

EDITORIAL

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# **Probiotics and Women's Health**

### Introduction

The term probiotic was derived from the Greek word, meaning for life. The concept of probiotics is very ancient. Mention of cultured dairy products is found in the Bible and the sacred book of Hinduism. Soured milk and cultured dairy products such as kefir, kourniss, leben and dahi were often used therapeutically before the existence of microorganisms was recognized. The use of microorganism in food fermentation is one of the oldest methods for producing and preserving food.

The Nobel Laureate Dr. Elias Metchnikoff, the father of modern immunology, in his book entitled Prolongation of Life, spoke highly about the health benefits of the leutin acid bacteria (LAB) - Lactobacillus bulgaricus and streptococcus hemophilus <sup>1</sup>.

The rationale for using probiotics is that the body contains a miniature ecology of a number of bacteria known as natural flora. The flora can be thrown out of balance by a wide range of circumstances including the use of antibiotics or other drugs, excess alcohol, stress, disease, exposure to toxic substances, and even the use of antibacterial soap. In these circumstances, symbiotic bacteria decrease in number and allow to thrive pathogenic organisms which are detrimental to health.

The Food and Agriculture Organization (FAO) of the United Nations defines probiotics as live microorganisms which when administered in adequate amounts, confer a beneficial health effect on the host . The World Health Organisation (WHO) has outlined certain guidelines for a bacterial strain to be used as a probiotic <sup>2</sup> viz., i) it must be of human organ, ii) it must survive during gastric transit, iii) it must tolerate bile salts, and iv) it must adhere to gut epithelial tissue.

### Microbiology

Currently, there are only a few recognized lactobacilli or bifidobacterial strains which meet WHO and FAO criteria. The most documented strains include L. rhamnosis G.G (Vativ, Finland), L. rhamnosus GR-1 and L. ferment RC-14 (Urex Biotech, Canada), L. casei Shirota (Yahurut, Japan), Lacidophilus NCFM (Rhodia, USA), L. reuten MM-53 (Blogara, Sivder), L. plantarniu 299v (Brobil, Sweden), L. johnsomel LT1 (Nestle, Switzerland), B. lactis BB 12 (Hanse Denmark), and B. longum BB 536 (Morinaga, Japan). In terms of urogenital health only GR-1 and RC-14 have supportive data <sup>2</sup>. The probiotics that are marketed as nutritional supplements and used in foods, such as yogurt, are principally the bifidobacteria species and the lactobacillus species.

#### Pharmacology

The effectiveness of probiotics is related to their ability to survive in the acidic environment of the stomach and the alkaline conditions in the duodenum, as well as their ability to adhere to the intestinal mucosa of the colon and to colonize the colon  $^{3}$ .

Typical doses of probiotics range from one to ten billion colony forming units (CFU), to be taken a few times a week, to maintain their effect on the microecology.

The microrganisms need to be alive when they are consumed and therefore maintaining suitable conditions for their storage and transport before consumption is important. In general, probiotics are well tolerated and do not have any serious side effect, except for flatulence and constipation.

Probiotics may have antimicrobial, immunomodulatory, anticarcinogenic, antiallergeic, antidiarrheal and antioxidant properties. The various mechanisms include chelation of metallic ions, scavenging of reactive organs species, and reduction of bacterial activity <sup>2</sup>.

#### Mechanism of action <sup>4</sup>

Probiotics have multiple modes of action -

- 1) They colonize and adhere to the colon and reinforce the barrier function of the intestional mucosa helping in the management of intestinal infection and food allergies.
- 2) They secrete antimicrobial substances called bacteriocins.
- 3) They incerase the levels of circulating immunoglobulins especially immunoglobulin A in infants infested with rotavorin.
- 4) They enhance the nonspecific immunophagocytic activity of circuiting blood granulocytes.

- 5) They potentiate intestinal immune response to viral infection.
- 6) They increase the frequency of interferon garning and producing peripheral blood monocytes.
- 7) They secrete proteolytic enzymes which digest the bacterial toxins.
- 8) They alter the initiation and or promotional events of the chemically induced tumors by binding to the chemical carcinogen.

