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Industrial Applications of Synbiotics and Future Works on Health Claims

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Historical Background

The ready availability of antibiotics in the 1950s resulted in their widespread use as therapeutic agents and growth stimulants for farm animals. Since that time, there has been growing concern that the use of antibiotics as growth promoters was resulting in the development of resistant populations of bacteria which made subsequent use of antibiotics for therapy difficult. There is also a reaction against the use of antibiotics as therapeutic agents because of the intestinal upsets which often follow oral treatment with these agents. Although they are effective in curing the disease for which they are prescribed, the effect on the indigenous gut flora may persist after cessation of the treatment. The possibility of antibiotics ceasing to be used as growth stimulants for farm animals and the concern about the side-effects of their use as therapeutic agents has produced a climate in which both consumer and manufactures are looking for alternatives.

Definition and Characteristics

Probiotics are being considered to fill this role and already some farmers are using them in preference to antibiotics. Indeed, probiotics are selected cultures of microorganisms which are able to survive stomach/duodenum passage and which are able to multiply in the small and the large intestine. Otherwise, prebiotics are selected substrates which can not be digested in the upper intestinal tract, which enforce the growth of autochthonous microorganisms in the bowel, and which stimulate bowel movement (ballast substrates). In addition, synbiotics are mixtures of probiotic cultures and prebiotic substrates in dairy products. Probiotics might be described as follows; substances produced by one protozoan which stimulated another (Lilly and Stillwell, 1965); animal feed supplements which had a beneficial effect on the host animal by affecting its gut flora, that is, organisms and substances which contribute to intestinal microbial balance (Parker, 1974). However, this definition is unsatisfactory because it is too imprecise and it would include antibiotics; a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance (Fuller, 1989). This revised definition emphasizes the importance of live cells as an essential component of an effective probiotic and removes the confusion created by the use of the word 'substances'.

Probiotics

Practical results with probiotics might be described as follows; growth promotion of farm animals, effects on intestinal infections, alleviation of lactose intolerance, relief of constipation, antitumor activities, and anticholesterolaemic effects. In addition, possible modes of action of probiotics are as follows; suppression of viable count by production of antibacterial compounds, competition for nutrients, and competition for adhesion sites, alteration of microbial metabolism by increased and decreased enzyme activity, stimulation of immunity by increased antibody levels, and increased macrophage activity. And, features of a good probiotic; should be a strain which

is capable of exerting a beneficial effect on the host animals, e.g. increased growth or resistance to disease, should be non-pathogenic and non-toxic, should be present as viable cells, preferably in large numbers considering the minimum effective dose, should be capable of surviving and metabolizing in the gut environment, e.g. resistant to low pH and organic acids, and should be stable and capable of remaining viable for long periods under storage and field conditions.

Managing the Microbes in Human GI-Tract

- Over 400 species within the GI-tract can be identified. Average population levels 10^{12} CFU/g in colon
- The balance is influenced primarily by the host's individuality
- The composition of the diet influences on intestinal physiology and metabolism of microflora
- Variations in proteins, lipids and carbohydrates of the diet control the composition of microbes in the gut
- Fermentations in the colon by the intestinal microbes
  - Saccharolytic fermentations are considered to be favorable for the host's well-being
    : Formation of beneficial end products such as SCFA, lactate, ethanol
  - Protein fermentations result in the production of harmful products
    : BCFA, NH_3, amines, phenols

Desirable Properties of Probiotic Bacteria

Health and clinical properties
• Human origin • Resistance to acid and bile • Adherence to human intestinal cells • Colonization of the human gut • Production of antimicrobial substances • Antagonism against cariogenic and pathogenic bacteria • Safe for human consumption • Clinically validated health effects
Stability and technical properties
• Ability to maintain verified viability • Maintenance of good flavor and aroma profile after fermentation • Maintenance of mild acidity throughout storage: good acidity profile • Maintenance of colonizing properties throughout processing and storage • Development of good storage stability in fermented products • Stability after freeze drying and other drying methods • Accurate strain identification • Dose-response data for required effects

Requirements for Good Clinical Studies of Demonstration

The unique probiotic properties for functional foods use are as follows; defined and well-characterized strains of bacteria, well-defined studies and well-designed clinical trials, double-blind placebo controlled, randomized human studies, results confirmed by different groups, publication in peer-reviewed journals, each strain documented and tested independently on its own merit, and extrapolation of data from closely related strains not acceptable.

