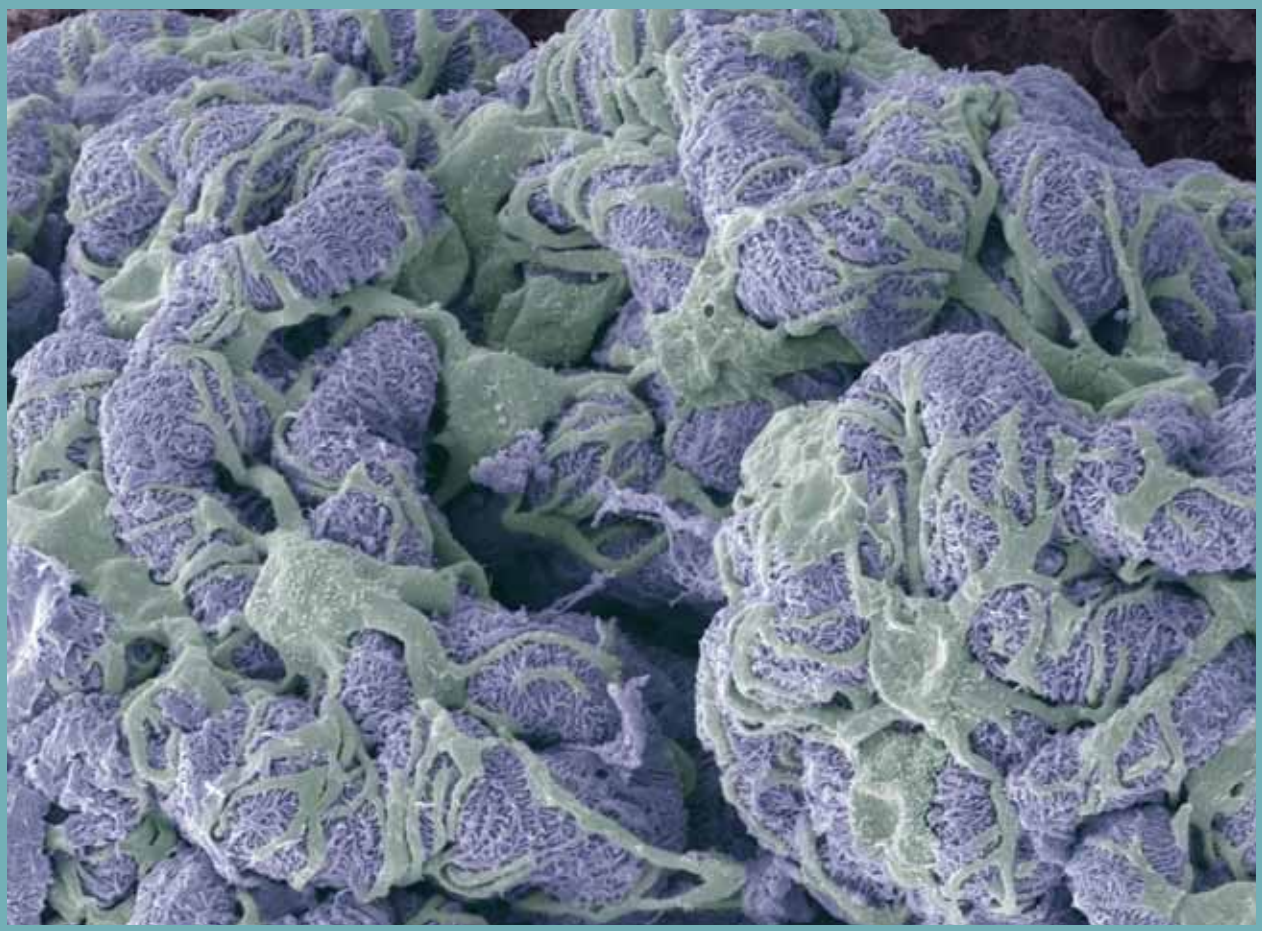
amr
Alternative Medicine Review®
A Journal of Clinical Therapeutics

