BACTERIOLOGY, COLONIZATION, AND CLINICAL EFFICACY OF DDS-1 LACTOBACILLUS ACIDOPHILUS

A WHITE PAPER

POWERED BY PROBIOTICS

Authored By,
Michael N. Pakdaman, M.D., and Michael Shahani

For more information please contact sales@nebraskacultures.com
OBJECTIVE: The aim of this white paper is to present a comprehensive review of literature regarding the clinical and laboratory evidence behind *Lactobacillus acidophilus* on supporting health, with a focus on the DDS-1 strain. Discovered in 1959, the DDS-1 strain of *Lactobacillus acidophilus* has been used in numerous laboratory, animal, and human clinical studies, and has been shown to have a positive effect on digestion, immune function, and skin conditions.

REVIEW: The human gastrointestinal (GI) microbiome consists of up to 500 different species that live in symbiosis with humans, providing nutrients, aiding in digestion, and supporting increased immunity. This white paper reviews the role of the microflora and the path to development of commercially available probiotics. *Lactobacillus* is a genus of bacteria found naturally in the bowel and known for its sugar fermenting properties. *Lactobacillus* is also a common component of many probiotic formulations. Bacteriology of the *L. acidophilus* species is discussed, particularly the variability of different strains of *L. acidophilus* in terms of efficacy and ability to colonize the GI tract. The DDS-1 strain of *L. acidophilus* is a unique strain that has been shown in human studies to successfully colonize the GI tract.

Many studies show many potential health benefits including inhibition of pathogenic bacteria and support for antibiotic-associated diarrhea. The DDS-1 strain of *L. acidophilus* has also been shown in a randomized clinical trial to support improved GI symptoms in response to a lactose challenge. Longitudinal comparison between the DDS-1 group and placebo group in this study demonstrated statistically significant reductions in abdominal symptom scores during the 6-hour Lactose Challenge at week 4 for diarrhea (p=0.033), abdominal cramping (p=0.012), vomiting (p=0.0002), and overall symptom score (p=0.037). Laboratory and human studies have also shown a potential link between DDS-1 consumption and immune health. Safety studies demonstrate no significant adverse events among non-immunocompromised healthy adults. DDS-1 has been shown to reduce the symptoms of atopic dermatitis in young children.

CONCLUSIONS: *L. acidophilus* is a species of bacteria shown in clinical studies to support improved GI symptoms among those with lactose intolerance. Several strains of *L. acidophilus* exist, many of which lack any clinical evidence of gastrointestinal colonization or clinical efficacy. The DDS-1 strain of *L. acidophilus*, manufactured by Nebraska Cultures, is a probiotic that has been demonstrated to successfully colonize the colonic mucosa as well as reduce common symptoms related to lactose intolerance including diarrhea, abdominal cramping, and vomiting.
INTRODUCTION
Gastrointestinal Microflora

The human body contains numerous microorganisms that naturally exist in symbiosis along mucosal surfaces, including up to 500 different species of bacteria that reside in our GI tracts alone and the total bacterial count outnumbering all human cells by tenfold [1, 2]. These bacteria, or “microflora,” provide humans certain benefits such as facilitation of metabolism, immune support, and nutrient synthesis [3, 4]. The mature GI tract is composed of primarily anaerobic bacteria, mainly Bacteroides, Porphyromonas, Bifidobacterium, Lactobacillus, and Clostridium [13]. The DDS-1 product is a purified strain of the anaerobic bacteria Lactobacillus acidophilus. The significance of anaerobic bacteria is that it relies on the anaerobic cycle of glycolysis, rapidly breaking down carbohydrates such as lactose and producing lactic acid, the final byproduct of anaerobic metabolism [14]. This natural anaerobic mechanism of carbohydrate breakdown suggests a potential benefit in alleviating symptoms related to excess lactose in the GI tract, as seen among individuals with lactose intolerance.

Colonization Resistance and the Antibiotic Age

Early studies demonstrated that the loss of the bacteria making up the human GI microflora could be caused by antibiotic use and was in fact linked to increased risk of GI infection [15-18]. Treatment with anti-anaerobe antibiotics has been shown to result in both reductions in the concentration of intestinal microflora (“good bacteria”) as well as increased pathogenic bacteria (“bad bacteria”) such as vancomycin-resistant enterococcus (VRE), antibiotic resistant E. coli, and Clostridium difficile [18-21]. Based on these findings, research has increasingly been directed at providing exogenous bacteria in order to facilitate restoration of the normal gut flora [22]. Lactobacillus acidophilus is one such probiotic that is often administered to support a healthy gut microbiota. The DDS-1 strain of L. acidophilus has been shown to successfully colonize the GI tract, providing a potential for increased gut immune health in the face of antibiotic therapy [23]. The DDS-1 strain has been shown in one preclinical study to reduce antibiotic-associated bacterial grown in-vitro [24].