### Probiotics in health and disease

Probiotics have a broad scope in general health interventions. They have been used for a wide variety of purposes like managing lactose intolerance, for immunomodulation in chronic inflammatory and infetious conditions, managing oral absorption syndromes, prevention of colon cancer, and for cardioprotection by lowering blood pressure and cholesterol levels. The use of probiotics in obstetrics and gynecology is in early stages of experimentation and study. The major application has been in the treatment of vaginosis, candidiasis, and recurrent urinary tract infection (UTI)<sup>2</sup>.

The recurrent nature of urogenital infection, emergence of multidrug resistant bacteria, and patient dissatisfaction with side effects of drugs need better ways to diagnose, treat, and prevent infection. Alternative strategies like probiotics would be a beneficial treatment option. Lactobacili have been shown to produce biosurfactants and collagen binding proteins that inhibit pathogen adheniousness and displace the pathogens. They also modulate the host immunity by decreasing IL-1 and IL-8 levels which are elevated in bacterial vaginosis (BV). Probiotics also lead to production of cell signaling molecules which down regulate pathogen molecule signal of mucous production which acts as a barrier to antiinflammatory cytokine production.

Studies have shown that absence or depletion of lactobacillus in vagina is one of the main reasons for BV infections and this results in significantly increased risk of HIV as well as gonnorrhoea, chlamydia and Herpes simplex viral infections <sup>5</sup>.

Hallen et al <sup>6</sup> in 1992 were the first to perform a controlled cross over study to examine whether daily ingestion of yogurt containing lactobacillus acidophillus prevents vulvovaginal candidial infection. They proposed that twice a day use of hydrogen peroxide producing 108-9L acidophilus in a product called Vivag for 6 days led to 43% improvement compared to none in the placebo group. Neri et al <sup>7</sup> were the first to achieve favorable results by using intravaginal applications of yogurt to treat woman with BV in the first trimester of pregnancy. Their results indicated that the continous

correction of vaginal pH and lactobacillus flora are crucial for normal regional ecology.

BV has been associated with a 40% increased risk of preterm labor. Reid et al <sup>8</sup> in a placebo controlled study of 64 women reported that oral ingestion of L. rhamnesus GR-1 and L. fermentrum of RC-14 for 60 days resulted in a cure rate of 87.6%. Thus lactobacilus as an adjunct to antibiotics may be helpful in increasing cure rates and preventing recurrence.

Shalev <sup>9</sup> enumerates the following potential pathways by which lactobacillus can reduce the risk of preterm labor –

- i) LRC 14 secrete collagen binding proteins that prevent pathogen adhesion.
- ii) RC-14 and GR-1 adhere to epithelial cells and inhibit pathogen binding and translocations.
- iii) Production of  $H_20_2$  bacteriocino that kill pathogerms.
- iv) Increase in TGF- beta and IL-10 which decreases NO (nitric oxide) synthetase
- v) Degradation of lipids.
- vi) Stimulation of IgA at distant sites.
- vii) Production of conjugated linoleic acid.

As regards recurrent UTI, extensive studies of various lactobacilli strains and of the properties believed to be important for protecting the host, led to the selection of a two strain combination for vaginal use. This includes distal urethral isolate L. rhamnosus GR-1 selected primarily for its antigram- negative activities and resistance to spermicide. More recently L.fermentum B-54 is replaced by RC-14 for antigrampositive local activities and  $H_2O_2$  probiotics. Results from various studies, show that the recurrence rates of UTI can be significantly reduced by using one or two capsules vaginally per week for one year with no side effect of yeast infection.

#### Conclusion

The primary aim of probiotics is to restore the vaginal lactobacilli microflora such that the indigenous lactobacilli recover, and the patient retains some degree of acidic pH and protection against infection. Probiotics are not magic bullets but evidence is accumulating that the use of protein probiotic strains and manipulation of the host's own intestinal and vaginal or urethral microbiota will provide valuable options to help restore and maintain urogenital and intestinal health. Thus daily intake of scientifically selected probiotics would provide natural, safe, and effective means of regulating the fluctuating vaginal flora and thereby lower the risk of infection in healthy and sick women.

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