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Neutraceuticals: Prebiotics and Probiotics

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Abstract: The introduction of probiotics, prebiotics, or synbiotics into human diet is favourable for the intestinal microbiota. They may be consumed in the form of raw vegetables and fruit, fermented pickles, or dairy products. Another source may be pharmaceutical formulas and functional food. This paper provides a review of available information and summarises the current knowledge on the effects of probiotics, prebiotics, and synbiotics on human health. The mechanism of beneficial action of those substances is discussed, and verified study results proving their efficacy in human nutrition are presented. As only few experimental studies on nanoprebiotics and nanoprobiotics are available in the scientific literature, research on this prominent field is needed, covering effectiveness, bioavailability, and safety aspects.

Keywords: Introduction, History, Neutraceutical Market Overview, probiotics, prebiotics

Introduction:

Health and longevity have become the new mantras (consciousness) in people. The health benefits of certain foods containing bioactive compounds (matrices having positive effects on human health) have been realized for preventing many diseases. These compounds or foods used in promoting health are classified either as functional foods or nutraceuticals. These foods have been claimed to render health benefits and are marketed as functional foods¹. The health benefits imparted by these functional food aim to create foodstuffs which after ingestion multiply “healthy” bacteria in the intestine. Till date, Japan is the only country that has formulated a specific regulatory approval process for functional foods. Japanese coined the term Foods for Specified Health Use or FOSHU, to which a functional ingredient has been added for a specific healthful effect². The word “probiotic” comes from Greek, and it means “for life”. Most probably, it was Ferdinand Vergin who

invented the term “probiotic” in 1954, in his article entitled “Anti-und Probiotika” comparing the harmful effects of antibiotics and other antibacterial agents on the intestinal microbiota with the beneficial effects (“probiotika”) of some useful bacteria³. In 1995, prebiotics were defined by Gibson and Roberfroid as non-digested food components that, through the stimulation of growth and/or activity of a single type or a limited amount of microorganisms residing in the gastrointestinal tract, improve the health condition of a host⁴. Synbiotics have both probiotic and prebiotic properties and were created in order to overcome some possible difficulties in the survival of probiotics in the gastrointestinal tract⁵. Therefore, an appropriate combination of both components in a single product should ensure a superior effect, compared to the activity of the probiotic or prebiotic alone⁶.

The aim of the review was to discuss the mechanisms of action of probiotics, prebiotics, and synbiotics, as well as the current insight into their effect on human health. The selection of probiotic strains, prebiotics, and their respective dosages is crucial in obtaining a therapeutic effect, so separate sections are dedicated to this topic. Further research into the acquisition of new probiotic strains, the selection of probiotics and prebiotics for synbiotics, dose setting, safety of use, and clinical trials documenting the desired health effects is necessary. Effects should be confirmed in properly scheduled clinical trials conducted by independent research centres.

History-

Although different definitions for functional foods are used worldwide, there is no official or commonly accepted definition that exists, so far. However, broadly any food accompanying a particular health claim can be defined as functional foods. The concept of functional food was invented in Japan during the 1980s, when health authorities realized the need for enhancement in the life quality and expectancy so as to reduce the healthcare costs⁷.

Functional foods are categorized as (i) foods with naturally occurring bioactive substances (e.g. dietary fibre), (ii) foods supplemented with bioactive substances (e.g. probiotics) and (iii) derived food ingredients introduced to conventional foods (e.g. prebiotics), through a combination of probiotics and prebiotics (e.g. synbiotics). Probiotics, prebiotics, synbiotics, vitamins and minerals: coming under functional food and currently used for human consumption in the form of fermented milks and yoghurts, sports drinks, baby foods, and chewing gum⁸.

Nutraceutical Market Overview-

Health consciousness, awareness and willingness to spend on health-fortifying food among people are the main reasons behind the rapidly growing nutraceutical market in India. The Indian nutraceutical market has in the past been viewed as an export-focused industry, but with the changing market trends, most local

companies have started to launch products in India and expanded their product line according to Indian consumer needs. In 2013, the European nutraceutical market was valued at \$6.4 billion and is estimated to grow at an annual rate of 7.2% between 2013 and 2018, to reach a projected \$9.0 billion by 2018. According to a report, functional foods remained the fastest-growing segment of the North America nutraceutical market with a 6.5% CAGR during 2007–2011. Currently, dietary supplements are the largest segment of nutraceuticals in the USA⁹.

