Meta biotic-a novel ingredient for functional foods: A review

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Abstract
The probiotic products are gaining importance in disease management and health restoration. The regular consumption of probiotic could offer a wide range of health benefits. Although, probiotics are considered safe and beneficial for health and harmful effects of probiotic usage are rare, but recent data showed adverse effects of probiotic after long term consumption. Some medical reports specified that probiotic bacteria are rarely related with human opportunistic infections like sepsis, infective endocarditis, bacteremia, urological infections, allergic sensitization and autoimmune disorders. Metabiotics are the structural components of probiotics, their metabolites or small signalling molecules whose chemical structure is known that can affect the human metabolic and signalling pathways. Metabiotics are advantageous over probiotic and synbiotic because of their known chemical structure, which can provide accurate information regarding their dosage, safety, and shelf-life. Metabiotics are a natural evolution and can be considered as future of functional food industry.

Keywords: Metabiotic, probiotic, synbiotic, signalling pathways

Introduction
Nobel laureate, Elie Metchnikoff, reported that selective microbiota have beneficial role in gastro-intestinal tract. Probiotic organisms help in improving body’s natural defense mechanism [7]. The Food and Agriculture Organization provides official definition of ‘probiotic’ as living organisms that upon ingestion in certain numbers, exert benefits to the consumer’s health [4]. The food products termed as ‘probiotic’ must contain a microbial count of ≥6 log CFU per milliliter or gram at the end of their shelf-life to provide suggested health beneficial effect to the host [6]. According to recent proposal the concentration of probiotic bacteria should not be less than 8 log CFU/g of a product to provide health beneficial effect to host [5]. The idea of probiotic usage for disease management and health restoration is not new. However, lately, the renewed interest probiotics usage as bio-therapeutic agents has been observed mainly due to consumers’ awareness and press drive. Further research had revealed that regular consumption of probiotic could offer a wide range of health benefits. The inclusion of probiotic into different foods has created a new segment of functional food sector labelled as ‘probiotic foods’. Bacteria from Lactobacillus and Bifidobacterium genera are commonly considered as probiotic [3] and they regarded as safe and don’t have any harmful effects on host health [11]. The most commonly used organisms are lactobacilli and bifidobacteria spp [16]. Other lactic acid bacteria (LAB) include in probiotic family are Lactococcus, Streptococcus and Propionibacterium, etc. [18]. Some non-related microbes identified as probiotic are non-pathogenic E. coli Nissle 1917 and Clostridium butyricum [9] yeast spp (Saccharomyces boulardii), filamentous fungi (Aspergillus oryzae), and some spore forming bacilli [8]. A numerous health beneficial effects are claimed in favour of probiotic products including gastrointestinal health, pathogenic gut infections, improvement in lactose metabolism, anticarcinogenic effects, reduction in serum cholesterol, stimulation of immune system, improvement in inflammatory bowel disease, etc. [17]. Some health benefits are well established, while others need to be established, which have shown promising results in animal models. It is important to consider that no single strain will provide all proposed benefits, and not all strains of the same species will be effective against defined health conditions. There is enough evidence to support the opinion that oral administration of lactobacilli and bifidobacteria is capable to restore the normal balance of gut microbiota [11].

Adverse health effect of probiotic
Although, probiotics are considered to be safe and beneficial and harmful effect of probiotic application are rare, but recent data has disclosed regarding adverse effects of probiotic, even regarding to Lactobacillus or Bifidobacterium spp. [1,23].
It should be considered in mind that any probable adverse consequences will be apparent only after long-term consumption of probiotic. Medical reports specify that lactic acid bacteria and probiotic (specially bifidobacterial spp.) commonly used as probiotic are rarely related with human opportunistic infections like sepsis, infective endocarditis, bacteraemia, urological infections, etc. There are an increased evidence of these beneficial organisms being responsible for allergic sensitization and autoimmunity disorders. Elderly people, new borns and pregnant women are at elevated risk of potential probiotic infection as they are immune-compromised. Several Lactobacillus strains are characterized as naturally resistant to vancomycin, which is a matter of apprehension regarding the possible transfer of such resistance to pathogenic organisms residing in the gut.