March 2012 Volume 17, Number 1



ACAM AMERICAN COLLEGE FOR ADVANCEMENT IN MEDICINE

The Official Journal of The American College for Advancement in Medicine

Bacillus coagulans

Julie S. Jurenka, MT (ASCP)

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."[1] 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.[2] 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 sporulated 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*).[3] 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*).[4] 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.[4]

Julie S. Jurenka, MT (ASCP) - Contributing Editor, *Alternative Medicine Review*; Medical Affairs Research Assistant, Thorne Research, Inc. Correspondence address: Thorne Research, Inc., P.O. Box 25, Dover, ID 83825 Email: jjurenka@thorne.com

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,[5] 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).[4] *B. coagulans* is considered a transient colonizing probiotic, indicating it takes up only temporary residence in the human intestines.[3] Spores of *B. coagulans* are excreted slowly via the feces for approximately seven days after discontinuation of administration.[3]

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.[6-8] This is presumed to be a result of improving gastrointestinal ecology by replenishing the quantity of desirable obligate microorganisms and antagonizing pathogenic microbes.[3,6]

B. coagulans has also been shown *in vitro* to produce bacteriocins,[3] bacteriocin-like substances,[9] and short-chain fatty acids that nourish the colonic mucosa.[10] 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. coagulans* and demonstrate significant antibacterial activity.[9,11]

In vitro bioassays have also shown components of the cell wall and supernatant of certain strains of *B. coagulans* influence gut inflammation via cytokine modulation, inhibition of reactive oxygen species, and enhanced phagocytosis.[12] Research in humans has also shown *B. coagulans* GBI-30-6086 increased tumor necrosis factor-alpha (TNF-α) response to adenovirus by 250 percent over baseline after 30 days of treatment. A 1,709-percent increase in the TNF-α response to influenza A was also noted, but no effect was observed for other strains of influenza.[13] Antifungal activity by *B. coagulans* has also been demonstrated *in vitro* against Fusarium species, although the mechanism behind this has not been determined.[14]

B. coagulans possesses significant β-galactosidase (lactase) activity *in vitro* and may also have lactic acid dehydrogenase activity, thereby enhancing the digestibility of lactose in those who are lactose intolerant.[3,15] *B. 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).[16]

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. 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.[6,7] It has also been reported that *B. 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 *Lactobacillus acidophilus* or Bifidobacteria alone.[8] 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. 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. 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. coagulans*-fructo-oligosaccharide preparation for 10 days. At the end of the treatment period, only 29 percent of children in the *B. 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).[18]

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. 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. 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. 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

Author	Year	Material Used	Condition	Study Population	Daily Dose	Results
La Rosa et al	2003	*B .coagulans* with fructo-oligosaccharides (referred to as L .sporogenes in the study)	Antibiotic-associated diarrhea	98 children	Not specified	71 % of children in treatment group had resolution of diarrhea versus 38 % in placebo group; duration of diarrhea significantly shortened in treatment group
Dolin BJ et al	2009	*B. coagulans* GBI-30, 6086	Irritable bowel syndrome – diarrhea predominant (IBS-D)	52 adults	2 billion cfu	Decreased number of bowel movements; no statistically significant change in other IBS symptoms
Hun L	2009	*B. coagulans* GBI-30, 6086	IBS-D	44 adults	800 million cfu	Statistically significant improvements in abdominal pain and bloating in treatment group compared to placebo
Chandra RK	2002	*B. coagulans*	Acute rotavirus diarrhea	112 newborns	100 million cfu	Statistically significant decrease in frequency and duration of diarrhea in treatment group compared to placebo
Sari FN et al.	2011	*B. coagulans* (referred to as L,sporogenes in study)	Necrotizing enterocolitis (NEC)	221 very-low-birth-weight (VLBW) neonates (<1500 g, <33 weeks)	350 million cfu	No effect on rate of death or NEC on VLBW infants; significantly improved feeding tolerance in treatment group
Dutta P et al	2011	*B. coagulans* (referred to as L. sporogenes in study)	Diarrhea with dehydration (diverse etiology)	148 infants (6-24 months)	Not specified	No therapeutic effect on management of acute dehydrating diarrhea of diverse etiology, including rotavirus associated diarrhea in children
Kalman DS et al	2009	*B. coagulans* GBI-30, 6086 in Digestive AdvantageTM Gas Defense Formula	Intestinal pain, gas, bloating	61 adults	2 billion cfu	Significant reduction in intestinal gas and pain scores; strong trend toward improved abdominal distention scores; improved quality of life scores