Probiotic-

Probiotic products may contain one or more selected microbial strains. Human probiotic microorganisms belong mostly to the following genera: *Lactobacillus*, *Bifidobacterium*, and *Lactococcus*, *Streptococcus*, *Enterococcus*. Moreover, strains of Gram-positive bacteria belonging to the genus *Bacillus* and some yeast strains belonging to the genus *Saccharomyces* are commonly used in probiotic products¹⁰. In the USA, microorganisms used for consumption purposes should have the GRAS (Generally Regarded As Safe) status, regulated by the FDA (Food and Drug Administration). In Europe, EFSA introduced the term of QPS (Qualified Presumption of Safety). The QPS concept involves some additional criteria of the safety assessment of bacterial supplements, including the history of safe usage and absence of the risk of acquired resistance to antibiotics¹¹.

Mechanism of action of Probiotics-

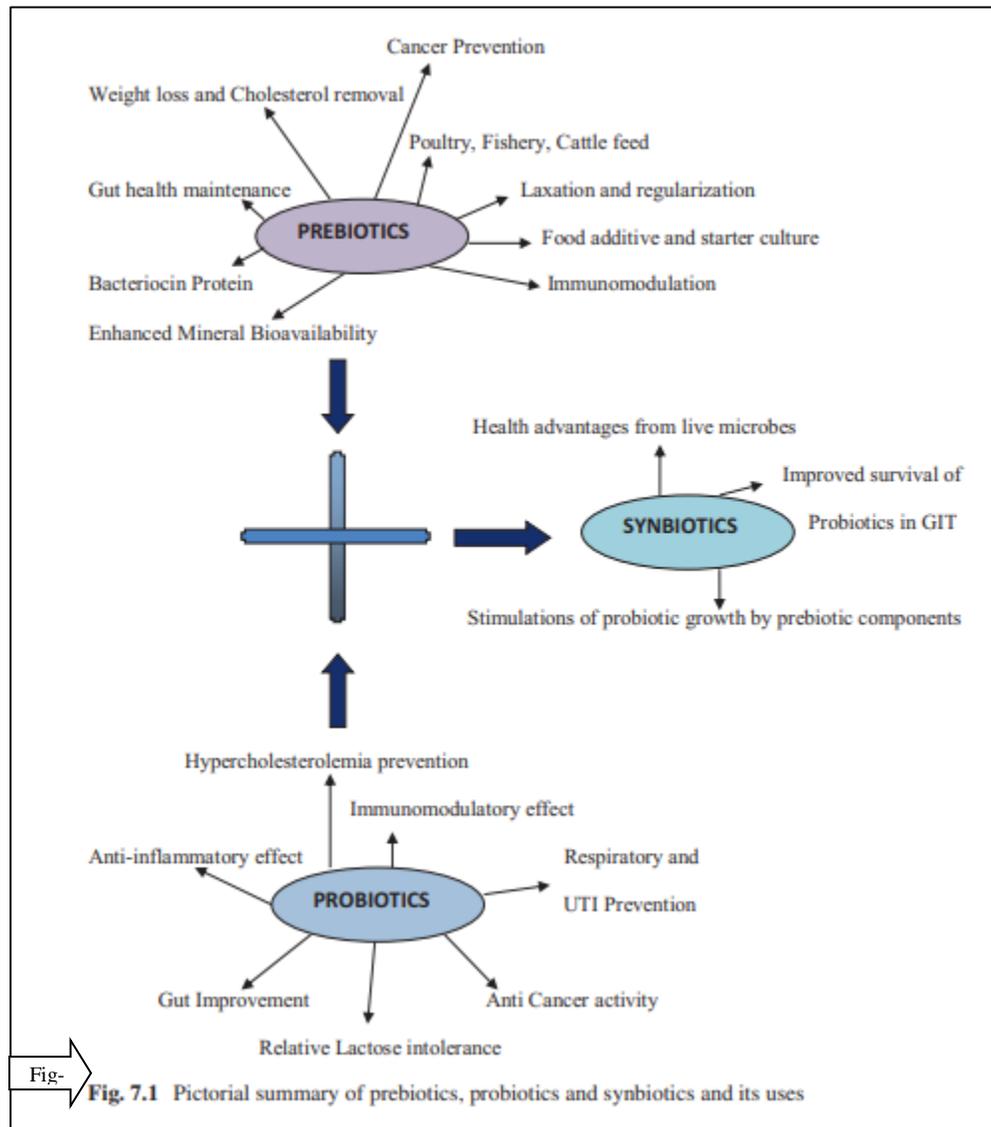
A significant progress has been observed lately in the field of studies on probiotics, mostly in terms of the selection and characteristics of individual probiotic cultures, their possible use, and their effect on health. Probiotics have numerous advantageous functions in human organisms. Their main advantage is the effect on the development of the microbiota inhabiting the organism in the way ensuring proper balance between pathogens and the bacteria that are necessary for a normal function of the organism¹². Probiotic microorganisms may also be able to produce enzymes, such as esterase, lipase, and co-enzymes A, Q, NAD, and NADP. Some products of probiotics metabolism may also show antibiotic (acidophiline, bacitracin, lactacin), anti-cancerogenic, and immunosuppressive properties¹³.

