

## **Bacillus coagulans: Probiotic of Choice**

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## **Introduction**

Probiotics have recently received considerable attention by the healthcare professionals and the public. Prior to considering *Bacillus coagulans*, we need to know what probiotics are. Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit on the host (Ref. 1). From this definition, it is concluded that probiotics can be a components of foods, dietary supplements and drugs. Furthermore, definition does not talk about the age of the subject or route of administration. It does not talk about type of the conferred health benefit either.

## **Bacillus coagulans (LactoSpore®)**

*Bacillus coagulans* is the taxonomic nomenclature of the microorganism deposited to the American Type Culture Collection (ATCC) facility under the number 7050. *Bacillus coagulans* was originally known as *Lactobacillus sporogenes*. Therefore, the names *Bacillus coagulans* and *Lactobacillus sporogenes* have been and are used in the literature interchangeably. LactoSpore® is Sabinsa Corporation's tradename for this probiotic. The most comprehensive review on LactoSpore® is written by Majeed and Prakash (Ref. 2).

## **Characteristic Features**

*Bacillus coagulans*, a nonpathogenic/nontoxicogenic microorganism, is a rod-shaped, Gram positive, endospore-forming (spore is formed within the cell) bacteria. It is facultative anaerobe, grows optimally at 37°C & pH in the range 5.5 to 6.2. *B. coagulans* requires nutritionally complex environment in which it derives energy via fermentation or catabolism of carbohydrates. It is more acid-tolerant than pathogenic and spoilage microorganisms

## **Probiotic Features**

When ingested, spores of *B. coagulans* can withstand the acidic environment of the stomach. Spores then germinate and proliferate within the GI tract within a few hours. After germination, *B. coagulans* is metabolically active as part of facultative anaerobes in the intestine, producing L (+) lactic acid, as primary product of fermentation. The main mechanism for survival and proliferation of *B. coagulans* is "Competitive Exclusion". Competitive exclusion is generally applied via competition for limited nutrients. However, the acidic environment created by production of L (+) lactic acid prevents the growth of pathogenic microbes and allows growth of *B. coagulans* which ultimately dominate the microflora. Furthermore, *B. coagulans* also produces bacteriocins (antimicrobial proteinaceous compounds) that are inhibitory towards both Gram positive and Gram negative bacteria. Suggested dose of *B. Coagulans* is 100 to 200 million spores, 3 times per day. *B. coagulans* is temporary resident of GI tract. In other words, following discontinuation of its administration, it is slowly excreted from body (usually within seven days).

## **Probiotic of Choice**

There are seven reasons why LactoSpore® can be considered as probiotic of choice:

### **Reason 1) History of Use**

Dietary ingestion of lactic acid producing bacteria has a substantial history of use and the safety record is excellent. For example, lactic-acid bacteria are used in starter cultures for fermentation in foods such as yogurt, kefir, sauerkraut, sausage, sourdough bread, Nigerian “Ugba” and Korean “Kimchi”. They are also utilized for production of enzymes that are used for food production (e.g., insoluble glucose isomerase enzyme). Lactic acid bacteria have also been used extensively in dietary supplements (alone or with vitamins, minerals, prebiotic, etc.).

### **Reason 2) Stability of Spores**

Due to its spore-forming nature, *B. coagulans* is resistant to most chemical and physical conditions (e.g., heat and acid) and survives manufacturing, shipping and storage with no loss of viable count. *B. coagulans* does not require refrigeration conditions and is room-temperature stable. Each batch of LactoSpore® produced in Sabinsa’s FDA-inspected biotechnology facility is inspected for sporulation and purity (Fig.1). The LactoSpore® powder produced in this facility is standardized to 15 billion spores per gram. Lower spore counts (e.g., 6 billion spores per gram) are also produced.

