Industrial Bioprocessing Alert (TechVision)

Probiotics in Nutraceuticals

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Probiotics in Nutraceuticals
Probiotics in Nutraceuticals – Introduction

Nutraceuticals are extracts containing biologically active food components supplied in forms other than food. On the basis of applications, nutraceuticals can be divided into functional foods, beverages, and dietary supplements.

Consumption of probiotics, which offers numerous health benefits by improving the intestinal microbial balance in consumers, through functional food products is the most popular approach at present. However, there are several challenges in using probiotics as nutraceutical ingredients, as identified by the industry.

This issue of the *Industrial Bioprocessing* TechVision Opportunity Engine features some of the recent technologies for using probiotics in nutraceuticals. The purpose of this profile is to:

1. provide an overview of factors and challenges affecting probiotics’ survival in nutraceutical applications;
2. highlight recent technological advances and their attributes in maintaining probiotics’ viability and stability for nutraceutical benefits.
**Strategic Perspectives**

### Key Market Trends

**Drivers**
- The rise in consumer awareness on probiotics
- Rising popularity of probiotic functional foods and beverages among consumers
- Active development of functional food varieties in the market
- The growing population and rising disposable incomes in developing Asian countries that spiked the demand for functional foods and dietary supplements

**Restraints**
- The maintenance of viability and stability of probiotics
- The inability of some probiotic strains to resist simple substance combinations, industrial conditions, and gastrointestinal stress factors
- Shortcomings in processing and storage, which affect the viability of probiotic organisms
- The negative effects of probiotics on product quality and sensory properties

Current, nutraceuticals is driving an emerging trend of personalized nutrition, whereby food and drinks are personally matched to consumers’ health, nutritional needs, and preferences.

Probiotics fit the nutraceuticals market trends as consumers demand for products that can promote healthy teeth, prevent digestive health issues and boost the immune system.

### Competitive Landscape

- **Drivers**
  - The leading nations in the global nutraceutical markets are the US, Japan, Israel, and Germany.
  - Germany, the Netherlands, and Sweden have emerged as the key nutraceutical innovation hubs in Europe.
  - The UK and Spain are the key test markets in Europe for new nutraceutical products.
  - As for the global functional food market, the Asia Pacific region is expected to be the second dominant participant behind the USA by 2020.

- **Patent Trend**
  - The global probiotics market is forecasted to grow steadily from 2014 to 2020 due to increasing demand from health-conscious consumers. This has influenced the patent trend for probiotics in nutraceuticals in 2014 – 2015.
  - The United States Patent and Trademark Office (USPTO) registered the largest number of patents (filed and granted).
Innovations for Probiotics in Nutraceuticals
**Problem Statement**

Microencapsulation is one of the solutions to maintain the viability and optimum protection of probiotics in capsule, tablet, and powder forms. However, there are challenges in applying probiotic microencapsulation technology, which include:

1. The appropriate selection of microencapsulation technique and encapsulating material
2. Unstable microcapsules due to incompatible formulations
3. Difficulty in producing uniformly sized microcapsules

**Features**

1. Patented probiotic encapsulation technology that uses gentle extrusion method and a proprietary biopolymers blend as shell substrate
2. Produces odorless and tasteless microcapsules ranging from 150-500 µm in diameter
3. Produces very stable microcapsules that can withstand increased temperatures, acidic pH, moisture, and increased oxygen concentrations
4. Cost efficient and easy-to-use, has potential for diversely different applications and applicable in most nutraceutical production facilities

**Potential Applications**

- Microcapsules are applicable in most known galenic formulations such as capsules, tablets, gels, liquids, and oils.
- Microcapsules can be mixed with powders such as formula milk and proteins and with cereals for cereal bars.
- Encapsulated probiotics can be mixed with various substances such as vitamins, high vitamin C doses, minerals, plant extracts, different salts, and other nutritious ingredients.
- Customized products can be developed according to customers’ formulations or specifications.

**Results**

Intelicaps’ probiotic microencapsulation technology enables optimum probiotics survival at production level to allow endless possibilities for substance combinations.
**ProDURA™ Bacillus coagulans, Nebraska Cultures, California, U.S.A**

**Unique probiotic strain**

**Problem Statements**

Probiotics are sensitive toward ingestion processes due to the pH level and enzymatic activities in the gastrointestinal tract.

Rigorous nutraceutical production processes and activities may disrupt probiotics’ viability and quality.

**Tech Profile**

The bacterium ProDURA™ Bacillus coagulans from Nebraska Cultures continues the legacy of the company's founder, the late Dr. Khem Shahani's scientific probiotic research.

**Where**

Nebraska Cultures is located in California, USA.

