Bacillus coagulans

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Introduction

Probiotics are defined by the World Health Organization as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host." Worldwide, there are numerous strains of probiotics used in dietary supplements and foods, but most are unstable at room temperature and need to be freeze-dried or encapsulated via special processes to remain viable during manufacturing, storage, and exposure to stomach acid and bile. Consequently, for most probiotics, only a very small percentage of the starting material is actually viable at the end of shelf life. Bacillus coagulans is a notable exception which, due to its sporeulated form, survives without special handling and proliferates in the gastrointestinal environment.

Description

Bacillus coagulans is a gram-positive, spore-forming, microaerophilic, lactic-acid producing bacillus. It was originally isolated and described in 1932 by Horowitz and Wlassowa and named Lactobacillus sporogenes (L. sporogenes). In 1957, the organism was reclassified in Bergey's Manual of Determinative Bacteriology based on its biochemical properties, and the current correct nomenclature is Bacillus coagulans (B. coagulans). However, the organism is still sometimes referred to as L. sporogenes; for the purposes of this monograph, the correct nomenclature — B. coagulans — will be used. B. coagulans is unique among probiotics in that it possesses a protective, spore-like protein coating, which allows it to survive stomach acid, reach the small intestine, germinate, and multiply. The organism requires a complex mixture of organic substrates for growth, including fermentable carbohydrates and peptides.

Pharmacokinetics

Subsequent to oral administration, B. coagulans arrives in the stomach in its spore form, where it is exposed to the stomach's churning action and acidic pH that causes the spore coating to absorb water, swell, and begin the germination process. Upon arrival in the duodenum, the spores germinate and multiply rapidly. Estimates suggest the average duration of time between oral dosing and germination is 4-6 hours, with approximately 85 percent of the starting material reaching the intestinal tract. After germination, B. coagulans is metabolically active in the intestines, producing levorotatory L(+)-lactic acid, the form most readily metabolized in glycogen synthesis by the body (i.e., the isomeric form that would not be expected to contribute to metabolic acidosis). B. coagulans is considered a transient colonizing probiotic, indicating it takes up only temporary residence in the human intestines. Spores of B. coagulans are excreted slowly via the feces for approximately seven days after discontinuation of administration.

Mechanisms of Action

Despite the transient nature of this organism in the digestive tract, it is thought to produce a shift in the intestinal environment in support of a complex gastrointestinal flora. This is presumed to be a result of improving gastrointestinal ecology by replenishing the quantity of desirable obligate microorganisms and antagonizing pathogenic microbes.

B. coagulans has also been shown in vitro to produce bacteriocins, bacteriocin-like substances, and short-chain fatty acids that nourish the colonic mucosa. Bacteriocins are peptides produced by some strains of bacteria that inhibit the growth of...
other bacteria. Coagulin, a bacteriocin-like substance,\(^9\) and lactosporin, a unique antimicrobial protein with a lipid moiety,\(^11\) have been isolated from \(B.\) \textit{coagulans} and demonstrate significant antibacterial activity.\(^9\)\(^11\)

\textit{In vitro} bioassays have also shown components of the cell wall and supernatant of certain strains of \(B.\) \textit{coagulans} influence gut inflammation via cytokine modulation, inhibition of reactive oxygen species, and enhanced phagocytosis.\(^12\) Research in humans has also shown \(B.\) \textit{coagulans} GBI-30-0066 increased tumor necrosis factor-alpha (TNF-\(\alpha\)) response to adenovirus by 250 percent over baseline after 30 days of treatment. A 1,709-percent increase in the TNF-\(\alpha\) response to influenza A was also noted, but no effect was observed for other strains of influenza.\(^13\) Antifungal activity by \(B.\) \textit{coagulans} has also been demonstrated \textit{in vitro} against \textit{Fusarium} species, although the mechanism behind this has not been determined.\(^14\)

\(B.\) \textit{coagulans} possesses significant \(\beta\)-galactosidase (lactase) activity \textit{in vitro} and may also have lactic acid dehydrogenase activity, thereby enhancing the digestibility of lactose in those who are lactose intolerant.\(^15\)\(^16\) \(B.\) \textit{coagulans} assimilates and incorporates cholesterol into its cellular structure, binds cholesterol in the gut, and may inhibit the cholesterol-producing enzyme 3-hydroxy-3-methylglutaryl coenzyme reductase (HMG-CoA reductase).\(^17\)

### Clinical Indications

#### Gastrointestinal Disorders

An optimal balance between indigenous beneficial bacteria and potentially pathogenic bacteria in the gut is essential for efficient digestion and nutrient absorption. Imbalances in the gastrointestinal milieu can occur during antibiotic therapy, immune suppression, allergy insult, and stress. Probiotic administration has been shown to be an effective therapy for modulating a variety of gastrointestinal disorders (Table 1).

