species of Bifidobacterium have been found to reduce the incidence of tumour in the liver, colon, small intestine and mammary gland of rats[24]. Bacterial enzymes like ג–glucuronidase and nitroreductase play a vibrant role in the development of cancer by hydrolaysing carcinogenic compounds. Studies have reported that probiotics, including species of *Bifidobacteria*, decrease the activity of these enzymes thereby reducing various cancers[25].

A recent study has reported that probiotic supplements containing *B. longum* and other species of *Bifidobacterium*, suppress the total number of colon cancer cells in rats[26]. Many studies have concluded that certain strains of probiotics can be used as an adjuvant in cancer treatment[22].

***Bifidobacteria* in allergic disorders**

The shift of Th1/Th2 cytokine balance towards Th2 response is associated with allergic disorders which cause the activation of Th2 cytokines and release of interleukin 4, 5 and 13 and also IgE production[27]. Studies have reported that long term consumption of *Bifidobacterium* lactis significantly reduces the allergic symptoms in children. A study evaluated the clinical and

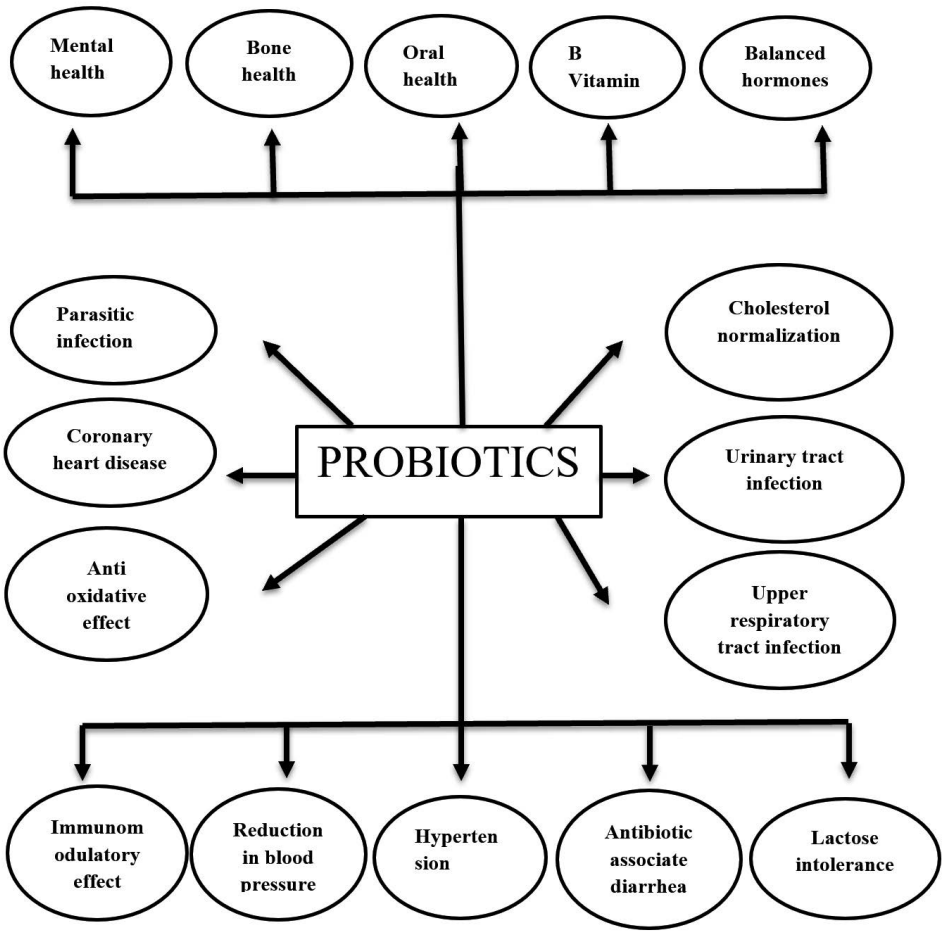

Fig. 1. Health attributes of Probiotics

immunological changes of atopic dermatitis after consuming probiotics containing *B.animalis* and *L.acidophilus* found to play a major role in the treatment of atopic dermatitis[28,29,30,31] .

