Review of scientific evidence for efficacy of Lactobacillus acidophilus DDS-1 as a probiotic strain

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INTRODUCTION

For more than 25 years, Lactobacillus acidophilus DDS-1 strain has been marketed commercially worldwide as an effective probiotic strain. It has been the subject of a variety of in vitro, human and animal studies for more than 40 years. The focus of the efficacy research on this strain has been on its nutritional, anti-bacterial and anti-pathogenic, anti-carcinogenic and technological properties. At the same time, the microbiological and technological properties of DDS-1 have been studied.

IDENTITY

Lactobacillus acidophilus DDS-1 is a unique endogenous human strain extensively researched at University of Nebraska and is protected by US patent, and commercially manufactured and trademarked by UAS Laboratories. The morphological and cultural characteristics of Lactobacillus acidophilus DDS-1 have been determined in order to confirm the genus and species of the isolate called “Acidophilin”22,26. When grown in skim milk, the organisms were found to be Gram positive rods 0.6 to 0.9Hm by 1.5 to 6.0Hm, occurring singly, in pairs and in variable dimension short chains with rounded ends. These organisms were non-motile. Optimum growth temperature was 37°C and no growth occurred below 22°C or above 45°C. Further, this culture was observed to be microaerophilic and produced acid from glucose, galactose, fructose, lactose, sucrose, mannose and maltose. It had the ability to grow in acidic media and could ferment amygdalin, cellubiose and salicin. Raffinose, trehalose and dextrin were fermented very slightly. Xylose, arabinose, rhamnose, glycerol, mannitol, sorbitol, dulcitol and inositol were not fermented. Additionally, the organism grew in tomato juice both containing 2% NaCl or bile salts but not in broth containing 4% NaCl or bile salts. These characteristics are attributable to L. acidophilus and thus confirmed the identity of the isolate DDS-1.

NUTRITIONAL EFFECTS

DDS-1 produces enzymes such as proteases and lipases, which can help with the breakdown of protein and fats. Acidophilus milk (both fermented and unfermented) containing DDS-1 was shown to have a higher protein digestibility than heated milk when tested in rats11. However, ability of these enzymes produced in situ to improve digestion has not been documented. Cultured dairy products fermented with DDS-1 had higher levels of folic acid and vitamin B1218, suggesting the metabolic ability of this strain to produce some B vitamins.

Cholesterol lowering effect of DDS-1 has been demonstrated early24. Whether fermentation of milk by lactic cultures increases its anticholesteremic activity needs to be investigated further. Nevertheless, based upon his preliminary studies, Sinha reported that even unfermented sweet acidophilus milk demonstrated such an activity. He observed that feeding milk to rats had little or no effect upon their serum cholesterol while incorporation of cholesterol in the diet increased serum cholesterol. The addition of 4 million L. acidophilus DDS-1 cells per milliliter of milk lowered cholesterol significantly.

Traveler’s diarrhea: The effect of Lactobacillus acidophilus DDS-1 supplementation on traveler’s diarrhea was studied by Senhert20 during 1987-1989. Seventy persons participated in three studies. Each person received 2 DDS-100 Acidophilus capsules (UAS Labs) containing Lactobacillus acidophilus DDS-1 at the rate of 2 billion CFU per gram (2 capsules) before breakfast for a week before their trip and during the entire period of the trip to Guatemala, Mexico and Nepal. Lactobacillus acidophilus DDS-1 provided substantial protection against traveler’s diarrhea to the individuals who received this supplement. Only two reported digestive disorders. The usual incidence on such trips is 25 to 30%.

BILE AND ACID TOLERANCE

Bile tolerance has been considered to be an important characteristic of Lactobacillus acidophilus that enables it to survive, grow, and exert its action in the small intestine27. Strains that are able to grow and metabolize in the presence of physiological levels of bile should logically be more likely to survive intestinal transit19. Studies have shown that the DDS-1 strain is capable of growing in bile concentrations of up to 3%. An in vivo study demonstrated that the DDS-1 strain survives in
the presence of human gastric juice.

In a preliminary study, Peterson\textsuperscript{16} fed 2 capsules containing 2x10\textsuperscript{10} CFU/gm \textit{L. acidophilus DDS-1} to 10 patients for three weeks and examined the stool before and after feeding. He reported a 100 fold increase of \textit{L. acidophilus} in the stool after \textit{L. acidophilus DDS-1} feeding of the patients. This demonstrates the survival of DDS-1 and its implantation and multiplication in the intestine.

