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"Postbiotics" - One Step Ahead of Probiotics

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A B S T R A C T

Food is the basic necessity of mankind. Human gastrointestinal tract resident microflora contains good bacteria that extend therapeutic benefits which are termed as Probiotics. The use of probiotics, prebiotics that stimulates probiotics and synbiotics which is a combination of pro and prebiotics improve the gut homeostasis, has been blooming for the past decade. Recent work on relevant probiotic strains has also led to the isolation and characterisation of certain probiotic derived metabolites called as postbiotics. The different forms of postbiotics include peptidoglycans; exopolysaccharides; organic acids or short-chain fatty acids, peptide molecules; and bacteriocins. These have favourable absorption, metabolism and distribution abilities which could indicate a high capacity to signal different organs and tissues in the host thus eliciting several biological responses. The incorporation of live probiotic bacteria in foods is dependent on propagation, processing steps, viability, survival number, colonization and so on. To overcome these problems their metabolites may be a good alternative to probiotics. In contrast, postbiotics are supposed to be more stable than the probiotics allowing their application in a wide variety of functional food products.

Introduction

Food is an essential part of everyone's life. It gives us the nutrients to grow and develop, be healthy and active. Human body needs all the essential nutrients like carbohydrates, proteins, fat, minerals and vitamins in a required quantity which covers the meaning of balanced food providing a good health. A zoo within us the gastrointestinal tract comprising of friendly bacteria like *Lactobacilli* and *Bifidobacteria* conferring positive benefits and unfriendly bacteria like *E. coli*, *Salmonella* spp, *Shigella* spp etc involved in causing diseases.

Savage in 1977 has defined and categorized the gastrointestinal microflora into 2 types – Autochthonus flora which are indigenous flora and Allochthonus flora which are transient through food and water. It is known for the decades that what we eat can balance the microbes in our digestive tract. By eating good foods, a healthy balance of microflora of the gut is maintained which is termed as Eubiosis. At the start of 20th century, Russian Nobel prize winner and father of probiotics Elie Metchnikoff proposed that regular consumption of fermented milk products containing acid producing bacteria could

prevent "putrifaction" in the large intestine leading to a longer healthier life.

Human gut micro ecosystem

Human intestine is the largest immune organ contributing to 70% immunity to human body. Our intestine is about 300 to 400 sq.cm surface area predominated by trillions of living bacteria, colonized by approximately 10^{14} bacteria of >500 species.

The prevalence of bacteria in different parts of GIT appears to be dependent on several factors such as pH, redox potential, bacterial adhesion, mucin secretion, diet, nutrients availability and bacterial antagonism.

Stomach is the foremost organ of digestive system containing of *Lactobacillus* species to a range of 10^2 to 10^3. The pH of the stomach lies between 1.5 and 2.0 where mostly the acid tolerant bacteria like *Lb. acidophilus* exists. Next to the stomach, small intestine is divided into duodenum, jejunum and ileum which contain *Lactobacillus* species and *Enterococcus s*pecies to a range of 10^4 to 10^5. The pH of the small intestine is 4.0 because the cholesterol is synthesised in liver, stored and concentrated in gall bladder and transported to duodenum after food intake. The large intestine is divided into colon, cecum and rectum containing *Lactobacilli*, *Bifidobacteria*, Enterobacter, Enterococci, Bacteriodes, Peptococci, Clostridia of about 10^9 to 10^{12} cfu/ml of intestinal content pH is 6-7.

Factors influencing the gut micro ecosystem

Several factors like Mother's microflora, mode of birth, feeding practices during infancy and microbial infections, antibiotics, diet (highly processed, low fiber), chronic diarrhea and stress in the later life influence the gut. All these factors tends to complication of imbalance in the gut health.

One such complication is Dysbiosis which means disturbance in the balance of microflora in the gut. Dysbiosis is the condition where pathogenic bacteria in the gut are dominated. Administration of antibiotics for longer time in the treatment of Tuberculosis and chemotherapy involved in the cancer prevention are the major factors for dysbiosis. Eubiosis is a condition where healthy balance of the microflora exists in the GIT. In this condition, *Bifidobacteria* and *Lactobacilli* species are associated with the health (Tannock, 1983).

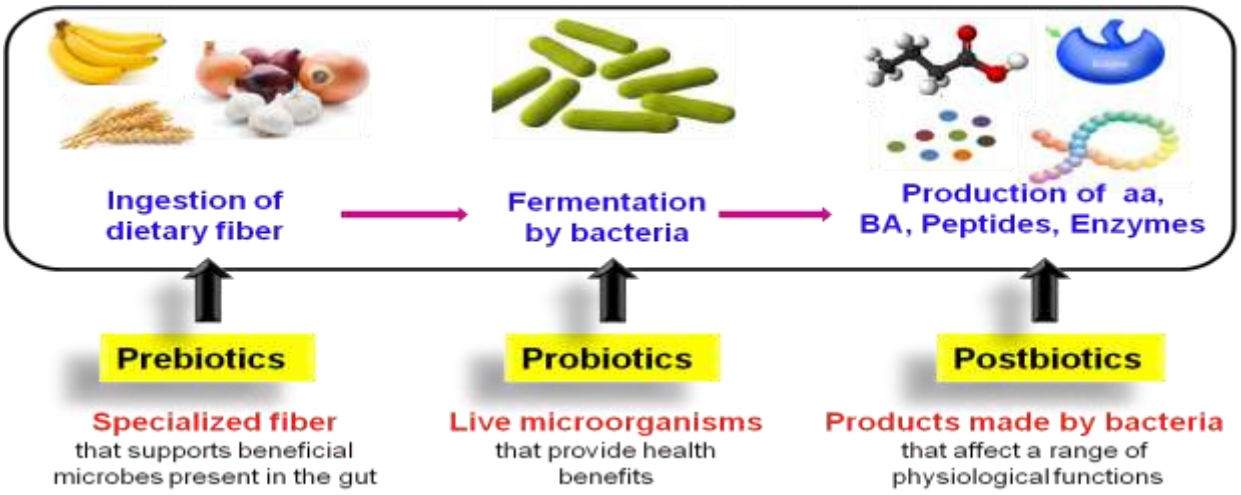
To overcome the imbalance in the gut microflora, restoration or modulation of gut health can be made by the consuming foods containing probiotics (pro = early life), prebiotics (pre = before life) and synbiotics (Syn = add life). All these terms have got historical interventions and shining in today's era.

