

Rethinking “probiotics”

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The term “probiotic” has scientific, regulatory and public dimensions, and we may have reached a point where the term needs be reclaimed as a useful, commonly understood concept. While hundreds of human trials are published, the term is in danger of falling into disrepute as a result of negative publicity associated with the rejection of numerous health claims by regulatory agencies such as EFSA, who are demanding quasi-medical standards of proof in a bid to “protect the consumer.”¹ We may well lose the term at a time when scientists, healthcare practitioners and consumers are beginning to recognize its value. How can we ensure that we are able to realize the benefits of this wealth of scientific research, while ensuring that misleading information is not promoted and good research is encouraged?

The evidence that probiotics can benefit health has been reinforced by hundreds of reports of human studies in the scientific literature. Not all reports are positive, and surely some studies with null results are not published—a problem not unique to the probiotic field. Even so, numerous meta-analyses across a variety of health endpoints conclude that probiotics are more effective than placebo in randomized controlled trials. Consider just one of many of these recent meta-analyses which looked at the benefits of probiotics across a range of gastrointestinal diseases, which assessed 74 studies and 84 trials involving 10,351 patients and numerous probiotic preparations.² It concluded that “across all diseases and probiotic species, positive significant effects of probiotics were observed for all age groups, single vs. multiple species and treatment lengths.” As with most meta-analyses,

this report included the caveat that the studies were not consistently performed, and legitimate criticisms include issues such as small sample sizes, considerable heterogeneity relating to the probiotic strains investigated, different clinical methodologies and various clinical endpoints. While this is often presented as a weakness, one could argue that this weight of evidence actually indicates that most of the investigated strains, regardless of study size, dose, methodological nuances and clinical endpoints, improve the health of the participants beyond any placebo effect. This endorses the very definition of probiotics, that they are “live microorganisms, which when administered in adequate amounts confer a health benefit on the host.”³ In any other area of research, this data set would surely be regarded as excellent evidence to support the original hypothesis.

Perhaps we need to reconsider one of the central dogmas of probiotic science and regulation, which has been that evidence of a health benefit must always be provided on an individual strain-by-strain basis. Where it has already been established by a very significant body of experimental research that certain genera or species are beneficial to health it may well be reasonable to allow the use of the term “probiotic,” primarily to inform the consumer of the likely benefits of consuming high levels of safe, live microbes. It is entirely rational to predict that where common microbial structures or functions mediate a health benefit, similar effects would be expected for other strains sharing the same mechanistic capability.

In this revised view of probiotics, we could reclaim the term for its original

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intention; that probiotics are safe, live microbes associated with improving or maintaining health if consumed regularly in adequate doses. Most *Lactobacillus* species and members of the *Bifidobacterium* genus would be expected to qualify as probiotics, as acknowledged in the Canadian approach to probiotic claims on foods.⁴ These organisms may work by eliciting a benign immune response or by temporarily improving barrier function, and it would be expected that most members of those species or genera with a significant body of supportive scientific literature would be included in this category. Any specific health claim beyond this general claim of “probiotic” would have to be supported by robust evidence of the benefit. Such evidence could be targeted toward a single strain, a combination of strains, or members of a group of microbes defined by similar mechanistic capabilities. These might include effects such as immunomodulatory interactions or production of beneficial metabolites (e.g., SCFAs) or enzymes (e.g., lactase). Or strains might possess mechanisms that may well be rare or strain-specific, such as the ability to produce a bioactive molecule demonstrated to be effective in a target condition. These probiotic strains could be eligible for a specific health claim based on the human evidence.

References

1. Commission Implementing Decision of 24 January 2013 adopting guidelines for the implementation of specific conditions for health claims laid down in Article 10 of Regulation (EC) No 1924/2006 of the European Parliament and of the Council [Internet]. Official Journal of the European Union: 24 January 2013 [cited 11 March 2013]. Available from: <http://eur-lex.europa.eu/JOHtmldo?uri=OJ:L:2013:022:SO M:EN:HTML>.

This would lead to a situation for probiotics somewhat similar to that which already exists in medical microbiology when describing pathogens. All members of a particular pathogenic genus or species are assumed to be harmful a priori, but it is accepted that individual strains may differ in their virulence or may even be avirulent. We also accept that not all individuals exposed to the pathogen will fall ill or that all will experience the same consequences and even accept that many people may carry pathogenic microbes without any ill effects. These nuances do not lead to widespread confusion about the definition of pathogens (“microbes that cause disease in their host”), nor do they prevent excellence in research in this area. We believe the same reasoning should apply to probiotics, together with the same nuances and difficulties commonly encountered when dealing with such complex ecosystems as the human body.

We believe that the balance of evidence strongly favors the beneficial effects of consuming safe microbes for people with certain chronic health concerns, including gastrointestinal and atopic conditions. It may well be that the best advice to healthy consumers interested in probiotics is to consume a bolus of safe microbes, and many different microbes may serve this purpose equally well. Perhaps an important dietary

2. Ritchie ML, Romanuk TN. A meta-analysis of probiotic efficacy for gastrointestinal diseases. *PLoS One* 2012; 7:e34938; PMID:22529959; <http://dx.doi.org/10.1371/journal.pone.0034938>

3. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria [Internet]. World Health Organization and Food and Agricultural Organization of the United Nations: 2001[cited 11 March 2013]. Available from: http://www.who.int/foodsafety/publications/fs_management/en/probiotics.pdf.

guideline should include advice to ingest an “adequate microbial load every day.” Such a recommendation would build on the “old friends” hypothesis, which suggests that regular exposure to microorganisms can benefit human health.⁵ However, we would restrict the term “probiotic” to those genera, species and strains for which there is a convincing body of literature documenting a health benefit. When claiming a specific health benefit that goes beyond simple use of the term “probiotic,” strain-specific data would still be needed.

In conclusion, instead of viewing probiotic effects as necessarily strain-specific, perhaps we need to recognize that there is a spectrum of beneficial probiotic functionalities, some of which are unique to only one or a few strains, but others which are common to larger groups of microbes. It seems reasonable that the term probiotic should be allowed among certain taxonomic groups when there is such a body of evidence to suggest that probiotic functionality is in fact widespread. We also strongly encourage further rigorous research into specific genera, species and strains to identify additional specific health benefits.

Disclosure of Potential Conflicts of Interest

No potential conflict of interest was disclosed.

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