**IMPACT ON FECAL MICROECOLOGY**

The impact of feeding DDS-1 on the microflora and enzyme activities in feces of human subjects was determined\textsuperscript{2}. Low fat milk (3 – 8 oz glasses/d) with or without other blood assessments were different. These results suggest group had a statistically high hematocrit than treated, but no difference in colonic region of the stomach were observed. The control observed with conventional animals, except higher levels in the treatment groups. No difference in fecal lactobacilli was observed in different tissues were observed between control and inoculated intragastrically with \textit{DDS-1}. Results of the fecal microbiology analysis indicated that there was no change in total aerobic flora and no consistent change in coliforms. However, total lactobacilli increased by 1-2 logs. Enzyme activity assessment showed no consistent changes in \(\beta\)-glucosidase or \(\beta\)-glucuronidase activities. These results demonstrate that consumption of DDS-1 can increase levels of fecal lactobacilli.

Two trials were conducted to determine the impact of DDS-1 on physiological markers in germ-free and conventionally colonized pigs\textsuperscript{15}. In the first trial, the effect of oral administration of DDS-1 (2x10\textsuperscript{11} per day for 3 consecutive days) on 5-day old germ-free pigs was determined. Three pigs were sacrificed from the control and test groups 3, 5, 7 and 9 days after DDS-1 administration. Blood and tissue (from seven gastrointestinal sites: 2 stomach sites, duodenum, jejunum, ileum, cecum and colon) were collected. Blood was evaluated for red and white cell counts, hematocrit, serum albumin, serum globulin and urea nitrogen. Tissue was evaluated for the presence of lactobacilli. DDS-1 consuming pigs had higher \textit{L. acidophilus} counts than the controls, with concentrations the highest in the large intestine. Increased counts were maintained through 9 days post DDS-1 feeding. However, the colonic contents were not separated from the tissue, so conclusions on association of the lactobacilli with the tissue cannot be made. No impact of DDS-1 feeding on serum proteins, urea nitrogen, hematocrit or red blood cell counts was observed. White blood cell counts increased. In the second trial with conventional animals, pigs at 2 days of age were inoculated intragastrically with DDS-1 or sterile water. All parameters for the first trial were included in the second trial in addition to assessment of weight gain and addition of coliform counts on tissues. Small to no differences in Lactobacillus levels in different tissues were observed between control and treatment groups. No difference in fecal lactobacilli was observed with conventional animals, except higher levels in the cardiac region of the stomach were observed. The control group had a statistically high hematocrit than treated, but no other blood assessments were different. These results suggest mild effects of a three-day feeding regime in a conventional pig model. The short duration of the feeding regime likely contributed to these findings.

**ANTIBACTERIAL AND ANTIPATHOGENIC EFFECTS**

A compound with antibacterial properties is produced by DDS-1. Named ‘acidophilin’, this compound was isolated from milk in which DDS-1 was grown. Other \textit{L. acidophilus} strains did not produce significant amounts of this compound. Once dried, this milk was extracted with methanol, acetone and subjected to column chromatography. Active fractions were concentrated and tested using an agar zone inhibition assay against some common food-borne pathogens. Activity against \textit{Bacillus subtilis}, \textit{Clostridium botulinum}, \textit{clostridium perfringens}, \textit{Escherichia coli}, \textit{Proteus mirabilis}, \textit{Salmonella enteritidis}, \textit{Salmonella typhimurium}, \textit{Staphylococcus aureus} and \textit{Staphylococcus faecalis} was observed\textsuperscript{22,23}. As an important follow up to this in vitro demonstration of activity, Zychowicz\textsuperscript{26,30} demonstrated the effectiveness of acidophilus milk on decreasing the carrier state and on the incidence and duration of \textit{Salmonella} and \textit{Shigella} dysentery in children.

The ability of DDS-1 to inhibit \textit{Staphylococcus aureus} was further demonstrated. \textit{S. aureus} growth was inhibited in acidophilus yogurt likely due to a combination of activity of hydrogen peroxide, lactic acid and bacteriocin\textsuperscript{1}.