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 neonates[22] 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-α 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 mutans 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 mutans Streptococci. A statistically significant reduction ($p<0.001$) in salivary mutans 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.[10]

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.[30] *B. coagulans* at a concentration of 1.36×10^{11} CFUs/g was used in the study, corresponding to 95.2×10^{11} CFUs for a 70-kg human. Typical human dose range for *B. coagulans* is 100×10^{6} (100 million) to 3×10^{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.[10]

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

1. Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. London, Ontario, Canada; April 30 and May 1, 2002.
2. Gilliland SE. Health and nutritional benefits from lactic acid bacteria. *FEMS Microbiol Rev* 1990;7:175-188.
3. Majeed M, Prakash L. *Lactospore : The Effective Probiotic*. Piscataway, NJ: NutriScience Publishers, Inc.; 1998.
4. Bergey D. *Bergey's Manual of Determinative Bacteriology*. 9th ed. Baltimore, MD: The Williams and Wilkens Company; 1993.
5. Ghandi AB. *Lactobacillus sporogenes*, an advancement in Lactobacillus therapy. *East Pharm* 1988:41-43.
6. Adami A, Cavazzoni V. Occurrence of selected bacterial groups in the faeces of piglets fed with Bacillus coagulans as probiotic. *J Basic Microbiol* 1999;39:3-9.
7. Smirnov VV, Reznik SR, V'iunitskaia VA, et al. The effect of the complex probiotic Sporolact on the intestinal microbiocenosis of warm-blooded animals. *Mikrobiol Z* 1995;57:42-49. [Article in Russian]
8. Voichishina LG, Chaplinskii Vla, V'iunitskaia VA. The use of sporulating bacteria in treating patients with dysbacteriosis. *Vrach Delo* 1991;(12):73-75. [Article in Russian]
9. Hyronimus B, Le Marrec C, Urdaci MC. Coagulin, a bacteriocin-like inhibitory substance produced by *Bacillus coagulans* I4. *J Appl Microbiol* 1998;85:42-50.

