Synbiotic product

Synbiotics = combination of pro- & prebiotics
Probiotics = life cells positively influencing gut flora
  Lactic acid bacteria & several yeast strains
Prebiotics = non- or slow digestible food components:
  positive influence on particular gut bacteria
Types & numbers of microbes

In human gut system

In healthy person everything is in balance

→ Homeostasis
3 situations have something in common

- Children with atopic eczema
- Operation patients
- Elderly people

Living examples showing
Probiotics +/- or Prebiotics
Help promoting their health

Potential target groups
Working of Probiotics

Probiotic strain

- Inhibits adhesion of pathogen cells
- Acts as biosurfactants
- Produces acids
- Produces bacteriocins
- Inhibits growth of pathogen cells
- Modulates cytokine production
- Produces hydrogen peroxide
- Inhibits growth of pathogen cells
- Work as co-aggregation molecules
- Block the spread of pathogens
- Strengthen the immune system
- Detoxification
Working of Prebiotics

1. Prebiotics contained in foods or supplements are consumed
2. Prebiotics are not digested in the stomach or small bowel
3. Prebiotics remain intact until they pass into the large bowel
4. Prebiotics are used as food by beneficial bacteria in the large bowel
5. Increased beneficial bacteria in the large bowel lead to a variety of health effects
Working of Synbiotics

FOS = Fructo-oligosaccharides
GOS = Galacto-oligosaccharides

Absorption by gut
10% of daily energy req

Lowers pH
Clostridia

FOS
GOS

Lactobacilli
Bifidobacteria

Succinate
Lactate
Acetate

Anaerostipes caccae
Eubacterium halli

Butyrate
Propionate
Acetate
Vulnerable groups

High meat diet

Eldery people

Decrease of bifidobacteria relative to peptide degrading bacteria
Protein degradation in colon:

Sugar at low pH: hexoses $\rightarrow$ HMF  pentoses $\rightarrow$ fufural

Maillard reaction in food:

Tuohy et al 2006 Mol Nutr Food Res 50:847-857
Heterofermentative: \textit{L. reuteri}

Two glycolytic pathways operating simultaneously

PKP alone:

\[ \text{Lac} : (\text{Ac} + \text{EtOH}) = 1 : 1 \]

\textit{L. reuteri}:

\[ \text{Lac} : (\text{Ac} + \text{EtOH}) = >1 : 1 \]

EMP alone:

\[ \text{Lac} : (\text{Ac} + \text{EtOH}) = 2 : 0 \]

PKP: net 1 ATP

EMP: net 2 ATP

\[ \text{Årsköld et al 2008 J Bact} \]
Metabolic map *L. reuteri*

Reducing equivalents:
Not to Ac CoA, but instead to Furfural

Then AcP to Acetate:
1 xtra ATP

van Niel et al. accepted
Proof of principle: L. reuteri with/without furfural as model compound

Control: 25 g/L Glucose

Furfural: 25 g/L Glucose + 0.1% Furfural (arrow)
Next steps: different levels of getting evidence

• More testing:
  ❖ How will prebiotics improve probiotics?
  ❖ Which probiotics – prebiotics combination(s)?

• Lab reactors → Artificial systems or animals?

• Voluntary humans – who?

• To justify any health claims
Health claims true?

Meet the Bacteria

These microorganisms have been shown to boost health in scientific studies:

<table>
<thead>
<tr>
<th>Strain</th>
<th>Benefits</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bifidobacterium animalis</em></td>
<td>Gut health and faster digestion</td>
<td>Dannon Activia yogurt</td>
</tr>
<tr>
<td>DN-173 010 (marketing name: Bifidis Regularis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Bifidobacterium infantis</em></td>
<td>Alleviates symptoms of irritable bowel syndrome</td>
<td>Procter &amp; Gamble’s Align supplement</td>
</tr>
<tr>
<td>35624</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Bifidobacterium lactis</em></td>
<td>Helps immune system and digestive health</td>
<td>Yo-Plus yogurt, Nestle Good Start infant formula</td>
</tr>
<tr>
<td>Bb-12</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus casei</em></td>
<td>Helps immune system and digestive health</td>
<td>Yakult fermented dairy drink</td>
</tr>
<tr>
<td>Shirota</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus casei DN-114 001</em> (marketing name: L. casei Immunitas)</td>
<td>Helps immune system; lessens duration of colds and flu in older people</td>
<td>Dannon’s DanActive dairy drink</td>
</tr>
<tr>
<td><em>Lactobacillus rhamnosus</em></td>
<td>Improved vaginal health; helps eradicate vaginal</td>
<td>RepHresh Pro-B and Fem-Dophilus dietary supplements</td>
</tr>
<tr>
<td>GR-1 in combination with Lactobacillus reuteri</td>
<td>infections</td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus reuteri</em></td>
<td>Helps treat colic, gingivitis, antibiotic-associated diarrhea</td>
<td>BioGaia tablets, drops and lozenges</td>
</tr>
<tr>
<td>55730</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Saccharomyces boulardii</em></td>
<td>Helps prevent and treat antibiotic-associated diarrhea</td>
<td>Florastor dietary supplement</td>
</tr>
<tr>
<td>yeast</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EFSA
European Food Safety Authority