#### Dysbiosis

In laboratory animals with bacterial dysbiosis, \(B.\) \textit{coagulans} supplementation inhibits growth of pathogenic microorganisms and results in renewal of desirable obligate gastrointestinal organisms to normal levels. Reports suggest that supplementation produces a rapid resolution of acute gastrointestinal infection induced by pathogenic bacteria in animals.\(^5\)\(^1\) It has also been reported that \(B.\) \textit{coagulans} treatment in conjunction with traditional probiotics results in 20- to 30-percent higher treatment efficacy in humans with bacterial dysbiosis than traditional probiotics such as \textit{Lactobacillus acidophilus} or \textit{Bifidobacteria} alone.\(^6\) It should be noted that English full-text versions of these studies\(^7\)\(^8\) were not available, so detailed information is lacking.

### Antibiotic-associated Diarrhea

In a 2007 systematic review of the literature including 10 randomized trials and 1,986 children, \(B.\) \textit{coagulans} was shown to be among the most promising probiotics for preventing antibiotic-associated diarrhea.\(^17\) In a multi-center, randomized, double-blind, placebo-controlled trial, the effect of \(B.\) \textit{coagulans} on antibiotic-associated diarrhea was investigated in 98 children. Subjects were divided into placebo and treatment groups, with those in the treatment group given a \(B.\) \textit{coagulans}-fructo-oligosaccharide preparation for 10 days. At the end of the treatment period, only 29 percent of children in the \(B.\) \textit{coagulans} group continued to experience diarrhea compared to 62 percent in the placebo group. The average duration of diarrhea was also significantly shorter in the treatment group (0.7 days) when compared to the placebo group (1.6 days).\(^17\)

### Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a chronic gastrointestinal condition of multi-factorial etiology, presenting with episodic abdominal bloating, pain, diarrhea and/or constipation. Management of irritable bowel symptoms can be challenging and may significantly impact the patient’s quality of life. Because probiotics have the ability to improve bowel health, strains of \(B.\) \textit{coagulans} have been studied as a therapy for IBS in two randomized, double-blind clinical trials.

In one eight-week study, 52 men and women (ages 30-67) with diarrhea-predominant IBS (IBS-D) were randomized to receive one capsule daily of \(B.\) \textit{coagulans} with two billion colony forming units (CFUs) \((n=26)\) or identically appearing placebo (microcrystalline cellulose; \(n=26)\). Patients were monitored at baseline and daily for eight weeks and were assessed for compliance, frequency of bowel movements, abdominal pain, distention, flatulence, and urgency. The average number of bowel movements decreased significantly in the \(B.\) \textit{coagulans} group when compared to placebo \((p=0.042)\); differences between treatment and placebo groups for other parameters did not reach statistical significance.\(^19\)