From Microflora to Probiotics

The use of cultured bacteria such as L. acidophilus to support improved GI health has been popular long before scientific studies were performed. Yogurt, a common source of L. acidophilus has long been promoted for the perceived health benefits of the bacteria it contains [25]. These bacteria are called probiotics, which are defined by the World Health Organization (WHO) as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host” [26]. Research directed at the benefit of probiotics such as L. acidophilus focuses on the ability of the ingested bacteria to colonize the GI tract and on potential benefits such as aiding in metabolism, immune support, and nutrient synthesis [3, 4]. Recent studies have also evaluated the role of these probiotics, including the DDS-1 strain of Lactobacillus acidophilus, in relieving common GI symptoms such as bloating, diarrhea, and flatulence. Of note, clinical research on the efficacy and colonization of probiotics is often conflicting due to the high variability in strain selection, dose, and delivery vehicles of the numerous probiotics in the market today [27]. For this reason, a purified strain that has been shown to both successfully colonize and improve symptoms in humans is of critical value.
DDS-1 strain of *L. acidophilus* has been shown in humans to both colonize the gastrointestinal tract as well as improve symptoms of diarrhea, cramping, and vomiting [23, 28].

**LACTOBACILLUS OVERVIEW**

*Lactobacillus acidophilus*

*Lactobacillus* is a genus of rod-shaped, gram-positive, lactic acid-producing bacteria belonging to the phylum Firmicutes [29]. Lactic acid production occurs through fermentation of carbohydrates, with lactic acid as the primary end-product [14]. *Lactobacillus acidophilus* is a species of *Lactobacillus* that was first isolated from feces in 1900 and known to ferment various carbohydrates including lactose, glucose, N-acetylglucosamine, and fucose [29, 34]. *Lactobacillus* species are popular in food supplements, commercial foods, and in research, with its popularity largely due to its widespread use in foods such as yogurt.

In contrast to autochthonous species of *Lactobacillus* such as *L. reuteri* and *L. mucosae*, *L. acidophilus* is an allochthonous species that only colonizes the GI tract after exogenous consumption [23, 35]. *L. acidophilus* may be found in various food products, including wine, milk, meat, fruits, vegetables and cereal grains [36]. It is also commonly added to dairy products, most commonly yogurt [37].

*L. acidophilus* is widely available in numerous formulations and strains, leading to high variations in product quality and efficacy. A recent study assessing both the accuracy of probiotic labeling and actual bacterial content found that only 2 of 25 evaluated products were of acceptable quality [38].

“*There are numerous L. acidophilus products on the market today, many of which have not been evaluated in clinical studies and may be of unacceptable quality.*”

**DDS-1**

The DDS-1 strain of *Lactobacillus acidophilus*, discovered in 1959 by Dr. Khem Shahani at the University of Nebraska, is a unique strain of *L. acidophilus* on deposit with the FDA Agricultural Research Service (ARS) with the catalog number B-3208. It is known to have a high tolerance to acidity, making it ideal for passage through the stomach and into the bowel where it can colonize. It is currently manufactured by Nebraska Cultures, Inc. A recent study compared *L. acidophilus* to autochthonous species *L. reuteri* and *L. mucosae* in the ability to colonize the human GI tract. All three organisms were found to successfully colonize the GI tract, as quantified by assessment of fecal samples [23]. Naturally, the autochthonous species demonstrated higher quantities in fecal stool compared with *L. acidophilus*, and only one of the twelve human subjects was found to have detectable bacteria 8 days after the end of consumption. These findings indicate that while these probiotics successfully colonize the GI tract, even preparations of autochthonous species must continue to be consumed on a regular basis to ensure persistence in the gut.

