Probiotics and Immunomodulation

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1. INTRODUCTION

Probiotics are defined as live microbial food supplements that beneficially influence the health of the host (1). Generally, this was considered to occur by improving the microbial balance (2); however, it is becoming increasingly clear that probiotics elicit at least some of their health benefits from immunomodulation. The gastrointestinal (GI) tract fulfills many functions aside from digesting and absorbing nutrients. One of these other functions is the gut hosts a complex mixture of microbes that comprise our resident gut microflora, some of which may play a key role in maintaining human health. Bifidobacterium and Lactobacillus are strongly associated with optimum microbial balance in the gut, and it is for these two genera that the greatest body of evidence for health-promoting properties exists.

Interest in functional foods, particularly the use of probiotics by the general public for maintenance of general health, as well as the prevention of certain chronic diseases (e.g., cancer, diabetes, and allergies), gained momentum during the past decade. The rising cost of medical treatment; the increasing number of patients suffering from “Western diseases,” such as allergies, autoimmune, inflammatory, and gut-related problems; the aging population; and the overall increasing interest of the general population in their own health are all key factors driving the surge of interest in probiotics for health.

Despite that man has consumed fermented food products for thousands of years and there is anecdotal evidence suggesting the health-promoting properties of such products, it is only now that a considerable volume of evidence supporting certain health benefits after the consumption of specific bacterial strains is mounting. The pathway to conclusively demonstrating a health benefit for a probiotic strain in humans is rather slow and arduous. Often, particularly if the bacterial strain to be tested is one not normally consumed by humans, it begins with evidence from animal trials, which aim to support a specific health claim and demonstrate safety of consumption. Conclusive evidence is then sought via a series of carefully controlled human clinical trials. Unfortunately, trials demonstrating the prevention of certain diseases or conditions, for example, traveler’s diarrhea, can be extremely difficult to conduct for numerous reasons. This has added to problems in obtaining documented evidence of the efficacy of certain probiotics and functional foods and adds to the consumer’s confusion, who often must make his or her
purchasing decision based solely on the product’s packaging information. Products are often sold with unsubstantiated or general health claims, and it is becoming increasingly clear in probiotics that all probiotic strains are not created equal. Also, there is controversy concerning the level of consumption of viable probiotic organisms required to confer health benefits in man: levels ranging from $10^6$ colony-forming units (CFU) to $10^9$ CFU at the time of consumption have been suggested, and various minimum standards have been set throughout the world (3,4). Further controversy has arisen after reports that several probiotic products either did not contain the listed species or contained extra species or the levels of viable probiotics were less than one tenth of that stated on the package (5). Because consumers are encouraged to consume probiotics on a daily basis, it is important that information detailing the probiotic strains (including accurate viability counts, dose, delivery medium, and safety) for which specific health benefits have been conclusively demonstrated, be made available to the consumer, as well as to health professionals who are likely to recommend such products.

Probiotics confer an array of health benefits; however, not all are fully proven through rigorous clinical trials. Research supporting the use of certain probiotic strains in the treatment of diarrheal diseases and lactose intolerance are well documented (3). There is also a substantial body of evidence documenting specific probiotic strains’ ability to modulate the immune system, although it is unclear if this translates into disease resistance (6). Data supporting the use of probiotics to control inflammatory diseases, treat and prevent allergies, and prevent cancer are promising, and, no doubt, future research will soon be added in these areas.

2. INTESTINAL MICROFLORA AND THE ONTOGENY OF THE GUT IMMUNE SYSTEM

The GI tract provides a protective barrier between the internal environment and the constant challenge of externally derived food antigens and microorganisms. This includes the control of antigen transport by exclusion of antigens and elimination of foreign antigens, which have penetrated the mucosa, as well as the regulation of antigen-specific immune responses in the gut.

Colonization of the gut with healthy normal microflora, which begins immediately after birth, provides a source of microbial antigens that, along with dietary antigens, aid in the mucosal immune system’s development and maturation. This is supported by observations that the spleen and lymph nodes (secondary lymphoid tissues) in germ-free animals are poorly developed because of the lack of antigenic stimulation (7). The maturation process creates an environment in which inflammatory responses are maintained in a regulated, yet primed, state, hence promoting normal gut-barrier functions (8). Therefore, exposure to bacterial and dietary antigens is essential both for the early education of the immune system and to ensure the development of a balanced immune system.

It is becoming clear that in our effort to sterilize food products and eliminate as many potentially pathogenic bacteria from both our food supply and our environment we have, in fact, also inadvertently eliminated several potentially beneficial bacteria, possibly even decreasing the diversity of bacteria colonizing the gut. In doing so, we have decreased the range of antigens to which our gut is exposed. This lack of exposure to microbial antigens results in inadequate priming of Th1 cell activity, thus leading