***Bifidobacterium i*n Hepatic Encephalophathy**

Probiotics found to be effective against the treatment of hepatic encephalophathy[32]. Intake of different *Lactobacillus* and *Bifidobacterium* strains in an acute liver injury rat model has shown various effects on bacterial translocation and hepatocellular damage[33]. In another study five days of probiotic therapy with *Bifidobacterium* strains in alcoholic patients have significantly lowered AST and ALT activity at the end of treatment[34] .

Characterization of Strain

Bile and acid tolerance

Gastric acid and bile play a significant role in the body's defence against ingested microorganisms. In order to use bacteria as probiotics, it should be made to resist bile salts[19]. Bile salt plays a fundamental role in the defence mechanism of the gut.

Production of antimicrobial substances

Variety of antimicrobial substances has been produced by probiotic bacteria. Some of those compounds includes short fatty acids, bacteriocins, hydrogen peroxides etc. These have the ability to compete against gastrointestinal microbes and thereby inhibit pathogen bacteria[37,38].

Bifidobacteria produce antimicrobial proteins such as bacteriocins, which are substances for the inhibition of food borne pathogens[39]. Bacteriocins promotes antimicrobial activity through pore formation which causes cell lysis and prevents biosynthesis of cell wall[40].

Adhesion properties of *Bifidobacteria*

The adhesion onto mucin is used to evaluate the ability of the strains to colonise the intestine. This property is an important factor for the selection of probiotics[41]. Mucin in the intestine of hosts provides protection from enteric pathogens via steric hindrance specific binding for viruses and bacteria. Certain *Bifidobacterium* strains like *B. bifidum, B. longum* has *afcA* and *engBF* genes which express mucin degrading glycosidase [42].

Carbohydrate metabolism

Bifidobacteria are saccharolytic and play a significant role in the fermentation of carbohydrates in colon. It can also ferment different sources of carbon such as xylo-oligosaccharides. Bifidobacteria degrade hexose sugars through "bifid shunt" a metabolic pathway. In this, Fructose 6 phosphoketolase is broken down to fructose 6 phosphate in the presence of inorganic phosphate[43]. F6PPK assay using different chemicals like CTAB and Triton X-100 (Sigma) is a reliable test for genus identification of *bifidobacteria* [35].

Culture media for *Bifidobacterium s*pecies

Due to the non-availability of appropriate selective media, the isolation of *Bifidobacterium sp* from various niches has been a difficult task. Several media for the enumeration of *Bifidobacterium* sp are tested, and Wilkins Chalgren's agar, containing 100 mg/L Mupirocin, is used as selective medium of *Bifidobacterium* species from milk and cheese [44]. Reinforced Clostridial Agar and MRS Agar containing cysteine, Columbia agar medium containing lithium chloride and sodium propionate are used as selective media in dairy products and in quality control laboratories[45]. MTPY medium is used for isolating *Bifidobacteria* from hens' gastrointestinal tract[46,47].

A study by Wasilewska *et al* (2003)[48] developed another selective medium from milk: Raffinose Propionate lithium Mupirocin. In the year 2003, Ewa isolated *Bifidobacteria* from infant feces by two newly-modified Gerche's media:

1). One with stimulating *Bifidobacteria* growth maltodextring instead of lactose.

2). Addition of lithium chloride (3g/L) and Penicillin G, Sodium salt (50 U/L).

Culture medium used in different samples for the enumeration of *Bifidobacterium* sp is shown in Table 2.

Species of *Bifidobacteria*

More than thirty two Bifidobacterium species have been identified by scientists[49,50]. Distribution of principal species of *Bifidobacterium* is represented in Table 3 and major findings on *Bifidobacterium* sp in Table 4.