**Common uses of Lactobacillus Acidophilus**

The intrinsic benefits of the intestinal microflora
primarily involve (1) delivery and production of essential nutrients and amino acids such as folate and vitamin K; (2) breakdown of dietary components not otherwise digestible by endogenous human enzymes; (3) protection against pathogenic bacteria such as *C. difficile* and *Enterococcus*; and (4) support of host immunity through stimulation of immunomodulatory signals by gut epithelium [39-42]. Another major function of intestinal microbia is the breakdown of unabsorbed dietary sugars such as lactose, and conversion into short-chain fatty acids [2]. Probiotic supplements have been marketed to support similar aspects of GI health.

**Gastrointestinal Colonization**

As noted above, there is a lack of strong evidence supporting long term colonization of exogenous sources of *Lactobacillus* after discontinuation of consumption, even for autochthonous species [23]. This is likely related to resistance from the endogenous bacteria, which while it may be the same species, has developed characteristics specific for the individual person in which they are endogenous. This concept is loosely analogous to organ or bone marrow transplantation, as while all humans are the same species, individual differences even between first-degree relatives lead the body to recognize the new organ as foreign. At this time, our knowledge of the specific bacteria-host interactions that lead to successful colonization is not entirely clear. Interestingly, a recent study evaluating consumption of *Lactobacillus casei Shirota* and *Bifidobacterium breve Yakult* for 4 weeks found beneficial effects of consumption persisted 3 months after discontinuation of the probiotic blend [43]. Although the study did not assess fecal samples, these findings suggest the benefits of probiotic consumption may persist, regardless of successful long-term colonization.

**LACTOSE MALDIGESTION AND LACTOSE INTOLERANCE**

**Lactase Non-Persistence**

Lactose is a disaccharide sugar consisting of glucose and galactose, and is a key source of calories and carbohydrates in milk and other dairy products [44-46]. Lactase is an endogenous enzyme critical in breaking down lactase into glucose and galactose. Lactase activity is found in the human fetus as early as 8 weeks gestation and reaches its peak at birth in preparation for metabolizing breast milk [47]. After termination of breastfeeding, lactase concentration in the gut begins to naturally decline, representing a normal physiologic process known as lactase non-persistence [47, 48]. As this is a normal human process, lactose non-persistence is asymptomatic, with GI symptoms seen only at doses greater than 25 grams (about two cups of whole milk) per day.

**Lactose Malabsorption**

While lactose non-persistence is considered a normal physiologic process, in some individuals the levels of lactase may decline to a point at which digestion of normal amounts of lactose is impaired. *Lactose malabsorption* is a condition characterized by decreased presence of lactase in the GI tract, resulting in impaired digestion of as low as 12-15 grams of lactose (about one cup of whole milk) [48]. Lactase tolerance is highly variable among individuals. Options for objective testing lactose malabsorption include biopsy of the small intestine mucosa (maldigesters show activity below 17-20 IU/g), genetic testing, blood glucose measurements after lactose consumption (i.e., the lactose tolerance test), and the “gold standard”, the hydrogen breath test (HBT) [49][50, 51] [52]. HBT evaluates the concentration of hydrogen (H2) in exhaled breath following the consumption of lactose. Increased breath hydrogen indicates bacterial digestion of lactose due to insufficiency of the lactase enzyme.

**Lactose Intolerance**

*Lactose intolerance* is defined as the presence of GI complaints (e.g. abdominal pain, bloating, cramps, flatulence) in the setting of lactose malabsorption [45, 46]. Thus in order to have lactose intolerance,
it is required to have lactose malabsorption. However those with malabsorption may not necessarily have lactose intolerance [53]. Symptomatology is both subjective and variable, with factors that affect GI symptoms including the amount of lactose ingested, lactase enzymatic activity, gastric and intestinal transit, and GI microflora composition [44, 54]. As such, individuals with lactose intolerance commonly retain a small amount of residual lactase activity, and can typically tolerate up to 12 grams of lactose (equivalent to an 8-ounce cup of whole milk) without developing GI symptoms[55, 56].

Conventional management of lactose intolerance aims to reduce GI symptoms of lactose intolerance. The first-line approach involves simply restricting ingested lactose by limiting dietary dairy intake [57-59]. Interestingly, symptoms of lactose intolerance are only triggered when lactose is consumed as part of dairy, and are well tolerated when lactose is consumed in pill form [60]. Thus, avoidance of medications that come in the form of lactose-containing pills is not recommended.

Lactase enzymes are also commercially available and have been shown to improve both GI symptoms as well as markers of lactose malabsorption, such as measured by HBT [61]. Interestingly, while both HBT results and symptoms were seen to improve after enzyme consumption, HBT results did not directly correlate with symptom improvement [62].