Molecular and genetic studies allowed the determination of the basics of the beneficial effect of probiotics, involving four mechanisms:

- Antagonism through the production of antimicrobial substances.
- Competition with pathogens for adhesion to the epithelium and for nutrients.
- Immunomodulation of the host.
- Inhibition of bacterial toxin production.

Some compounds found in prebiotics are soya-oligosaccharide, xylo-oligosaccharide, pyrodextrins, 4 of 24 gluco-oligosaccharide, lactulose, malto-oligosaccharide, galactans

(galacto-oligosaccharide (GOS)), oligofructose, isomalto-oligosaccharide (IOS), fructans (FOS and inulin), mannan-oligosaccharide (MOS), lactitol, and non-starch polysaccharides (NSP). Figure gives an overview of prebiotics¹⁴.



Prebiotics-

Different prebiotics will stimulate the growth of different indigenous gut bacteria. Prebiotics have enormous potential for modifying the gut microbiota, but these modifications occur at the level of individual strains and species and are not easily predicted a priori. Furthermore, the gut environment, especially pH, plays a key role in determining the outcome of interspecies competition. Both for reasons of efficacy and of safety, the development of prebiotics intended to benefit human health has to take account of the highly individual species profiles that may result. Prebiotics may be used as an alternative to probiotics or as an additional support for them. Long-term stability during the shelf-life of food, drinks, and feed, resistance to processing, and physical and chemical properties that exhibit a positive effect on the flavour and consistence of products may promote prebiotics as a competition to probiotics. Additionally, resistance to acids, proteases, and bile salts present in the gastrointestinal tract may be considered as other favourable properties of prebiotics. Prebiotic substances selectively stimulate microorganisms present in the host's

intestinal ecosystem, thus eliminating the need for competition with bacteria. Stimulation of the intestinal microbiota by prebiotics determines their fermentation activity, simultaneously influencing the SCFA level, which confers a health benefit on the host¹⁵.

Mechanism of Action of Prebiotics-

Prebiotics are present in natural products, but they may also be added to food. The purpose of these additions is to improve their nutritional and health value. Some examples are: inulin, fructooligosaccharides, lactulose, and derivatives of galactose and β -glucans. Those substances may serve as a medium for probiotics. They stimulate their growth, and contain no microorganisms.

The mechanism of a beneficial effect of prebiotics on immunological functions remains unclear. Several possible models have been proposed-

- Prebiotics are able to regulate the action of hepatic lipogenic enzymes by influencing the increased production of short-chain fatty acids (SCFAs), such as propionic acid.
- The production of SCFAs (especially of butyric acid) as a result of fermentation was identified as a modulator of histone acetylation, thus increasing the availability of numerous genes for transcription factors.
- The modulation of mucin production.
- It was demonstrated that FOS and several other prebiotics cause an increased count of lymphocytes and/or leukocytes in gut-associated lymphoid tissues (GALTs) and in peripheral blood.
- The increased secretion of IgA by GALTs may stimulate the phagocytic function of intra-inflammatory macrophages¹⁶.