***Bifidobacterium* Sp in probiotic foods**

Bifidobacterium bifidum grew better in milk under anaerobic conditions than standard strains. This strain gave the best results when it was added at 5-10% to milk and when stored at pH 5.0-5.3, and storage at lower pH adversely affected growth and acid production. Kanbe *et al* (2007)[51] reviewed the characteristics of

Bifidobacterium spp. growth factors and evidence for its beneficial effects on protein metabolism, vitamin metabolism, fecal excretion, kidney problems and the immune response. Fernandes *et al* (1987) [52]and Guo *et al* (2010)[53] mentioned that *Lactobacillus spp*. along with *B. bifidum* constituted health benefits. Hughes and Hoover (2011)[54] discussed *Bifidobacteria*, a group of lactose-utilizing bacteria, with emphasis on classification. Recent research has focused on these organisms and the benefits obtained from the ingestion of bifid-containing food products. Misra and Kuila (2001)[55] summarized the biological activities, the role of *Bifidobacteria*, preparation and the antimicrobial activity and therapeutic properties of bifidus milk. Consumption of bifidus milk with a high number (108 cfu/g) of this organism will provide L (+)-lactic acid, antibiotic factor and live *Bifidobacteria* in addition to other nutritional components. The combined action of these factors will create favorable conditions for the proliferation of intestinal *Bifidobacteria,* and discourage the growth of harmful organisms [56].

Bifidobacteria and functional foods

Functional foods are "food containing some health promoting components, also called as super food, designer foods etc., and functional by means of adding probiotics[10]. Certain Lactic acid bacteria including *Lactobacillus* and *Bifidobacterium* genus are used as functional ingredients in probiotic food products[9]. *Bifidobacterium* sp, isolated from different food products, is shown in Table 5. The main challenge associated with the application of probiotic cultures in functional food is their viability during processing. *B. animalis* subsp. lactis BB-12 is a widely used probiotic strain in food manufacture because of its viability[57].

Table 2. Culture medium used in different samples for enumeration of *Bifidobacterium sp*

Sample Type	Media Used	Reference
Breast milk	MRS supplemented with 0.5 g/L L-cysteine HCL	35
Infant feces	MRS + 0.25 g/L L-cysteine , Bifidobacterium Agar	1,70,6
Dairy products	TPY agar	2
Milk	MRS broth , Bifido selective medium TOS-Propionate Agar+ Mupirocin	71
Animal feed	BSM agar, MRS supplemented with cysteine HCL and Mupirocin	72
Yogurts	Galactose (GL) Agar	1
Infant gut	Garches broth	73

Table 3. Distribution of species of *Bifidobacterium*

Human Groups	Rabbit Species	Cow	Swine Faeces	Honeybee Species
B.adolescentis	*B.magnum*	*B.bifidum*	*B.pseudocatenulatum*	*B.indicum*
B.bifidum	*B.saeculare*	*B.breve*	*B.choerinum*	*B.coryneforme*
B.breve	*B.cumiculi*	*B.boum*	*B.aerophilum*	
B.angulatum		*B.magnum*	*B.thermoacidophilum*	
B.catenulatum		*B.ruminantium*	*B.thermophilum*	
B.gallicum		*B.thermophilum*	*B.suis*	
*B.pseudo-*catenulatum		*B.infantis*		
B.longum		*B.pseudolongum*		

General features of *Bifidobacterial* genomes

The NCBI knowledge base presently holds 254 publicly-out *Bifidobacteria* ordering sequences, of which lxi represents a complete ordering sequence. 3 or a lot of complete ordering sequences are *Bifidobacterial* species, like *B. animalis, B. adolescentis B. breve, B.bifidum, B. longum* and *B. angulatum*. The typical size of a *Bifidobacterial* ordering is 2.2 Mb, with appreciable differences in size. For instance, *B.indicum* LMG11587 has an ordering size 1.73 Mb, whereas *B. scardovii*JCM12489 has 3.16 Mb. *Bifidobacterium* orderings generally have 52–58 RNA genes per genome, except the ordering *of B. longum subsp. infantis* ATCC15697, which has seventy nine tRNA genes. The amount of rRNA