**Lactobacillus acidophilus and Lactose Intolerance**

Lactic acid bacteria have long been studied for their ability to cleave carbohydrates and potentially aid in digestion. Yogurt has been a dairy product of interest due to its tolerability among otherwise lactose intolerant individuals, which is believed to be related to the potential enzyme activity of lactic acid bacteria (LAB) such as *L. acidophilus* and *L. bulgaricus* [63-67]. *L. acidophilus* strains, such as those found in yogurt are now commercially available, with growing empirical evidence supporting their use in ameliorating GI symptoms among those with lactose intolerance. *L. acidophilus* maintains the characteristic ability of lactic acid bacteria to withstand highly acidic environments, allowing it to pass through the stomach and into the colon. This is thought to provide a superior delivery system of enzymatic lactase activity to the gut when compared to synthetic lactase pills. The DDS-1 strain of *L. acidophilus* is specifically formulated to withstand highly acidic environments in order to ensure optimal delivery. Clinical research supporting the use of probiotics, including the DDS-1 strain of *Lactobacillus acidophilus*, are described below.

**PRECLINICAL EVIDENCE**

Numerous preclinical studies have been performed to evaluate probiotic colonization and the effects on lactose digestion. An in-vitro study investigated six strains of lactic acid bacteria (*L. acidophilus*, *L. plantarum*, *L. fermentum*, *L. reuteri*, *Strep. thermophilus* and *Leuconostoc mesenteroides subsp. cremoris*) for the ability to digest human milk oligosaccharides and galactooligosaccharides. The study found that *L. acidophilus* ferments lactose, glucose, N-acetylglucosamine, and fucose in vitro [34]. Another in-vitro study evaluated the ability of *L. acidophilus* to colonize on human GI mucosa and whether this affected lactose digestion [68]. The *L. acidophilus* strain resulted in a significant decrease in lactose concentration compared with the control group. One animal study fed yogurt to rats and measured galactose in the blood in order to evaluate lactose absorption [69]. The authors found increased intestinal lactase activity as well as viable cultured microflora in the stool, suggesting that bacteria in yogurt may be able to colonize the gut and provide improvement in digestion of lactose.

An in-vitro analysis of six strains of *L. acidophilus* was performed and found several differences between strains with regard to beta-galactosidase activity and surface layer proteins involved in attaching the GI mucosa [70]. This brings up an important point that not all strains of *L. acidophilus* are equivalent,
which likely contributes to the high variability of clinical data as described below.

The DDS-1 strain – Preclinical Studies

With regard to the DDS-1 strain, a recent study by Frese et al. evaluated fecal stool samples after administration of three species of *Lactobacillus* (*L. acidophilus* DDS-1 strain, *L. reuteri*, and *L. mucosae*) [23]. While the autochthonous species *L. reuteri* and *L. mucosae* demonstrated superior colonization, all three organisms were found to successfully colonize the GI tract, including the DDS-1 strain of *L. acidophilus*. An in-vitro study found that investigating the effect of the DDS-1 strain of *L. acidophilus* resulted in reduced pathologic transformation of bile acids, suggesting support for a healthier gastrointestinal tract [71]. These findings were further corroborated by an animal study on rats [72]. A follow-up study by the same group found increased production of immune modulators such as interleukin-1 and tumor necrosis factor-alpha was stimulated by DDS-1 [73].

Another in-vitro study found a growth-inhibitory effect of the DDS-1 strain on growth of *Helobacter pylori*, a common gastrointestinal pathogen [24]. DDS-1 has been suggested to support improved oral mucosal health as well through an in-vitro study evaluating the role of DDS-1 against oral streptococcus biofilms [74].

**CLINICAL EVIDENCE**

**Diarrhea**

Clinical studies on probiotics center primarily on gastrointestinal conditions. One common condition noted in the literature is antibiotic-associated diarrhea (AAD). Antibiotics targeted against anaerobic pathogens can lead to the loss of intestinal microflora, which is also primarily anaerobic [16, 17].

This loss of the natural bacterial populations in the gut can result in impaired intestinal absorption and increased risk to pathogenic GI infection [15]. Probiotics have been introduced to potentially counteract the destructive effects of systemic antibiotics on GI flora, however clinical evidence has yielded mixed results. One large-scale multicenter randomized-controlled trial found no benefit of *L. acidophilus* in the prevention of AAD [75]. Another randomized study evaluating the role of *L. acidophilus* and *Bifidobacterium* on AAD found that although there was no significant change in the rate of AAD, the duration of diarrhea symptoms improved [76].