### **Reason 3) GRAS Status**

In December 2008, LactoSpore® was self-affirmed GRAS (Generally Recognized As Safe) by an independent panel of recognized experts qualified by their scientific training and relevant national and international experience to evaluate the safety of food and food ingredients. It was recommended by this panel of experts that 250 million CFU (Colony Forming Unit) of spores/person/day is safe. Up to 10 ppm of LactoSpore® at the concentration of 15 billion spores per gram may be used in the following selected food products:

*Baked Goods, Breakfast Cereals, Other Grains, Fats & Oils, Milk Products, Cheese, Frozen Dairy, Soft Candy, Confectionery & Frosting, Gelatins & Puddings, Soups, Snack Foods, Non-alcoholic Beverages, Imitation Dairy Products, Hard Candy, Sugar Substitutes and Instant Coffee & Tea.*

### **Reason 4) Documented Clinical Effectiveness**

#### ***Clinical Study 1: Gastrointestinal Health (Japan)***

In this double-blind, randomized clinical study, a total of 567 subjects participated in 19 independent health care institutions. Duration of study was 2-20 days and dosage of probiotic was 50 million to 750 million CFU/day (Ref. 3). As a result of receiving *B. coagulans*, 93.7% of diarrhea due to acute or chronic gastroenteritis, 85.9% of maldigestion accompanied with diarrhea, 87.9% of infantile diarrhea and 65.4% of Constipation conditions showed improvement (Table 1).

#### ***Clinical Study 2: Infant Gastrointestinal Health (India)***

In this study, 112 newborn infants in rural India were randomized to receive a daily oral dose of 100 million *Lactobacillus sporogenes* or a placebo for one year (Ref. 4). Morbidity was monitored each week for 12 months. Ninety four experienced diarrhea due to rotavirus infection. The group fed *L. sporogenes* had fewer episodes of diarrhea (3.4 vs. 8.6 in the placebo group) and less number of days of illness (13 days vs. 35 days in the placebo group). The episodes of diarrhea were of shorter duration (3.6 days vs.

6.8 days in the placebo group). These observations suggest that the prophylactic feeding of *Lactobacillus* has a preventive effect on the incidence and duration of acute rotavirus diarrhea.

#### ***Clinical Study 3: Serum Lipid Profile (India)***

In this study, short term hypolipidemic effects of oral *L. sporogenes* therapy (360 million spores/day in tablet form) were studied in 17 patients with type II hyperlipidemia in an open label fixed dose trial (Ref. 5). Total serum cholesterol (330 mg/dl vs. 226 mg/dl), LDL-cholesterol (267 mg/dl vs. 173 mg/dl) and total cholesterol to HDL cholesterol and LDL-cholesterol to HDL-cholesterol ratios were reduced significantly over a period of three months. HDL-cholesterol was marginally increased (43.6 mg/dl vs. 46.8 mg/dl); however there was no change in serum triglyceride levels (table 2).

#### ***Clinical Study 4: Infant Gastrointestinal Health (India)***

In this study, sixty diarrhea cases, three constipation and three jaundice cases were randomly selected. Dose administered was 15 million spores *L. sporogenes* per day and the recovery period was 1.8 days (Ref. 6). 81.7% of the diarrhea condition and 100% of the constipation and jaundice conditions were successfully treated. No complicating side effect was seen. The authors concluded that *L. sporogenes* has proved to be an efficacious and very safe drug for treatment of neonatal diarrhea.

#### ***Clinical Study 5: Acute & Chronic Diarrhea (China)***

In this study, the efficacy and safety of *Bacillus coagulans* tablets in the treatment of acute and chronic diarrhea was investigated (Ref. 7). Eligible patients were randomly allocated to two groups. There were 103 patients in the study group (51 with acute diarrhea and 52 with chronic diarrhea) and 101 in the control group (51 with acute diarrhea and 50 with chronic diarrhea). The study group received *B. coagulans* tablets at a dose of  $10^8$ CFU, three times daily for 3-7 days (acute diarrhea) and 14-21 days (chronic diarrhea), while the control group received Golden Bifid (*Bifidobacterium longium*) tablets at a dose of  $10^8$ CFU three times daily for 3-7 days and 14-21 days. Administration of these probiotic preparations was randomized and double-blind. The results showed that: (i) The best effectiveness rate of *B. coagulans* tablets in acute diarrhea was 78% and the total effectiveness rate was 98%, while the corresponding rates of Golden Bifid tablets were 70% and 92%, respectively (ii) The best effectiveness rate of chronic diarrhea of *B. coagulans* tablets was 48%, and its total effectiveness rate was 90%. The corresponding rates of Golden Bifid tablets were 37% and 80%, respectively. No statistically significant differences were found between these two groups. Moreover, no adverse reactions were found in either drug. (iii) The number of *Bifidobacterium* and *Lactobacillus* in gut significantly increased. The authors conclude that the *B. coagulans* tablets are an effective agent in the treatment of acute and chronic diarrhea and that their efficacy and safety are similar to that of Golden Bifid tablets (table 3).