10. Mandel DR, Eichas K, Holmes J. *Bacillus coagulans*: a viable adjunct therapy for relieving symptoms of rheumatoid arthritis according to a randomized, controlled trial. *BMC Complement Altern Med* 2010;10:1.
11. Riazi S, Wirawan RE, Badmaev V, Chikindas ML. Characterization of lactosporin, a novel antimicrobial protein produced by *Bacillus coagulans* ATCC 7050. *J Appl Microbiol* 2009;106:1370-1377.
12. Kodali VP, Sen R. Antioxidant and free radical scavenging activities of an exopolysaccharide from a probiotic bacterium. *Biotechnol J* 2008;3:245-251.
13. Baron M. Apatented strain of *Bacillus coagulans* increased immune response to viral challenge. *Postgrad Med* 2009;121:114-118.
14. Czaczyk K, Trojanowska K, Mueller A. Antifungal activity of *Bacillus coagulans* against Fusarium sp. *Acta Microbiol Pol* 2002;51:275-283.
15. Kim YM, et al. Studies on the production of β-galactosidase by *Bacillus coagulans*. Properties and applications of β-galactosidase. *Korean J Applied Microbiol Bioeng* 1985;13;355-360. Cited in: Majeed M, Prakash L. *Lactospore : The Effective Probiotic*. Piscataway, NJ: NutriScience Publishers, Inc.; 1998.
16. Mohan JC, Arora R, Khalilullah M. Preliminary observations on effect of *Lactobacillus sporogenes* on serum lipid levels in hypercholesterolemic patients. *Indian J Med Res* 1990;92:431-432.
17. Johnston BC, Supina AL, Ospina M, Vohra S. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev* 2007;(2):CD004827.
18. La Rosa M, Bottaro G, Gulino N, et al. Prevention of antibiotic-associated diarrhea with *Lactobacillus sporogenes* and fructo-oligosaccharides in children. A multicentric double-blind vs placebo study. *Minerva Pediatr* 2003;55:447-452. [Article in Italian]
19. Dolin BJ. Effects of a proprietary *Bacillus coagulans* preparation on symptoms of diarrhea-predominant irritable bowel syndrome. *Methods Find Exp Clin Pharmacol* 2009;31:655-659.
20. Hun L. *Bacillus coagulans* significantly improved abdominal pain and bloating in patients with IBS. *Postgrad Med* 2009;121:119-124.
21. Chandra RK. Effect of Lactobacillus on the incidence and severity of acute rotavirus diarrhea in infants. A prospective, placebo-controlled double-blind study. *Nutr Res* 2002;22:65-69.
22. Sari FN, Dizdar EA, Oguz S, et al. Oral probiotics: *Lactobacillus sporogenes* for prevention of necrotizing enterocolitis in very low-birth weight infants: a randomized, controlled trial. *Eur J Clin Nutr* 2011;65:434-439.
23. Dutta P, Mitra U, Dutta S, et al. Randomised controlled clinical trial of *Lactobacillus sporogenes (Bacillus coagulans)*, used as a probiotic in clinical practice, on acute watery diarrhea in children. *Trop Med Int Health* 2011;16:555-561.
24. Kalman DS, Schwartz HI, Alvarez P, et al. A prospective, randomized, double-blind, placebo-controlled parallel-group dual site trial to evaluate the effects of a *Bacillus coagulans*-based product on functional intestinal gas symptoms. *BMC Gastroenterol* 2009;9:85.
25. Kumar ORM, Christopher KJ. Feeding of *L. sporogenes* to rabbits. *Indian Vet J* 1989;66:896-898.
26. Mathur SN, et al. Sporlac therapy in treatment of aphthous stomatitis. *Uttar Pradesh State Dent J* 1970;11:7-12. Cited in: Majeed M, Prakash L. *Lactospore®: The Effective Probiotic*. Piscataway, NJ: NutriScience Publishers, Inc.; 1998.
27. Sharma JK, Kapoor KK, Mukhija RD. Clinical trial of Sporlac in the treatment of recurrent aphthous ulceration. *Uttar Pradesh State Dent J* 1980;11:7-12.
28. Jindal G, Pandey RK, Agarwal J, Singh M. A comparative evaluation of probiotics on salivary mutans streptococci counts in Indian children. *Eur Arch Paediatr Dent* 2011;12:211-215.
29. Shirodkar NV, Sankholkar PC, Ghosh S, Nulkar SM. Multi-centre clinical assessment of Myconip vaginal tablets in non-specific vaginitis. *Indian Pract* 1980;33:207-210.
30. Endres JR, Clewell A, Jade KA, et al. Safety assessment of a proprietary preparation of a novel probiotic, *Bacillus coagulans*, as a food ingredient. *Food Chem Toxicol* 2009;47:1231-1238.

in continuous publication since 1996 – the leading peer-reviewed journal designed for sharing information on the practical use of alternative and complementary medicine

... your voice on PubMed

amr
Alternative Medicine Review®
a journal of clinical therapeutics

subscribe today

"For over sixteen years, AMR has been a nexus of excellent information and dialogue about natural medicine. AMR is relevant, timely, and articulate. Complementary and integrative health-care professionals regard AMR as the best journal our profession has".
David J. Schleich, PhD - President, NCNM

"As Alternative Medicine Review may be our only 'Medlined' journal for alternative articles, [its loss] would be like regressing 20 years to when none of us could get anything published." Davis Lamson, ND

Alternative Medicine Review
1610 Main Street,
Napa, CA 94558
www.altmedrev.com
info@altmedrev.com