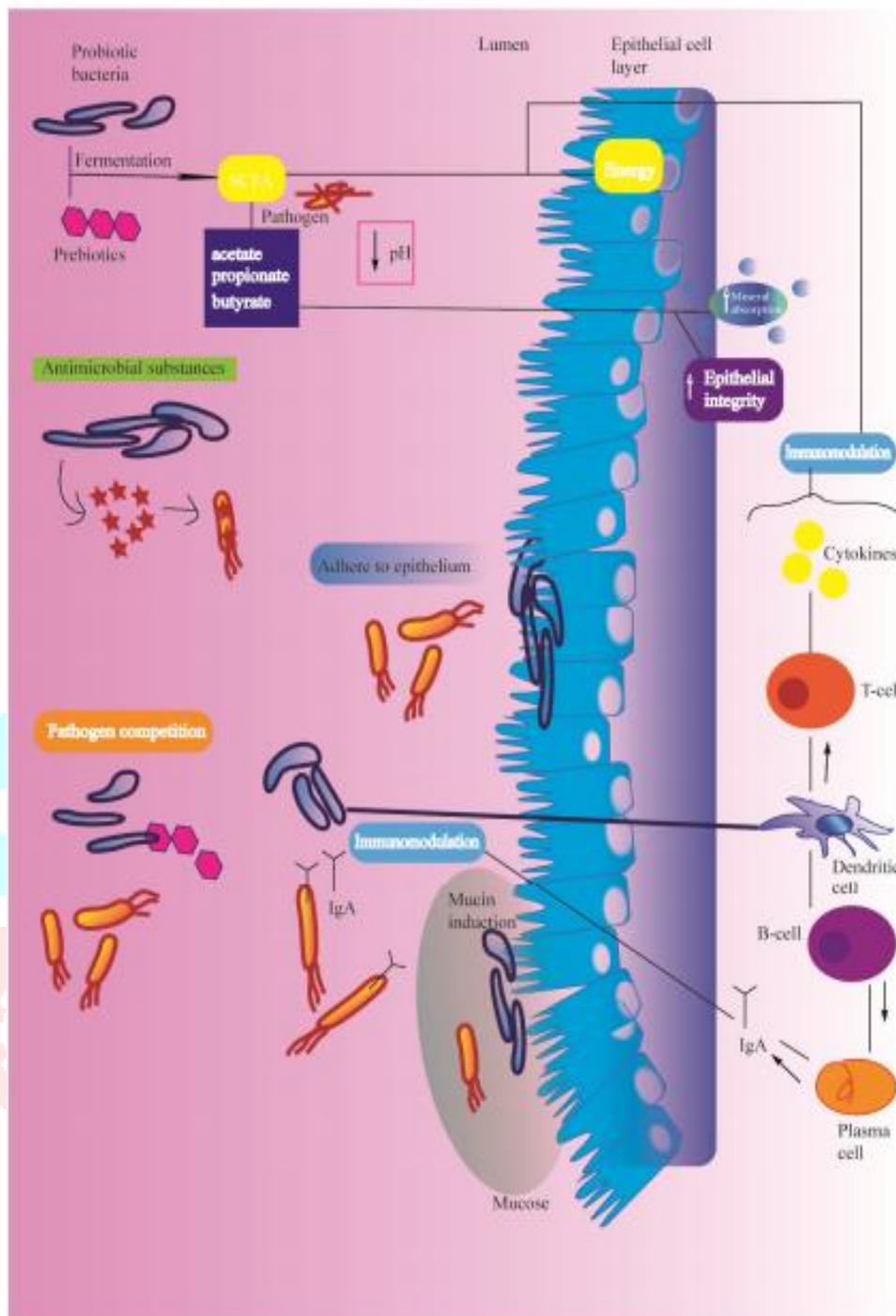


Figure 2. Overview of mechanism of action of pre and probiotics

It was also demonstrated that the administration of prebiotics increases the absorption of minerals, mostly of magnesium and calcium¹⁷.

Conclusion-

Probiotic organisms are crucial for the maintenance of balance of human intestinal microbiota. Numerous scientific reports confirm their positive effect in the host's health. Probiotic microorganisms are attributed a high therapeutic potential in, e.g., obesity, insulin resistance syndrome, type 2 diabetes, and non-alcohol hepatic steatosis. Nonetheless, in order to assess the effective use of food-grade nanoparticles, further studies are expected to exploit and assess safety, improved bioavailability, and efficacy. It turns out that the development of bio-therapeutic formulas containing both appropriate microbial strains and synergistic prebiotics may lead to the enhancement of the probiotic effect in the small intestine and the colon. Those "enhanced" probiotic products may be even more effective, and their protective and stimulatory effect superior to their components administered separately. It seems that we will see further studies on combinations of probiotics and prebiotics, and further development & Future studies may explain the mechanisms of actions of those components, which may confer a beneficial effect on human health.

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