Classification of Probiotic Organisms and Their Safety Status

Organisms	Infection potential
Lactobacillus	Mainly non-pathogens, some opportunistic infections (usually in immunocompromised patients)
Lactococcus	Mainly non-pathogens
Leuconostoc	Mainly non-pathogens, some isolated cases of infection
Streptococcus	Oral streptococci mainly non-pathogens (including *Str. thermophilus*): Some may cause opportunistic infections
Enterococcus	Some strains are opportunistic pathogens with haemolytic activity and antibiotic resistance
Bifidobacterium	Mainly non-pathogens, some isolated cases of human infection
Saccharomyces	Mainly non-pathogens, some isolated cases of human infection

Important Studies for the Safety Assessment of Probiotics

Type of property studied	Safety factor to be assessed
Intrinsic properties of lactic acid bacteria	Adhesion factors, antibiotic resistance, existence of plasmids and plasmid transfer potential, harmful enzyme profiles
Metabolic products	Concentration, safety, and other effects
Toxicity	Acute and subacute effects of ingestion of large amounts of tested bacteria
Mucosal effects	Adhesion, invasion potential, intestinal mucus degradation, infectivity in immunocompromised animals (e.g. following lethal irradiation)
Dose-response effects	Dose-response studies by oral administration in volunteers
Clinical assessment	Potential for side-effects, careful evaluation in healthy volunteers, and disease specific studies
Epidemiological studies	Surveillance of large populations following introduction of new strains and products

Prebiotics: Non-Digestible Oligosaccharides (NDOs)

- Resistant to upper gastrointestinal digestive enzymes but are fermented in the colon by specific colon bacteria
  - Galacto-oligosaccharides (GOS)
  - Fructo-oligosaccharides (FOS)
  - Isomalto-oligosaccharides (IMO)
  - Inulin and its hydrolysate, oligofructose
- Selectively stimulating the beneficial bacteria in the gut
- Increased production of short-chain fatty acids (SCFA)
  - The profile of SCFA dependent on the NDOs used
  - The aim is to increase levels of propionate and butyrate

Synbiotic, a New Tool for the Management

Probiotics+Prebiotics: Tools for managing the microbes in the gut

- Probiotics - Live microbial (food) ingredients that are beneficial to host health
- Prebiotics - Non-digestible food components that beneficially affect the host by selectively stimulating the growth and/or activity of one or limited number of bacteria in the colon that have the potential to improve host health
- Mixtures of probiotics and prebiotics that beneficially affects the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract
- For maintaining and improving host well-being
  - By modification of bacterial fermentation and bacterial composition
- Double-effect on bifidobacteria
  - Metabolic activities of microbes in the colon are altered towards enhanced functionality

Targets for tools

- Stimulation of bifidobacteria and lactobacilli
  - Bifidobacteria have several positive effects
    : Inhibition of pathogenic bacteria
    : Stimulation of vitamin synthesis
    : Supplementation in digestion and absorption
    : Stimulation of immune system
- Modification of metabolic activity of microbes in the gut
  - Enhancement of saccharolytic fermentation pattern instead of protein degradation and fermentation
- Specific dietary carbohydrates are known to promote the growth of the beneficial bacteria

Industrial Applications and Future Works on Health Claims

Probiotic cultures of lactic acid bacteria such as *Lactobacillus*, *Streptococcus*, *Leuconostoc*, *Pediococcus*, and *Bifidobacterium*, yeasts and molds (only or mainly for animals) are used for man and animals nowadays. And many kinds of yoghurt-like products, yoghurt drinks, pharmaceuticals, and baby foods are commercialized in Europe, USA, and Asian countries. For future works on health claims, researched effects of probiotic bacteria should meet target health benefits such as aid in lactose digestion, resistance to enteric pathogens, anti-colon cancer effect, small bowel bacterial overgrowth, immune system modulation, allergy, blood lipids/heart disease, antihypertensive effect, urogenital infections, infection caused by *Helicobacter pylori*, and hepatic encephalopathy.

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