More recently, Yasmin et al.\textsuperscript{28} reported the ability of DDS-1 to inhibit in a co-culture assay \textit{Helicobacter pylori} at ratios of 1:1 through 1:1000 (\textit{L. acidophilus DDS-1:H. pylori}) or higher. The mechanisms and in vivo impact are subjects for further study.

There is growing evidence suggesting that probiotics can be effective in the prevention of recurrent urinary tract infection (UTI). The proposed mechanism of action includes inhibition of growth and adhesion of pathogens at the vaginal and urethral mucosa before ascension of these pathogens into the bladder\textsuperscript{25}. In a case study, \textit{L. acidophilus DDS-1} with two billion viable organisms was given twice daily for a month and followed up with once daily to patients. It showed positive effects\textsuperscript{8}.

**Effect on Candida albicans**: Lactobacilli have been reported to produce hydrogen peroxide\textsuperscript{4}. \textit{Lactobacillus acidophilus DDS-1} is a producer of hydrogen peroxide\textsuperscript{7}. Several researchers have suggested that Lactobacilli may be used to supply hydrogen peroxide–thiocyanate anti-microbial system\textsuperscript{6,10,13}. Evidence has been presented that thiocyanate is involved in the inhibition of candida albicans by certain strains of Lactobacillus acidophilus\textsuperscript{9}.

In a case study at a primary health care clinic, Senhet\textsuperscript{20} provided \textit{Lactobacillus acidophilus DDS-1} at the rate of 4 billion CFU/gm daily to 42 patients for a period of three months and reported improvement in 22 cases.
ANTICARCINOGENIC EFFECTS

The anti-tumorogenic properties of DDS-1 were tested in a rat model of chemically induced colon tumors. A standard diet supplemented with DDS-1 was fed to a group of rats injected subcutaneously with N-nitrosobis (2-oxopropyl) amine to induce tumors. Tumor incidence was assessed at 26 and 40 weeks. At 26 weeks, the DDS-1 fed rats demonstrated a statistically significant reduction in tumor incidence, ornithine decarboxylase activity and metaphase arrest per crypt per hour compared to the control group. At 40 weeks, tumors in the DDS-1 group were fewer and smaller than in the control group. These results suggest that DDS-1 may delay the initiation process of chemically induced colon tumors in rats.

Methanol-acetone and silica gel fractionation extracts of DDS-1 were also evaluated in vitro against the KB-line and Hi-line of cancer cells in tissue culture and in a mouse model of Sarcoma-180. Morphological changes and growth inhibition of the KB cell line was observed in vitro and specific inhibitory activity was observed against Sarcoma-180 cells.

The mechanism of DDS-1 induced suppression of tumors was evaluated. Using a mouse macrophage cell line, investigators determined that DDS-1 was able to stimulate the production of immune components (interleukin-1α and tumor necrosis factor-α) that are known killers or inhibitors of tumor cells. DDS-1 performed this function better than three other strains of L. acidophilus (NRRL 0734, NRRL 6934, NRRL B4527) or Bifidobacterium bifidum (strain not designated). Interestingly, the effect was also observed with heat-killed DDS-1.

TECHNOLOGICAL PROPERTIES

With the incorporation of a patented technology from University of Wisconsin/WARF into the manufacturing of Lactobacillus acidophilus DDS-1 (UAS Labs) culture, L. acidophilus DDS-1 is stable for up to two years at ambient temperature (23°C) when blended with a recommended excipient such as low water activity microcrystalline cellulose. Stability of L. acidophilus DDS-1 was tested. L. acidophilus DDS-1 was combined with Bifidobacterium longum at equal ratio and fortified with fructooligosaccharide at five percent rate. This supplement called DDS-Plus manufactured by UAS Laboratories was tested for potency every month for 12 months using the Standard Methods for Dairy Products. The stability curve shows that L. acidophilus DDS-1 is very stable and the loss of potency was about 7% in one year.

SAFETY

Lactobacillus acidophilus DDS-1 has been consumed by humans as a dietary supplement or in dairy products for over 3 decades with no adverse effects. The species of L. acidophilus is recognized internationally as a safe microorganism.

Note: UAS Laboratories, 9953 Valley View Road, Eden Prairie, MN 55344, USA is the commercial manufacturer of Lactobacillus acidophilus DDS-1 and the owner of US Trademark DDS/DDS-1
REFERENCES


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