Probiotics Beneficial Even When Inactive, According To UCSD Study

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Sue Pondrom Probiotics, the trendy "good bacteria" found to aid disorders such as Inflammatory Bowel Disease (IBD), allergies and even some forms of cancer, contain immune system-stimulating DNA which makes them just as effective when inactivated, as when consumed as live microorganisms in dairy products such as yogurt.

Reported in the February 2004 issue of the journal *Gastroenterology* by researchers at the University of California, San Diego (UCSD) School of Medicine and the Shaare Zedek Medical Center in Jerusalem, Israel, the findings offer the potential to use inactivated probiotics in food products. In addition, the study provides a mechanism to determine and to select which probiotic bacteria are best for patients with IBD.

A probiotic is a bacterial organism that contributes to the health and balance of the intestinal tract. Although recent medical studies have proven the therapeutic benefit of these good bacteria, their use dates back thousands of years. People in ancient Babylon, for example, used sour milk to alleviate gastrointestinal problems.

Although the effectiveness of these bacteria has been attributed to their live, metabolic activity, viable probiotics can't be added to food because they induce fermentation, changing the taste, texture and freshness on an hourly basis. For that reason, the bacteria have only been used in a very narrow range of products such as yogurt.

"Our goal was to address whether the metabolic activity of probiotics was mandatory for their protective effect," said the study's senior author, Eyal Raz, M.D., professor of medicine at UCSD. Raz noted that previous studies had tried heat killing of probiotics to inactivate them, but this process destroyed the cellular structure and beneficial aspects. In the new experiments, the team used gamma radiation on the bacteria, reducing metabolic activity to a minimum.

Next, the team administered the irradiated probiotics to mice with experimentally induced colitis, which is similar to human IBD. The irradiated probiotics effectively ameliorated the colitis, as did the administration of viable, "live" bacteria to another group of mice with colitis. This indicated that inactivated probiotics were as effective as live probiotics.

The team reasoned that the beneficial, anti-inflammatory activities seen with the inactivated probiotics could be the product of the innate immune system, the body's instant response to invasion by pathogens. Specifically, the researchers looked at molecules called toll-like receptors (TLR) that are known to respond to a variety of signature microbial molecules. In order to determine which TLR responded to probiotics, the team administered a chemical called chloroquine to mice deficient with several different TLRs. Chloroquine had recently been demonstrated to inhibit TLR9 activation, and it was only in the TLR9-deficient mice that the probiotics were ineffective in alleviating colitis.

In addition to studying the normal and irradiated probiotics on mice, the researchers tested a synthetic form of bacterial DNA called immunostimulatory (ISS) oligonucleotide (ODN), a short segment of synthetic DNA with immunostimulatory properties, which mimics bacterial DNA. In a previously published paper in *Gastroenterology**,

ISS-ODN had been found to reduce the harmful effects of experimental colitis in mice, indicating that it worked in a manner similar to probiotics.

According to the study's first author, Daniel Rachmilewitz, M.D., Division of Medicine, Shaare Zedek Medical Center, evaluation of the immunostimulatory activities of probiotics may also provide an easy screening system for the selection of probiotic bacteria prior to their clinical use.

In another portion of the study, the team also demonstrated that probiotics and ISS-ODN could be administered either orally or subcutaneously.

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