S4-4

Regulatory Issues on the Probiotics in Korea

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In order to be approved as a Health/Functional Food, the petitioner should submit the documentation about the identity, safety and efficacy about their probiotics. On the contrary to botanical extracts, probiotics have a specific characteristics. In this presentation, I would like the evaluation point about probiotics, which was modified from WHO report.

Identity

It was recognized that it is necessary to know the genus and species of the probiotic strain. The current state of evidence suggests that probiotic effects are strain specific. Specification of the bacteria must be established using the most current, valid methodology. It is recommended that a combination of phenotypic and genetic tests be used. Nomenclature of the bacteria must conform to the current, scientifically recognized names. Protracted use of older or misleading nomenclature is not acceptable on product labels.

DNA-DNA hybridization is the reference method to specify that a strain belongs to a species; however, as it is time consuming and beyond the resources of many laboratories, requiring a large collection of reference strains, the use of DNA sequences encoding 16S rRNA is suggested as a suitable substitute. In this case, it is recommended that this genotypic technique be combined with phenotypic tests for confirmation.

Patterns generated from the fermentation of a range of sugars and final fermentation products obtained from glucose utilization are key phenotypes that should be investigated for identification purpose.

Strain typing has to be performed with a reproducible genetic method or using a unique phenotypic trait. Pulsed Field Gel Electrophoresis (PFGE) is the gold standard. Randomly Amplified Polymorphic DNA (RAPD) can also be used, but is less reproducible. Determination of the presence of extrachromosomal genetic elements, such as plasmid can contribute to strain typing and characterization.

Safety Consideration

Historically, lactobacilli and bifidobacteria associated with food have been considered to be safe.

However, probiotics may theoretically be responsible for four types of side-effects: systemic infections, deleterious metabolic activities, excessive immune stimulation in susceptible individuals, gene transfer.

In recognition of the importance of assuring safety, even among a group of bacteria that is Generally Recognized as Safe(GRAS), we recommends that probiotic strains be characterized at a minimum with the following tests:

1. Determination of antibiotic resistance patterns
2. Assessment of certain metabolic activities (e.g., D-lactate production, bile salt deconjugation)
3. Assessment of side-effects during human studies
4. If the strain under evaluation belongs to a species that is a known mammalian toxin producer, it must be tested for toxin production.
5. If the strain under evaluation belongs to a species with known hemolytic potential, determination of hemolytic activity is required
6. If the strain is not a granted as a food legally, acute toxicity data should be submitted.

Efficacy

In some cases, animal models exist to provide substantiation of in vitro effects and determination of probiotic mechanism. Where appropriate, we encourage use of these prior to human trials. Probiotics have been tested for an impact on a variety of clinical conditions. Generally in the form of randomized, double blind, placebo-controlled design, measure efficacy compared with placebo.

In vitro tests are useful to gain knowledge of strains and the mechanism of the probiotic effects. Appropriate target-specific in vitro tests that correlate with in vivo results are recommended. For example, in vitro bile salts resistance was shown to correlate with gastric survival in vivo. A list of the main currently used in vitro tests for the study of probiotic strains is shown in Table 1.

Table 1. Main currently used in vitro tests for the study of probiotic strains

Resistance to gastric acidity
Bile acid resistance
Adherence to mucus and/or human epithelial cells and cell lines
Antimicrobial activity against potentially pathogenic bacteria
Ability to reduce pathogen adhesion to surfaces
Bile salt hydrolase activity

Conclusions

Currently, the health claims on probiotics are allowed as well as botanical products as a Health/Functional Food in Korea. We approve specific claims only when sufficient scientific evidence is available. We think that further development of methods to evaluation the functionality and safety of probiotics should be made by academia.

References

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