#### **Reason 5) Potential Health Benefits**

Potential health benefits of LactoSpore® include:

A) Normalizing intestinal flora/immune enhancement [dysbiosis, infectious bacterial and viral diarrhea (e.g., rotavirus, shigella, salmonella, enterotoxigenic *E. coli*, *vibrio cholerae* and HIV), antibiotic-associated diarrhea, enteral feeding diarrhea, and travelers' diarrhea, constipation,

digestive discomfort (flatulence and bloating), relief of lactose intolerance symptoms, Irritable Bowel Syndrome (IBS), Inflammatory Bowel Disease (Crohn's Disease & Ulcerative Colitis), and inhibition of intestinal bacterial enzymes involved in the synthesis of colonic carcinogen].

B) Non-GI tract conditions [urinary tract infections, non-specific vaginitis, hyperlipidimia & hypercholesterolemia, hypertension, and respiratory tract infections].

### **Reason 6) Availability of Matching Prebiotic**

A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health (Ref. 8). Fenumannan<sup>®</sup> is the matching prebiotic for LactoSpore<sup>®</sup>. Fenumannan<sup>®</sup> is the soluble dietary fiber fraction of fenugreek seeds powder. Fenumannan<sup>®</sup> contains 35% - 45% galactomannans.

A synbiotics is a mixture of probiotics and prebiotics that beneficially affects the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare (Ref. 9). A mixture of approximately 2.5% LactoSpore<sup>®</sup> (Probiotic) and approximately 97.5% of matching Fenumannan<sup>®</sup> (Prebiotic) forms a synbiotic named LactoWise<sup>®</sup>. LactoWise<sup>®</sup> is a room temperature (RT) stable product and does not need refrigeration. Its shelf-life is two years at RT and delivers the scientifically-validated benefits of its constituents, LactoSpore<sup>®</sup> and Fenumannan<sup>®</sup>.

### **Reason 7) Support Services**

There are two support services for the use of LactoSpore<sup>®</sup>:

First Service) Sabinsa Manufacturing: It offers a turn-key operation (the entire formula) using technologies including blending, granulation, pre-mixes and dose forms such as capsules, tablets and stick packs. Sabinsa manufacturing is located in Payson, UT, United States.

Second Service) ClinWorld Contract Research Organization (CRO): ClinWorld conducts clinical trials according to Good Clinical Practice, GCP (randomized, double-blind and placebo-controlled). ClinWorld's scope of services is from trial design and protocol development to writing final report and helping with claim substantiation. ClinWorld has networks of dedicated principal investigators and reputed hospitals and research institutes. ClinWorld CRO is located in Mumbai, India.

### **Conclusion**

LactoSpore<sup>®</sup> may be chosen as the probiotic of choice for seven reasons: history of use, stability of spores, GRAS status, documented clinical effectiveness, potential health benefits (normalizing intestinal flora/immune enhancement and non-GI tract conditions), availability of matching prebiotic Fenumannan<sup>®</sup> (i.e., synbiotic LactoWise<sup>®</sup>), and two support services (manufacturing and CRO).

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## **Figure**

Fig 1) SAMI (Sabinsa) FDA-inspected facility for production of LactoSpore® (Bangalore, India)

## **Tables**

Table 1) Clinical Study 1: Gastrointestinal Health (Japan)

Table 2) Clinical Study 3: Serum Lipid Profile (India)

Table 3) Clinical Study 5: Acute & Chronic Diarrhea (China)