**The Concept of ‘Metabiotic’**

The term ‘metabiotics’ may be defined as small molecules, the structural components of probiotic (symbiotic), their metabolites or small signalling molecules whose chemical structure is known that can affect the human metabolic and signalling pathways. Several probiotic organisms can become a source of various LMW bioactive molecules with various activities like bacteriocins, short chain fatty acids, other fatty and organic acids, proteins, peptidoglycans, nucleic acids, peptides, amino acids, antioxidants, vitamins, etc. The probiotic organisms may be utilized as source for industrial production of such bioactive components. The information regarding quality and quantity of these bioactive molecules produced by potential probiotic strain will provide researchers the novel metabolics with increased health efficacy, optimum dosage, and mode of action. Large scale industrial production of metabolics could be a novel prophylactic and therapeutic approach to address human health problems in the near future. Metabiotics can be used as food supplements and development of future functional foods for prophylaxis and management of human health problems. Metabiotics are advantageous over probiotic and symbiotic because of their known chemical structure, which can provide accurate information regarding their dosage, safety, and shelf-life. Besides, metabiotics have better absorption, metabolism, distribution, and excretion abilities as compared to live probiotics microorganisms. Metabiotics are a natural evolution of the probiotic conception which has been found beneficial in human health and diseases over probiotic and can be considered as future of functional food industry. The following molecules can be considered as metabiotic:

- **Shot Chain Fatty Acids (SCFAs):** Lactic acid, propionic acid, acetic acid, succinic acid and butyric acid etc. come under the category of short chain fatty acids. These are useful in colon cancer and immunity.

- **Polyamines:** The molecules include in this category are putrescine, spermidine and spermine: the health beneficial effect associated with these molecules are: immunomodulation, cancer and inflammatory disorders.

- **Bacteriocins:** These are anti-microbial peptides having food preservation effect and health promoting activity like reduction of high blood pressure.

- **Bioactive Peptides:** Bioactive peptides are protein fragments produced during fermentation in cheese, fermented milk, milk protein hydrolysates having several health beneficial effects like antithrombotic, anti-hypertensive, immune-modulating, osteoprotective, anti-lipemic properties, antioxidants, opioid and opioid antagonists, angiotensin-converting enzyme inhibitors etc.

- **Quorum Signalling Molecules:** These compounds includes Acyl-Homoserine Lactone (AHL) & Autoinducer Peptide(AIP). These molecules are having health beneficial properties like anti-inflammatory, anti-cancer, etc.

Some commercial metabiotics products have been given below (Table 1).

**Preparation of functional Dairy Products with metabiotic**

Probiotic organism will be grown on suitable substrate for production of potential metabolitic components. The specific metabolite will be separated, collected and incorporated into suitable.

**Insert table. 1**

Dairy products as shown in fig. 1. Alternatively, probiotic strain will be added during product preparation and fermented for suitable time followed by heat processing and packaging.

**Insert fig. 1.**

**Conclusion**

Metabiotic, which is the metabolite of probiotic, found more beneficial and safe due to known chemical structure and can be used for the development of new generation functional foods. However, the concept has newly introduced in probiotic research and persistent research is required in this regard to establish their efficacy in several chronic diseases through *in-vitro* and *in-vivo* experiments.

<table>
<thead>
<tr>
<th>Name and Characteristics of the product</th>
<th>Health beneficial Property</th>
</tr>
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<tbody>
<tr>
<td>“Hylak Forte” (Ratiopharm/Merckle, Germany) Metabolite of <em>Escherichia coli</em> DSM 4087. <em>Streptococcus faecalis</em> DSM 4086, <em>Lactobacillus acidophilus</em> DSM 4149 and <em>L. helveticus</em> DSM 4183</td>
<td>Positive effects in gut health</td>
</tr>
<tr>
<td>“Zakofalk” (a blend of sodium butyrate and inulin)</td>
<td>Inflammatory intestinal diseases</td>
</tr>
<tr>
<td><em>E. coli</em> glycoprotein</td>
<td>Helpful in anorexia</td>
</tr>
<tr>
<td><em>Lactobacillus casei</em> polysaccharide - Glycopeptides</td>
<td>Antihypertension</td>
</tr>
<tr>
<td><em>Bioactive peptides by L. helveticus</em> (Val-Pro-Pro and Ile-Pro-Pro)</td>
<td>Decrease of blood pressure</td>
</tr>
<tr>
<td><em>Bactstatin</em> bacteria-free lyophilized <em>B. subtilis</em> culture fluid containing lysozyme, catalase, polypeptides, peptidoglycan, amino acids, and natural sorbent celite</td>
<td>Immune-modulation and restoration of gut-microbiota</td>
</tr>
</tbody>
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( Adopted from Shenderov, 2013)
Fig 1: Preparation of metabolite enriched dairy product

References
5. Ganguly NK, Bhattacharya SK, Sesikeran B, Nair GB, Ramakrishna BS, Sachdev HPS et al. ICMR-DBT guidelines for evaluation of probiotics in food. The Indian Journal of Medical Research. 2011; 134(1):22.