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REVIEW ARTICLE

Probiotics: an update☆

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Abstract
Objective: Triggered by the growing knowledge on the link between the intestinal microbiome and human health, the interest in probiotics is ever increasing. The authors aimed to review the recent literature on probiotics, from definitions to clinical benefits, with emphasis on children.
Sources: Relevant literature from searches of PubMed, CINAHL, and recent consensus statements were reviewed.
Summary of the findings: While a balanced microbiome is related to health, an imbalanced microbiome or dysbiosis is related to many health problems both within the gastro-intestinal tract, such as diarrhea and inflammatory bowel disease, and outside the gastro-intestinal tract such as obesity and allergy. In this context, a strict regulation of probiotics with health claims is urgent, because the vast majority of these products are commercialized as food (supplements), claiming health benefits that are often not substantiated with clinically relevant evidence. The major indications of probiotics are in the area of the prevention and treatment of gastro-intestinal related disorders, but more data has become available on extra-intestinal indications. At least two published randomized controlled trials with the commercialized probiotic product in the claimed indication are a minimal condition before a claim can be sustained. Today, *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii* are the best-studied strains. Although adverse effects have sporadically been reported, these probiotics can be considered as safe.
Conclusions: Although regulation is improving, more stringent definitions are still required. Evidence of clinical benefit is accumulating, although still missing in many areas. Misuse and use of products that have not been validated constitute potential drawbacks.

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PALAVRAS-CHAVE
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Probióticos: informações atualizadas

Resumo

Objetivo: Motivado pelo conhecimento cada vez maior da associação entre o microbioma intestinal e a saúde humana, o interesse nos probióticos vem crescendo cada vez mais. Os autores visaram analisar a última literatura a respeito dos probióticos, de definições a benefícios clínicos com ênfase nas crianças.
Fontes dos dados: Foi analisada a literatura relevante de pesquisas do PubMed, do CINAHL e dos últimos consensos.
Síntese dos dados: Apesar de um equilíbrio no microbioma estar relacionado à saúde, um desequilíbrio no microbioma ou disbiose está relacionado a vários problemas de saúde no trato gastrointestinal, como diarreia e doença inflamatória intestinal, e fora do trato gastrointestinal, como obesidade e alergia. Nesse contexto, a regulamentação rigorosa dos probióticos a alegações de saúde é urgente, pois a grande maioria desses produtos é comercializada como alimentação (suplementos), alegando benefícios à saúde que frequentemente não são comprovados com evidências clinicamente relevantes. As principais indicações de probióticos são feitas na área da prevenção e tratamento de doenças gastrointestinais, porém mais dados têm sido disponibilizados a respeito de indicações extraintestinais. Pelo menos dois ensaios clínicos controlados e randomizados publicados com o probiótico comercializado na indicação declarada são a condição mínima antes de uma afirmação poder ser mantida. Atualmente, o *Lactobacillus rhamnosus* GG e *Saccharomyces boulardii* são as melhores cepas estudadas. Apesar de efeitos adversos terem sido esporadicamente relatados, os probióticos podem ser considerados seguros.
Conclusões: Apesar de a regulamentação estar aumentando, ainda são necessárias definições mais rigorosas. As evidências de benefícios clínicos estão aumentando, apesar de ainda ausentes em várias áreas. O uso inadequado e a utilização de produtos não validados constituem possíveis desvantagens.

Introduction

The joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) Expert Consultation on evaluation of health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria defined probiotics as: ''live microorganisms that, when administered in adequate amounts, confer a health benefit on the host''.[1] In 2002, a joint FAO/WHO Working Group[2] released guidelines for the evaluation of probiotics in food. The minimum requirements needed for probiotic status include:

- assessment of strain identity (genus, species, strain level);
- *in vitro* tests to screen potential probiotics: e.g. resistance to gastric acidity, bile acid, and digestive enzymes, antimicrobial activity against potentially pathogenic bacteria;
- safety assessment: requirements for proof that a probiotic strain is safe and without contamination in its delivery form;
- *in vivo* studies for substantiation of the health effects in the target host.

Following the FAO/WHO definition, the International Life Science Institute (ILSI)[3] and the European Food and Feed Cultures Association (EFFCA)[4] have released similar definitions for a probiotic: ''a live microbial food ingredient that, when consumed in adequate amounts, confers health benefits on the consumers'' and ''live microorganisms that, when ingested or locally applied in sufficient numbers, provide the consumer with one or more proven health benefits''. These definitions *de facto* imply that probiotic ingestion provides benefits for host health.

The science related to probiotics is recent, and is thus in constant evolution. Probiotics used in food, supplied as dietary supplement, or as active components of a registered medication, should not only be capable of surviving passage through the digestive tract by exhibiting acid and bile survival, but should also have the capability to proliferate in the gut. Probiotics must be able to exert their benefits on the host through growth and/or activity in the human body. Topical or local application of probiotics is also proposed in view of the recent evolution of scientific data. Therefore, the ability to remain viable and effective at the target site should be studied and confirmed for each strain, or even better, for each commercialized product. Clinical studies should be performed with the commercialized product and not with the isolated strain. However, lack of protection contributes to the fact that some companies refuse to deliver information on the specific strains in their product.[5] Recent literature has demonstrated that one of the mechanisms of action of probiotics involves stimulation of the immune system. It is questionable whether the probiotics need to be ''alive'' to induce immune-modulation. Therefore, the definition may have to be revised in the future.