In the second study, 44 subjects with IBS-D (82 percent women; average age 48 years) were
Table 1. *Bacillus coagulans* GI Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Material Used</th>
<th>Condition</th>
<th>Study Population</th>
<th>Daily Dose</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>La Rosa et al.</td>
<td>2003</td>
<td><em>B. coagulans</em> with fructo-oligosaccharides</td>
<td>Antibiotic-associated diarrhea</td>
<td>98 children</td>
<td>Not specified</td>
<td>71% of children in treatment group had resolution of diarrhea versus 38% in placebo group; duration of diarrhea significantly shortened in treatment group</td>
</tr>
<tr>
<td>Dolin BJ et al.</td>
<td>2009</td>
<td><em>B. coagulans</em> GBI-30, 6086</td>
<td>Irritable bowel syndrome – diarrhea predominant (IBS-D)</td>
<td>52 adults</td>
<td>2 billion cfu</td>
<td>Decreased number of bowel movements; no statistically significant change in other IBS symptoms</td>
</tr>
<tr>
<td>Hun L.</td>
<td>2009</td>
<td><em>B. coagulans</em> GBI-30, 6086</td>
<td>IBS-D</td>
<td>44 adults</td>
<td>800 million cfu</td>
<td>Statistically significant improvements in abdominal pain and bloating in treatment group compared to placebo</td>
</tr>
<tr>
<td>Chandra RK</td>
<td>2002</td>
<td><em>B. coagulans</em></td>
<td>Acute rotavirus diarrhea</td>
<td>112 newborns</td>
<td>100 million cfu</td>
<td>Statistically significant decrease in frequency and duration of diarrhea in treatment group compared to placebo</td>
</tr>
<tr>
<td>Sari FN et al.</td>
<td>2011</td>
<td><em>B. coagulans</em> (referred to as L. sporogenes in study)</td>
<td>Necrotizing enterocolitis (NEC) (&lt;1500 g, &lt;33 weeks)</td>
<td>221 very-low-birth-weight (VLBW) neonates</td>
<td>350 million cfu</td>
<td>No effect on rate of death or NEC on VLBW infants; significantly improved feeding tolerance in treatment group</td>
</tr>
<tr>
<td>Dutta P et al.</td>
<td>2011</td>
<td><em>B. coagulans</em> (referred to as L. sporogenes in study)</td>
<td>Diarrhea with dehydration (diverse etiology)</td>
<td>146 infants (6-24 months)</td>
<td>Not specified</td>
<td>No therapeutic effect on management of acute dehydrating diarrhea of diverse etiology, including rotavirus associated diarrhea in children</td>
</tr>
<tr>
<td>Kalman DS et al.</td>
<td>2009</td>
<td><em>B. coagulans</em> GBI-30, 6086 in Digestive AdvantageTM Gas Defense Formula</td>
<td>Intestinal pain, gas, bloating</td>
<td>61 adults</td>
<td>2 billion cfu</td>
<td>Significant reduction in intestinal gas and pain scores; strong trend toward improved abdominal distention scores; improved quality of life scores</td>
</tr>
</tbody>
</table>

randomized to either the *B. coagulans* (n=22) or placebo (n=22) group. Those in the treatment group received one capsule daily of *B. coagulans* containing 800 million CFUs and those in the placebo group received an identical-appearing capsule. Subjects were assessed at baseline and treated for eight weeks with three follow-up visits. Within-group improvements over baseline frequency, abdominal pain, and bloating scores reached statistical significance for each week of
treatment in the *B. coagulans* group (p < 0.01), but only at weeks 6 and 8 for the placebo group. Between-group statistical comparison was not conducted. No significant adverse events were reported. Data from both studies suggest *B. coagulans* may be an effective therapy for decreasing bowel movement frequency, abdominal pain, and bloating in patients with IBS.20

**Neonatal and Infant Diarrhea**

Research conducted in India has shown *B. coagulans* is effective in decreasing frequency and duration of neonatal diarrhea caused by acute rotavirus infection. Administration of 100 million CFUs of *B. coagulans* or placebo daily for one year to 112 newborns resulted in statistically significant decreases in number of diarrhea episodes and duration of each episode – 3.6 days in treatment group versus 6.8 days in placebo group.21 Conversely, two more recent studies demonstrated *B. coagulans* administration had no impact on necrotizing enterocolitis or rate of death in very low birth weight neonates22 or in older infants (6-24 months) with diarrhea and dehydration.23

**Flatulence**

A randomized, double-blind, placebo-controlled trial was conducted to evaluate the effects of *B. coagulans* on post-prandial gas-related intestinal symptoms. Sixty-one adults (average age 36.5 years) were randomized to receive two billion CFUs *B. coagulans* or placebo daily for four weeks. Subjects were evaluated at baseline, two, and four weeks for abdominal pain, distention, flatus, and dyspepsia severity. Measured against the placebo, subjects receiving the probiotic capsules achieved significant improvements in abdominal pain and total gastrointestinal symptom score, as well as a non-significant trend toward improvement for abdominal distention. No statistical benefits were reported for the Severity of Dyspepsia Assessment Scale.24

**Hyperlipidemia**

*B. coagulans* may positively affect lipid levels in animals and humans. This is thought to be due to its ability to bind cholesterol in the gut, and possible inhibition of the cholesterol-producing enzyme HMG-CoA reductase. Administration of *B. coagulans* to rabbits resulted in a 90-percent inhibition in the rise of serum cholesterol secondary to feeding of high cholesterol diets.25 *B. coagulans* supplementation (360 million CFUs/day) in humans decreased total serum cholesterol from an average of 330 mg/dL to 226 mg/dL in 17 subjects with type II hyperlipidemia over a three-month time interval. LDL-cholesterol and LDL:HDL ratios were also significantly decreased, with a slight increase in HDL-cholesterol. No changes in serum triglyceride levels were observed.16

