


Scientific thoroughness of human studies showing immune-stimulating properties of yogurt

Dear Sir:

We read with great interest the review article “Immunologic effects of yogurt” by Meydani and Ha (1), which was published recently in the Journal. Although these authors agree that there are strong indications that yogurt containing certain probiotics have immunostimulatory effects, they argue that most of the studies that substantiated this evidence lacked thoroughness and that the data from these studies were often misinterpreted. In particular, Meydani and Ha claim that most of these studies were poorly designed and lacked appropriate placebo groups and proper statistical analysis. We note that our human studies that showed several immunostimulating properties of Lactobacillus johnsonii strain La1 (reviewed in reference 2) are different. Even though our initial longitudinal studies that showed increased phagocytic activity and antigen-specific immunoglobulin A lacked placebo control groups, the data were analyzed by using repeated-measures analysis of variance, followed by least-significant-difference multicomparison procedures (3–5). More recent studies with La1 bacteria were carried out in a double-blind placebo-controlled fashion and differences within groups were tested by paired t tests (6–8).

A second concern of the authors is that many studies investigated immune stimulation by probiotics given to animals parenterally or in vitro in cell culture systems. It is true that immunization of animals with probiotics via a different route from that by which yogurt is usually consumed (ie, orally) is somewhat artificial. The results of these studies merely suggest that antigenic epitopes from probiotics have the potential to induce immune responses when put in direct contact with immunocompetent cells in vivo. This is why in all of our studies of both animals and humans (3–9), La1 bacteria were administered orally and, in most studies, in fermented milk. To ensure that La1 bacteria exert the above-mentioned functions in the final product (ie, yogurt), most observations made with the use of fermented milk were repeated in trials using a commercially available Lc1 yogurt that contained La1 bacteria and that included a placebo group that received an identical yogurt that did not contain La1 bacteria (6, 10). These studies, therefore, addressed effects that may have been due to bacteria used in the starter culture used for the fermentation process.

Last, Meydani and Ha criticize the short duration of most of the studies conducted with probiotics. Indeed, most studies were performed over relatively short periods and, in some studies, immune stimulation peaked after a few days and declined thereafter. According to Meydani and Ha, this result suggests that administration of probiotics has short-term adjuvant effects on the immune response. In our studies, La1 bacteria were usually administered over 3 wk, after which time all volunteers resumed a diet that did not contain probiotics or any other fermented product. In these studies, we showed that immune stimulation was maintained as long as the probiotic was administered, but declined 6 wk after administration ended (3, 5, 7). This finding suggests that, at least for La1 bacteria, immune stimulation is maintained as long as the bacteria is provided. Furthermore, we showed in a recent study of patients infected with Helicobacter pylori that the beneficial effects of La1 bacteria were measurable 6 wk after administration of the bacteria ended (8). Thus, even though the immune-stimulating properties of La1 bacteria may not be maintained in the absence of the bacteria, some beneficial effects are still observed long term. Whether these long-term effects are immune mediated remains to be shown. Nevertheless, the fact that innate immune responses are not only important for early containment of pathogens, but also crucial in shaping the subsequent acquired immune response that is responsible for long-term memory, makes this hypothesis conceivable. Because most studies of probiotics focused on innate immune markers, they may have overlooked long-term acquired immune functions because such functions are more difficult to address.

In summary, the review by Meydani and Ha provided excellent insight about all available tools and studies of immune modulation by probiotics and their components. These authors concluded that most of these studies conducted thus far were poorly designed and lacked scientific rigor. We hope that we have convinced Meydani and Ha that not all studies fall into this category.

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REFERENCES


Erratum