**Innovation Attributes**

1. **Scientifically proven to reduce total cholesterol and LDL levels and raise HDL levels in the blood**

2. **Able to withstand high temperatures**, up to 110 degrees C, applicable for food, soft gel and gummy processing

3. **pH stability**

   - Stable at both very high and low pH conditions, deliver higher counts of probiotics

4. **Robust**

   - Can survive extreme processing, shipping, storage and natural challenges of the digestive tract

**Features**

- ProDURA™ Bacillus coagulans is a probiotic strain that is effective, stable, and potent. It is in free flowing powder form and its cells in spore form.
- It is developed to fit and adapt to food manufacturing-related processes and human consumption.
- The strain’s protective coating only works under optimum heat, pH, and moisture of the large intestine. It is a powerful shield for the probiotics to withstand extreme conditions and manufacturing activities. The potency of the probiotic can be well maintained for up to 3 years at room temperatures.
- The strain is highly resistant to stomach acid and bile.

**Potential**

The protective coating ProDURA™ has been shown to be superior to other Bacillus coagulans strains in the market in terms of heat resistance.

Laboratory research has also shown that it can potentially reduce incidences of lactose intolerance, promote healthy growth and reduce bacterial infections in animals.
**BIO-tract®, Nutraceutix, Washington, USA**

*Probiotic controlled-release technology for nutraceuticals*

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**Problem Statement**

Controlled-release technology is very beneficial as it improves nutrient availability, lessens chances of side effects, heightens product effectiveness, simplifies dosing and improves dosage compliance. However, the related challenges include:

1. **High investment required for nutraceuticals company in opting for controlled-release technology**
2. **Disruption from stomach acids in the digestive tract, which highly affects probiotic functions**

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**Solution**

**BIO-tract®** controlled-release technology by Nutraceutix is made for nutritional supplement application, which may involve probiotics as the nutritional ingredient. It is effective for controlled and extended release of nutritional ingredients.

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**Advantages**

- Delivers an optimal amount of probiotics at a predictable rate
- Accommodate a wide range of active ingredients (suitable for combined probiotic ingredients)
- Simplifies and improves dosage compliance
- Enhances the absorption of active ingredients
- Protects a supplement’s probiotics from gastric acid, while providing optimal release of live organisms throughout the digestive tract
- Reduce production cost and complications

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**The Features**

- Programmable, consistent release
- Specially designed for extended and controlled ingredient release
- Effective to protect sensitive ingredients such as probiotics
- Keeps preferred amounts of active ingredients available for absorption over a desired period of time

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Nutraceutix partners with leading commercial and academic research institutions in probiotic research.

It has worked on various occasions with researchers including those from **Bastyr University** (USA) and the **German Diabetes Center** to produce probiotic supplements in the **BIO-tract®** caplet format.
SYNTEK®, SynbioTech Inc., Taiwan
Optimized probiotic production

Unmet Needs
1. High levels of viable probiotics are recommended in probiotic foods for efficacy.
2. There is difficulty in maintaining probiotic counts throughout preparation, processing, and storage.
3. The survival of probiotics during the drying process depends on strain, drying process and culture media.

Innovative Technology Attributes
- Growth medium, fermentation conditions and coating materials are designed specifically according to strain’s characteristics.
- Strains are applied with patented coating and freeze-drying techniques.
- It produces probiotics with enhanced lactic acid bacteria adhesion, acid and bile salt tolerance, immunity and storage ability.

Tech Profile
SynbioTech Inc.’s “SYNTEK® thorough” system is a probiotics optimizing development system that designs the medium, incubation conditions and coating materials for producing probiotics using its coating technology and freeze-drying technologies.

Advantages
- Easy and convenient production
- Reduced labor cost
- Reduces the risk of probiotics contamination
- Product value can be maintained
- Uses relatively lower temperatures than for the spray-drying technique

Results
- The survival rate of powdered freeze-dried probiotics is higher compared to other drying techniques.
- The high viability of dried probiotics is vital for health-promoting effects of nutraceuticals.
Opportunities for Probiotics in Nutraceuticals
Funding and Technology Roadmap

Maintenance of low production costs will remain challenging for future probiotic processes and formulation technologies. The advancement of the technologies needs strong financial support from funding bodies, which will lead to smooth technology progress along the roadmap. The Young Investigator Grant for Probiotics Research contributes to the advancement of probiotics research in the USA with an annual grant of $50,000 per grant recipient. The Ontario Research and Development Challenge Fund (ORDCF) has allocated $500 million in order to promote research and partnerships between business and research institutions in Canada. The Dannon Yogurt and Probiotics Fellowship Program by Dannon offers $25,000 to graduate students who show a strong interest in research on the nutritional value and importance of yogurt and probiotics. It was found that the source of funding does not influence the majority of outcomes in favor of the sponsors’ products.