**Viral Conditions**

The effect of *B. coagulans* on the immune response after exposure to adenovirus and influenza A was investigated in 10 subjects (average age 44 years) for 30 days. Subjects were given a daily dose of *B. coagulans* with two billion CFUs per capsule and assessed at baseline and after 30 days, acting as their own control. Whole blood samples were assessed for cytokine levels after T-cell exposure to the two viruses. In the nine subjects that were evaluable, 250- and 1,709-percent average increases in the TNF-a response to adenovirus and influenza A viruses, respectively, were observed after 30 days of treatment.13

**Oral Conditions**

**Aphthous Stomatitis**

Mathur et al reported Sporlac® (*B. coagulans*) at a dose of two tablets daily (120 million CFUs) was efficacious in clearing outbreaks of aphthous stomatitis, with resolution occurring within 2-3 days.26 Sharma et al found that *B. coagulans* given at 120 million CFUs daily resolved aphthous stomatitis in as little as 2-3 days.27

**Dental Caries**

Dental caries in children are caused in part by salivary mutants Streptococci and are a common problem both in modern and underdeveloped countries. A freeze-dried powdered preparation of *B. coagulans* (CFUs not noted) mixed in 20 mL of water was given to 50 children for 14 days and they were instructed to swish and swallow the mixture. Fifty additional children received a similar preparation containing *L. rhamnosus* and *Bifidobacterium* species, while another group of 50 children were given an identically appearing placebo. Saliva samples were collected on day 1 and 14 and cultured for salivary mutants Streptococci. A statistically significant reduction (p < 0.001) in salivary mutants Streptococci counts was observed in both probiotic treatment groups after 14 days, suggesting *B. coagulans* may be a cost-effective probiotic for preventing dental caries in children.28
Vaginitis

Vaginal administration of a commercial formulation of *B. coagulans* tablets called Myconip® was given to 44 women with non-specific vaginitis twice daily for 14 days. Total CFUs per tablet was not specified. Subjects with Trichomonas or Candida vaginitis were excluded from the study. Complete relief of pruritis and discharge was reported by 91 percent of subjects. These results were thought to be due to a beneficial change in vaginal acidity via lactic acid production by *B. coagulans*. Postmenopausal subjects had a slower response to therapy but eventually had complete relief as well.29

Rheumatoid Arthritis

The anti-inflammatory and immune-modulating properties of *B. coagulans* and other lactic acid-producing probiotics theoretically may have an impact on the symptoms of arthritis. In a randomized, controlled trial, 44 adult men and women (average age 62) with rheumatoid arthritis for at least one year received either *B. coagulans* with two billion CFUs or placebo daily for 60 days, in addition to their regular arthritis medications. Evaluations were conducted at baseline, 30, and 60 days for pain, disability, and global assessment by both patients and physicians. Subjects in the treatment group experienced statistically significant improvement in pain scale scores, patient pain assessment, and patient global and disability assessment when compared to placebo. Although physician assessment showed slight improvement in all categories, the results did not reach statistical significance. A reduction in C-reactive protein was seen in the treatment group, but not in the placebo group. Subjects in the treatment group also demonstrated greater ability to walk two miles, reach, and participate in daily activities.30

Toxicity and Side Effects

Toxicological safety assessments for *B. coagulans* indicate no mutagenic, clastogenic, or genotoxic effects. Results of an acute and 90-day subchronic oral toxicity study in rats yielded a No Adverse Effects Level (NOEL) greater than 1,000 mg/kg per day.31 *B. coagulans* at a concentration of $1.36 \times 10^{11}$ CFUs/g was used in the study, corresponding to 95.2 x $10^{11}$ CFUs for a 70-kg human. Typical human dose range for *B. coagulans* is $100 \times 10^{6} (100$ million) to $3 \times 10^{9} (3$ billion) CFUs daily, so this data represents a safety factor ranging from 3,173 to 95,200 times the recommended daily dose. In humans, adverse reactions following supplementation have not been reported in the peer-reviewed literature. For example, in the rheumatoid arthritis study, the authors mentioned that there were no treatment-related adverse events reported throughout the treatment period.30

Dosage

*B. coagulans* daily dosages reported in peer-reviewed research range from 100 million to 5 billion CFUs. Beneficial effects were noted in earlier studies, even at dosages as low as 100 million CFUs daily. Currently, for *B. coagulans* supplied in capsules, a typical dosage recommendation is 100 mg 2-3 times daily, with each 100 mg containing approximately 1.5 billion colony-forming units. It should be noted that several of the human studies cited in this monograph were conducted using a patented/proprietary strain of *B. coagulans* GBI-30,6086.

References