Probiotics have also been studied in patients with diarrhea from causes other than antibiotics. One study evaluated the use of *Lactobacillus* on mild acute diarrhea in children and found a shorter duration of diarrhea in the *Lactobacillus* group compared to the placebo group [77]. A randomized-controlled trial of 71 infants with acute watery diarrhea found shortened duration of diarrhea among those consuming *L. acidophilus* plus *Bifidobacterium infantis* [78].

**Lactose Maldigestion and Lactose Intolerance**

Numerous clinical studies have evaluated the role of probiotics on lactose maldigestion and intolerance. A summary of all clinical trials on *L. acidophilus* and related strains on lactose maldigestion and intolerance is provided in Table 1. Pertinent studies on *L. acidophilus* are described below.

One open-label study was on healthy men and women who were provided single doses of milk, yogurt, heated yogurt, yogurt with lactose, heated yogurt with lactose, sweet acidophilus milk (SAM), and sonicated SAM [79]. Both heated and non-heated yogurt demonstrated superior breath hydrogen testing compared with milk. Additionally, sonicated SAM resulted in improved HBT scores compared with plain SAM, indicating that cell lysis may cause release of intracellular lactase from the probiotic bacteria. A similar study found that yogurt and milk with hydrolyzed lactose resulted in improved
HBT compared with other milk formulations [80]. A randomized trial comparing plain milk to combinations of milk with four different L. acidophilus strains found variations in lactose digestion and tolerance among all four strains, yet all were superior to plain milk. This again reiterates the wide variations in formulations of the same species of L. acidophilus.

Studies have yielded mixed results on the efficacy of probiotics in improving HBT scores or improving abdominal symptoms [54, 81-83]. A study comparing plain milk to milk containing L. acidophilus found lactase-deficient patients were as intolerant to acidophilus milk as to unaltered milk [84]. Another randomized trial of 24 lactose intolerant subjects who were administered the BG2FO4 strain of L. acidophilus daily for 7 days found the probiotic to be present in stool samples after 7 days, yet no change was seen on breath testing [82].

The reasons for these variations are multifactorial. Subjective symptom scores are not only highly variable, but may also have conditions unrelated to lactose maldigestion causing their symptoms. Additionally, as noted above, the high variability of strains within the same species as well as variability in the quality of each probiotic preparation play a key role in efficacy. Individual differences in human colonic mucosa may affect the ability of certain strains to colonize the intestinal tract. This is further demonstrated by the study described earlier that assessed both the accuracy of probiotic labeling and actual bacterial content, noting that only 2 of 25 evaluated products were of acceptable quality [38].

The DDS-1 strain – Clinical Studies

The DDS-1 strain is a unique strain of Lactobacillus acidophilus discovered by Dr. Khem Shahani at the University of Nebraska in 1959. A recent single-blind, crossover study of twelve subjects revealed that Lactobacillus acidophilus DDS-1 persisted in the GI tract 1 day after consumption, indicating that the strain survived gastric passage [23]. Another study on intestinal colonization of probiotics using a variety of probiotic blends that contain DDS-1 (Flora Renew, Traveler’s Relief, Daily Balance, and Kids Probiotic) also demonstrated survival and colonization of DDS-1 in the GI tract [85].

We recently published results on a randomized, double-blind placebo-controlled crossover trial comparing the DDS-1 strain of Lactobacillus acidophilus to placebo with regard to GI symptoms of bloating, abdominal cramping, diarrhea, vomiting, and increased bowel sounds [28]. The study found improved symptom scores for diarrhea, vomiting, and overall symptoms in response to a lactose challenge. Although no significant changes were observed for HBT, the DDS-1 strain of Lactobacillus acidophilus can help improve GI symptoms of lactose intolerance such as diarrhea, abdominal cramping, and vomiting. Longitudinal comparison between the DDS-1 and placebo group demonstrated a statistically significant difference at week 4 in the diarrhea symptom score (p=0.033; 1.34 in the active group compared to 1.69 in the placebo group), as well as abdominal cramping (p=0.012; 1.94 compared to 2.39 in the placebo group), vomiting (p=0.002; 0.08 compared to 0.36 in the placebo group), and overall (p=0.037; 9.28 compared to 10.51 in the placebo group). As noted earlier, previous studies have demonstrated that improvement in GI symptoms may occur in the absence of changes in HBT [62]. The lack of significant effects on HBT further establishes that lactose malabsorption and lactose intolerance carry some degree of mutual exclusivity, as noted by the Saltzman et al. study described above [28, 82].