Regulation
Your project aim

• To design a new functional food based on synbiotics
• Take in account:
  o What you have to acquire for exhibiting health claims (research & animal/human tests)
  o A plan how to educate the public about your product
  o Choose target group
Starting literature

Elin E-book library
Elin journals library

Internet for news on Market Business
Report

- Objectives
- Time schedule/time plan
- Formulation of the product (required research)
- Plan for testing health claims (EFSA regulations as a guide)
- Quality control/GMP/Hazards
- Product preparation – shelf life
- Cost estimation (investment/manufacturing/cash flow)
- Environmental aspects
- Packaging/labeling – legislation
- Health claims
- Marketing aspects – target group/evaluation existing market
- Business plan
- Conclusion
- References
How Do I Know Probiotics Work?
Each probiotic that is used in a product has to undergo many trials to show that it is safe, effective and has proven health benefits. One of the tests which a probiotic bacterium must pass is its ability to pass through the stomach and reach the large intestine. A bacterium which falls at the first hurdle of stomach acid, digestive enzymes and bile would be no use! The probiotic used in Marks and Spencer foods has been shown to navigate the gut successfully.

What are Prebiotics?
- Prebiotics are complex carbohydrates that stimulate the growth of our natural intestinal bacteria and can help to promote a healthy digestive system.
- Prebiotics occur naturally in a range of foods such as asparagus, chicory, leeks, artichokes, bananas, onions, garlic, wheat, oats and soya beans. These days, you'll find a number of foods with added prebiotics too - like yogurts, yogurt drinks, cheeses, breakfast cereals and cereal bars.

The “Global Market Review of Functional Foods” estimates Worldwide functional food market ~ $90.5 billion by 2013
http://www.preparedfoods.com/articles/article-synbiotics-in-focus-july-2010
## TABLE 6.1 Species from which probiotics used in humans have been isolated

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Bifidobacterium</th>
<th>Leuconostoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactobacillus</td>
<td>bifidus</td>
<td>Pediococcus</td>
</tr>
<tr>
<td>acidophilus</td>
<td>infantis</td>
<td>Propionibacterium</td>
</tr>
<tr>
<td>johnsonii</td>
<td>longum</td>
<td>Enterococcus</td>
</tr>
<tr>
<td>plantarum</td>
<td>thermophilus</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>rhamnosus</td>
<td>adolescentis</td>
<td>Lactococcus</td>
</tr>
<tr>
<td>delbruecki</td>
<td>catenulatus</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>reuteri</td>
<td>pseudocatenulatus</td>
<td>niger</td>
</tr>
<tr>
<td>fermentum</td>
<td>lactis</td>
<td>oryzae</td>
</tr>
<tr>
<td>brevis</td>
<td>Streptococcus</td>
<td>Yeast and fungi</td>
</tr>
<tr>
<td>lactis</td>
<td>lactis</td>
<td>Saccharomyces</td>
</tr>
<tr>
<td>cellobiosus</td>
<td>cremoris</td>
<td>boulardii</td>
</tr>
<tr>
<td>paracasei</td>
<td>salivarius</td>
<td></td>
</tr>
<tr>
<td>helveticus</td>
<td>intermedius</td>
<td></td>
</tr>
<tr>
<td>Health claim system</td>
<td>Japan</td>
<td>China</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Foods for Specified Health Uses (FOSHU)</td>
<td>Health food</td>
<td>ANVISA 1999</td>
</tr>
<tr>
<td>Definition</td>
<td>FOSHU is foods officially approved to claim specific health physiological effects on the human body.</td>
<td>Health food is food officially approved to claim specific health efficacy and/or replenishment of vitamins specified regulate not be so. The food any acute disorder.</td>
</tr>
<tr>
<td>No. of trials required</td>
<td>One.</td>
<td>One.</td>
</tr>
<tr>
<td>Subjects</td>
<td>Local population except for oral health.</td>
<td>Local population.</td>
</tr>
<tr>
<td>Publication on result</td>
<td>Required to publish in peer reviewed journal.</td>
<td>Not required.</td>
</tr>
<tr>
<td>Claim on probiotics</td>
<td>Approved in ‘improve in GI conditions’ category.</td>
<td>Approved in ‘regulating gastrointestinal tract flora’, ‘enhancing immunity’, ‘facilitating feces excretion’, ‘facilitating digestion’, ‘improving skin water content’ categories.</td>
</tr>
<tr>
<td>Approved probiotics</td>
<td>10 single strain and 3 strain combinations in 73 products, as of Nov 2008.</td>
<td>12 species in 40 products, as of April 2009.</td>
</tr>
<tr>
<td>Novel food registration for probiotics</td>
<td>Not required.</td>
<td>Not required.</td>
</tr>
<tr>
<td>Remarks</td>
<td>Nutrient function claim is separately ruled under Food with Nutrient Function Claims (FNSC), where 12 vitamins and 5 minerals with fixed claims are allowed without any requirement for application.</td>
<td>In 2005, new rules for vitamins and minerals were added, and claim categories were expanded.</td>
</tr>
</tbody>
</table>

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