Table 4. Major Findings on *Bifidobacterium* species

Bifidobacterium species	Major findings	Reference
B. longum	• One amongst the foremost common strains within the gut with excellent antioxidative activity. • Consumption of *B. longum* plus fructo-oligosaccharides (FOS) helps in the treatment of Minimal Hepatic Encephalopathy (MHE). • Anti-obesity and immunomodulatory effects. • Continuous intake of BB536 decreases the incidence of influenza and fever, probably by potentiating innate immunity. • Has vital anti-aging benefits, fewer issues with regularity, higher memory recall and improved bone health. • BB536 ingestion modulates the intestinal environment and also improves health care of early patients receiving enteral feeding.	74,75,76,77,78,79
B. breve	• *B.breve* plays a significant role in mucosal host defense and helps in preventing infectious diseases. • Antiallergic strain. • Administration of live *B.breve* strain Yakult and GOS (galactose oligosaccharides) improves the clinical condition of patients with ulcerative colitis. • Oral administration of B. breve alleviates UV induced barrier changes and oxidative stress in skin.	80,81
B. lactis	• Intestinal anti-inflammatory activity. • Daily intake of ice-cream which contains *B.Lactis* reduces the salivary levels of mutants streptococci in young adults. • Partially inhibits the gluten/gliadin-induced damage in small intestinal mucosa. • Utilizes Resistant Starch (RS) as substrate and up regulate the acute apoptotic response to a carcinogen in colon.	82,83,84
B.bifidum	• Inhibit *H.pylori* both invitro and invivo. • *B.bifidum* G9-1 is useful for prophylactic treatment in IgE-dependent allergic disease. • Invitro study, *B.bifidum* S17, highly adherent strain with potent anti-inflammatory capacity. • Combination of both *L. acidophilus* and *B.bifidum* reduces body weight among 53 obese people.	21,86
B.coagulans	• Invitro *B.coagulans* has antioxidant and free radical scavenging properties.	87
B.infantis	• *B.infantis* 35624 a probiotic strain relieves many of IBS symptoms.	88

Table 5. *Bifidobacterium* species isolated from different food products

Product type	Species isolated	Reference
Yogurt	*B.animalis , B.lactis*	70
Butter milk	*B. bifidum , B.animalis, B. longum* BB536.	89
Fermented Soymilk	*B.lactis Bb-12, B.longum Bb-46, B.bifidum B3.2, B.bifidum B7.1 and B.breve B9.14*	90,91,92
Fermented milk	*B.animalis ssp. lactis BB-12, B.animalis ssp. animalis*	93

operons among *Bifidobacterial* genomes generally ranges from 2 to 5, and it has been recommended that the amount of rRNA operons present on a genome correlate to the variation of a specific species to environmental conditions[58,59].

CONCLUSION

The growing attention in each basic analysis and industrial importance of probiotics and the role of *Bifidobacterium* species is highlighted during this work. *Bifidobacteria,* as probiotics, may become an important means of reduction of serum cholesterol, alleviation of lactose intolerance, treatment of inflammatory bowel diseases, acute diarrhea, colorectal cancer and other intestinal infections. And these days there is a growing trend in the market for food supported with probiotics. And also it is applied in a variety of products such as powdered health food and medicines, tablets, capsules etc. Most of the *Bifidobacterium* species currently being studied and in use appear to be safe, with no adverse effects on health. However, it is safe to conclude that *Bifidobacterium* species holds a great potential as probiotics.

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CONFLICT OF INTEREST

The authors declares that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors have made substantial, direct and intellectual contribution to the work and approved it for publication.

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DATA AVAILABILITY

All datasets generated or analysed during this study are included in the manuscript.

ETHICAL STATEMENT

This article does not contain any studies with human participants or animals performed by any of the authors.

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