**Technology Roadmap**

- **2016**
  Technologies on probiotic encapsulation techniques, processing alteration, controlled-release systems and improvisation of storage conditions.

- **2020**
  Exploitation of food-grade raw materials (for instance, herbs) into which probiotic ingredients can be successfully incorporated – broadens the food type range.

- **2018**
  Further development in manufacturing processes and formulations of probiotic strains.

- **2023**
  Adoption

- **2024**
  New product categories with regard to probiotics technology for the functional food markets
Key Patents and Contacts
<table>
<thead>
<tr>
<th>Title</th>
<th>Patent Number</th>
<th>Issue/Publication Date</th>
<th>Assignee/Applicant</th>
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<tbody>
<tr>
<td>ACIDIC LACTIC ACID BACTERIA BEVERAGE AND METHOD OF PRODUCING ACIDIC LACTIC ACID BACTERIA BEVERAGE</td>
<td>US 20100247711 A1</td>
<td>09/30/2010</td>
<td>Kanetada Shimizu</td>
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<tr>
<td>An acidic lactic acid bacteria beverage having a favorable flavor and an improved survival rate for bifidobacteria. The acidic lactic acid bacteria beverage of the present invention includes bifidobacteria and inulin, wherein the inulin is not fermented by the bifidobacteria. The inulin content is preferably within a range from 1 to 10% by mass, and the pH of the acidic lactic acid bacteria beverage is preferably within a range from 4.1 to 4.8.</td>
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| PHARMACEUTICAL COMPOSITION, FOOD OR DRINK, OR FEED FOR INTESTINAL DISEASE. | US 20110262421 A1 | 10/27/2011             | Kouichirou Shin          |
| It is intended to provide a pharmaceutical composition, a food or drink, or a feed which has an effect on the prevention and/or treatment of an intestinal disease such as ulcerative colitis, Crohn's disease or irritable bowel syndrome. A preferred embodiment is the pharmaceutical composition, food or drink, or feed which contains lactoperoxidase as an active ingredient and has an effect on the prevention and/or treatment of an intestinal disease, wherein the intestinal disease is at least one disease selected from ulcerative colitis, Crohn's disease and irritable bowel syndrome. |

<p>| A method for producing naturally derived beneficial compounds including dispersing a microbiological culture media including at least one live probiotic organism, and at least one nutraceutical and/or at least one nutritive agent in distilled water to form a broth, incubating the broth at a predetermined temperature for a select period of time to induce probiotic activity; halting the probiotic activity, and separating the desired compound from the broth. |</p>
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<th>Issue/Publication Date</th>
<th>Assignee/Applicant</th>
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<tr>
<td>DRY FOOD PRODUCT CONTAINING LIVE PROBIOTIC</td>
<td>US 9072310 B2</td>
<td>07/07/2015</td>
<td>Advanced Bionutrition Corp.</td>
</tr>
<tr>
<td>The disclosure relates to a probiotic delivery system that can be consumed as a snack-food or added to a food product. In particular, the disclosure describes a crisp and tasty treat that comprises viable probiotic microorganisms preserved in a vacuum dried matrix of sugars, proteins, and polysaccharides. The probiotic remain viable within the treat for a longer time without the need for additional moisture barrier coating. The probiotic also remain viable in the animal gastrointestinal tract.</td>
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<td>PROBIOTIC COMPOSITION USEFUL FOR DIETARY AUGMENTATION AND/OR COMBATING DISEASE STATES AND ADVERSE PHYSIOLOGICAL CONDITIONS</td>
<td>US 8192733 B2</td>
<td>05/06/2012</td>
<td>Cobb &amp; Associates</td>
</tr>
<tr>
<td>A probiotic composition including the bacilli (1) Bacillus subtilis, (2) Bacillus coagulans, and (3) Enterococcus faecium. The composition may further include a carrier medium, such as fructo-oligo-saccharides (FOS), as incorporated in a dose form such as a pill, capsule, powder or sachet. The compositions of the disclosure may be usefully employed as health or nutritional supplements, food additives, or therapeutic agents for combating a wide variety of physiological disorders, such as irritable bowel syndrome, autism, and fibromyalgia.</td>
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<tr>
<td>LONG-LIFE PROBIOTIC FOOD PRODUCT</td>
<td>EP 2276357 B1</td>
<td>21/09/2011</td>
<td>Friesland Brands Bv</td>
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<tr>
<td>Disclosed is a food product such as a dairy product or fruit product of long-life nature (i.e. it can be stored non-refrigerated for an extended period of time) and that provides probiotic activity to the consumer. The latter is done by the inclusion of spores of probiotic bacteria. The product particularly is selected from the group consisting of dairy products (like e.g. dairy drinks, dairy derived food products and dairy food ingredients), fruit drinks, or concentrates thereof.</td>
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