Postbiotics: an evolving term

Probiotics when present in known amounts are known to produce postbiotics. Synonyms of postbiotics are metabolites, biogenics, cell free supernatants, metabiotics and metabolic waste of probiotic activity.

They are probiotic produced soluble, non-viable bacterial products with molecular weight of 50 to 100kDa. They have biological activity in the host. Overall postbiotics determines the fitness of probiotic bacteria.

Postbiotics are defined as "any factor resulting from the metabolic activity of a probiotic or any released molecule capable of conferring beneficial effects to the host in a direct or indirect way" (Tsilingiri *et al.,* 2013).



Classification of postbiotics

The different forms of postbiotics are derived both extracellularly and intracellularly. Cell wall components include Exoploysaccharide and petidoglycans. Intracellular major metabolites are organic acids like Lactic acid and acetic acid, Short chain fatty acids like butyric acid, acetate and propionate, bacteriocins like acidophilin, bifidin, reuterin, peptides including p40, p75 and Lactocepin (Matsuguchi *et al.*, 2002).

Production and identification postbiotics

Usually production of postbiotics involve cell disruption techniques like heat and enzymatic treatments, solvent extraction and sonication followed by post production steps such as additional extraction and centrifugation, dialysis, freeze-dried and column purification have been used to assist obtaining procedures (Amaretti *et al.*, 2013).

Postbiotics have been identified by qualitative and/or quantitatively. Magnetic resonance spectroscopy (1H NMR) was used to identify and characterize polysaccharide-glycopeptide complexes of *Lactobacillus casei* YIT9018. Chromatography with spectrometry and Fourier transform ion cyclotron resonance mass spectrometry have been used for identification of bacterial metabolites like short chain fatty acids, glycerolipids, purines, sphingolipids and oligosaccharides (Kok *et al.*, 2013).

Therapeutic benefits of postbiotics

The postbiotics have been proved to exert health benefits exihibiting local effects on specific tissues of the gut epithelium with immunomodulatory, anti-inflammatory and antibacterial properties, also exhibit systematic effects by affecting the multiple organs or tissues with anticarcinogenic, antiproliferative benefits along with the prevention of celiac disease (Sharma and Shukla, 2016).

Applications of postbiotics

Food industry

Cell free supernatant from probiotic *Lb. plantarum* YML 007 strain having biopreservative effect on soybeans resulted in improved shel life of unshelled soybeans upto 2 months (Rather *et al.,* 2013). Exopolysaccharide from *Lb. rhamnosus* showed 8.2% increase in Cheddar cheese yield with *L.lactis* (Torino and Mozzi, 2015**)**. Bifidin from *Bifidobacterium lactis* Bb-12 resulted in increasing Shelf life of minced

meat upto 3 months at -18˚ C by 100 % reduction of *E. coli* O157:H7.

Pharmaceutical industry

In USA, a company Pure Research Products, LLC, Boulder, CO. produces a drug Del-Immune VÒ containing of muramyl peptides extracted from *L.rhamnosus V* aids in relieving gastrointestinal distress in children (Roberts and Sichel, 2013). BioRay Inc., Laguna Hills, CA, USA, has marketed CytoFloraÒ containing cell wall lysates of *B. longum*, *Str.thermophilus* and *L. plantarum* is usefull in preventing Dysbiosis and autisim in children (Sherlock and Woods, 2010). HylakÒ Forte drug from Ratiopharm/Merckle GmbH, Germany contains short chain fatty acids from *L. acidophilus* and *L. helveticus* cures dysbacteriosis of patients with chronic gastritis (Omarova and Sarsenova, 2014).

Significance of LAB of fermented milk products

LAB used as Starter culture in various fermented dairy products are approved as General recognized as safe (GRAS) by Food and drug administration authority. All Starter cultures and lactic acid bacteria used in fermented milk products may not be probiotics. Through Fermented dairy products bacteria reach the stomach and die releasing metabolites which may be postbiotics with some examples LA, Peptidoglycan, bacteriocin. Other naturally fermented products like pickle, kimchi, sauerkraut, dosa batter and so on also delivers postbiotics to health benefits.

Future Prospective

Future in-vivo studies need to be carried in animal models and human clinical trials that help to determine the feasibility of postbiotics that improvement of GI health. Research with respect to production methods is to be fulfilled. Further studies on postbiotics would be a pathway to develop newer Pharmabiotic products and development of Functional foods.

In conclusion, probiotic, prebiotic and synbiotic concepts may be evergreen trend. Some of the drawback of probiotic is Colonization that extends therapeutic benefits and problems in propagation, proper processing if added to food. New approach incorporation of postbiotics in foods may be a good alternative with high therapeutic value and increased shelf-life of food products.

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