The DDS-1 strain has also been shown in a randomized, controlled trial to result in improved symptoms of atopic dermatitis (i.e., eczema) [86]. The study found reduced subjective symptom scores, reduced duration of steroid use, and corresponding lymphocyte changes among the group of children administered a mixtrure of L. acidophilus DDS-1, B.
BACTERIOLOGY, COLONIZATION, AND CLINICAL EFFICACY OF DDS-1 LACTOBACILLUS ACIDOPHILUS

A WHITE PAPER

lactis UABLA-12, and fructo-oligosaccharide, when compared to placebo. These findings support the potential immune benefits of DDS-1 as shown in the in-vitro studies described above [71-73].

Safety & Adverse Events

Theoretical risks for ingestion of commercially developed probiotics include infectious infiltration of the ingested bacteria, development of antibiotic resistance to gut microbial, and potential adverse changes in immune function [87].

While Lactobacillus bacteremia and sepsis have been reported, these cases are rare and almost exclusively associated with severely ill or an immunocompromised health status [88-90].

A recent prospective study administered the 821-3 strain of Lactobacillus acidophilus DDS-1 to 9 individuals

L. ACIDOPHILUS DDS-1 CLINICALS

Our Lactobacillus acidophilus DDS-1 shows reduction in symptoms of lactose intolerance.

18.8% : 77.8% : 20.7%

REDUCTION IN ABDOMINAL CRAMPING

REDUCTION IN VOMITING

REDUCTION IN DIARRHEA

OVERALL SYMPTOMS

A systematic review of adverse event data associated with consumption of probiotics found 387 studies on human consumption of probiotics. Overall, the authors found that the studies reviewed did not report significantly increased risk of adverse events associated with probiotic consumption [91].

Another systematic review of adverse events related to L. acidophilus consumption reported no significant adverse events, however the authors contended that this was due to limited reporting of data on adverse events in the literature and that further research is required to determine the safety of L. acidophilus consumption [92].

Specific symptom results of L. acidophilus DDS-1 Clinical Trials
CONCLUSION
The GI microflora forms naturally as part of human development and is essential in providing nutrients, supporting healthy metabolism, and protect from pathogenic infections. Based on this, commercially available bacteria have been developed to help promote healthy intestinal bacterial colonies. Lactobacillus acidophilus is a lactic acid producing anaerobic bacteria most commonly found in vaginal mucosa, which is commonly consumed in dairy products as well as in individual preparations. Both the efficacy and the ability of L. acidophilus to successfully colonize the GI tract are highly variable, with factors affecting successful colonization including the architecture of each individual’s mucosa, individual diet, and the quality of the specific L. acidophilus strain. Because of this, clinical research has yielded highly variable results. The DDS-1 strain of L. acidophilus has been demonstrated to successfully colonize the GI tract in humans as well as result in improved GI symptoms in response to lactose challenge.

ACKNOWLEDGMENTS AND STATEMENT OF AUTHORS’ CONTRIBUTIONS TO MANUSCRIPT
Pakdaman Consulting has ongoing research support grants from Nebraska Cultures, Inc., Walnut Creek, CA. Dr. Pakdaman has provided consulting services to Nebraska Cultures, Inc. The authors of this study do not endorse any brand or product.

SOURCES OF FINANCIAL SUPPORT
This review was conducted independently by Michael Pakdaman MD, under the sponsorship of Nebraska Cultures, Inc. Nebraska Cultures was not involved in the formulation, conceptualization, or write up of this review.

Michael Pakdaman is affiliated with Pakdaman Consulting, Inc., an independent research organization that was funded by Nebraska Cultures for preparation of this manuscript. Michael Shahani is affiliated with Nebraska Cultures. Mr. Shahani’s involvement in the manuscript involved description of the study product preparation. Mr. Shahani was not involved in literature review or discussion.
REFERENCES

BACTERIOLOGY, COLONIZATION, AND CLINICAL EFFICACY OF DDS-1 LACTOBACILLUS ACIDOPHILUS

A WHITE PAPER


