The future landscape of digestive health

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- The importance of digestive health
- Digestive health: What are consumers looking for?
- Digestive health solutions: more than pro- & prebiotics
- Digestive enzymes
- Case study Gluten Digestion
The importance of digestive health

- Digestive wellness is one of consumers' top health concerns\(^1\)
- 2 out of 3 adults experience some type of gastrointestinal issue\(^2\)
- Continuous yearly increases are reported in prevalence of digestive discomfort due to:
  - Reduced quality of diet (high fat, low fruit & vegetable, alcohol etc)
  - High stress, less eating moments, eating on the go
  - Obesity
  - Ageing

**Top 5 problems:**

1. Gas, bloating, or flatulence
2. Heartburn, acid reflux
3. Diarrhea
4. Constipation
5. Ingestion

\(^1\) Euromonitor 2014, after general wellbeing and obesity
\(^2\) Lightspeed GMI/Mintel, Digestive health, July 2015, US
What is the consumer approach?

Treatment Approach to issues

- Proactive treatment: 44%
- Reactive treatment: 27%
- Don't actively treat: 29%
- Medications
- Supplements
- Diet
- Lifestyle

Source: Lightspeed GMI/Mintel, Digestive health, July 2015, US
Diet major contributor for digestive health

Diet modifications to manage digestive health issue

<table>
<thead>
<tr>
<th>Diet Modification</th>
<th>Not interested</th>
<th>Interested in trying</th>
<th>Currently use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eat/drink high-fiber foods</td>
<td>17%</td>
<td>35%</td>
<td>48%</td>
</tr>
<tr>
<td>Eat/drink probiotics</td>
<td>28%</td>
<td>32%</td>
<td>40%</td>
</tr>
<tr>
<td>Change diet eliminating problem foods</td>
<td>23%</td>
<td>41%</td>
<td>36%</td>
</tr>
<tr>
<td>Eat packaged foods with digestive claims</td>
<td>46%</td>
<td>35%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Source: Lightspeed GMI/Mintel, Digestive health, July 2015, US
Market size of foods supporting digestive health is growing along with the increasing consumer interest

- Sales of foods with digestive health as prime positioning
  US$ 77.2 billion globally, with > 10% CAGR (13% 2009-2014)

- In reality the category for digestive health is bigger and more dynamic;
  → Should also include the ‘intolerance/free from’ category
  → CAGR 36% reaching US$ 13.2 billion globally in 2105

Main categories:
✓ Lactose-free : US$ 5.0 billion
✓ Gluten-free : US$ 3.42 billion

Source: Euromonitor, statista
Digestive health; not only a consumer or market trend
Digestive health & ingredients

Digestive Enzymes
- Nutrient breakdown
- Breakdown undesirable food components
- Protease
- Lipase
- Carbohydrase
- Lactase
- Glutenase
- Phytase

Gut Microbiota
- Right balance of microorganisms
- Feeding the right microorganisms
- Probiotics
- Fibers/Prebiotics

Gut Wall
- Gut endocrine function
- Optimal gut barrier function/mucus
- Vitamin A, B2,3,7, D
- PUFA
- Resveratrol
- Vitamin A, D probiotics

Gut Immune system

Probiotics
- Ronozyme®
- Maxilact®
- Tolerase®
- Maxipro®
- MaxiLact®
- Culturelle®
- Maxipro®
- Culturelle®

Fibers/Prebiotics
- Oatwell®, Fabuless®
- Life’s DHA®
- ResVida®
- Quali-A,B,D®
- Quali-A,D®

Enzymes
- Protease
- Lipase
- Carbohydrase
- Lactase
- Glutenase
- Phytase

Ingredients
- Vitamin A, B2,3,7, D
- PUFA
- Resveratrol
- Vitamin A, D probiotics
Digestive enzymes: fundamental to life

External energy

Dietary macronutrients (carbohydrates, fats, proteins)

Enzymes (carbohydrases, lipases, proteases)

Particles available to metabolism (glucose, fatty acids, glycerol and amino acids)

Internal energy
Digestive Enzymes

**Digesting nutrients**
- Carbohydrases
- Lipases
- Proteases

**Degrading anti-nutrients**
- Phytase
- Tannase
- Proteases (to break down natural enzyme-inhibitors)

**Degrading unwanted food compounds**
- Lactase
- Glutenase
- α-Galactosidase
- Protease for milk allergy

Improved availability nutrients and energy
Sources of digestive enzymes

**Plant derived Enzymes**
- Papain (papaya)
- Bromelain (pineapple)
- Actinidin (kiwi)

**Animal-derived Enzymes**
- Chymosin, lipase
- Pepsine, (chymo)trypsin
- Pancreatin

**Microbial Enzymes**
- protease, peptidase, lipase, amylase
- glucoamylase, invertase, lactase, $\alpha$-galactosidase,
- cellulase, hemicellulase, pectinase and phytase

- Broad substrate specificity
- Can be modified to optimize pH or temperature profile
- Controlled manufacturing of high enzyme activities and purity
- Can be blended to targeted applications
Case study

Proline Specific Protease for Gluten digestion
Gluten intolerance

Gluten: protein found in wheat, barley, and rye

Many individuals cannot tolerate gluten
  - Coeliac disease: 0.4%-1%
  - Gluten sensitivity: 0.6%-6%

Proline-rich epitopes
  - Poorly digested in GI tract
  - Trigger immune response in coeliac disease
  - Gluten sensitivity: mechanism unknown

Gluten-free diet

Low gluten grain cultivars

Enzymes
  - Food processing
  - Supplements
PSP: Proline-Specific Protease

- Unique and patent-protected protease
- Isolated from food-grade fungus *Aspergillus niger*
- Specifically cleaves peptides after proline residues
Proline specific protease for use in dietary supplements (Tolerase G®)

- PSP is active and stable at low pH (3-5) and 37°C
- PSP is not digested by pepsin
- PSP reduces immunogenic response (T-cell proliferation) to gliadin

1 Stepniak D et al. AJP-Gastrointest Liver Physiol • VOL 291 • 2006
Tolerase™ G digests gluten in the stomach of the TIM gastrointestinal model

**Study design**

- A standard fast food menu was processed in the TIM system with and without co-administration of Tolerase™ G
- Samples taken from the stomach, duodenum, jejunum and ileum compartments from T0 until T4h
- Immunogenic peptides from gliadins and glutenins assessed by monoclonal antibody-based competition assays, Western blot analysis and T-cell proliferation assays

**Results**

Tolerase G: degrades gluten in the GI-tract

Stomach
- Placebo
- Tolerase G

Small intestine
- Placebo
- Tolerase G

limit of quantitation: 21 mg*min/L

Liquid meal: 4 g gluten
Liquid AN-PEP or placebo
Acetaminophen (gastric emptying)

Gastric sampling
Duodenal sampling

Salden B et al. AP&T 2015
Proline specific protease for gluten-free beer (Brewers Clarex®)

• Beer chill-haze: Proline-rich peptides form a haze by complexing with polyphenols in the beer

• “Brewers Clarex ®”: PSP can clarify beer without affecting foam and taste

• Brewers Clarex-treated beer: Gluten-Free without compromise!
Gluten Removal with Brewers Clarex®

Worth:
>1000ppm Gluten + Brewers Clarex (2-3 g/hl)

Green beer:
<10ppm Gluten (R5 Elisa)

<table>
<thead>
<tr>
<th>Product</th>
<th>Prolamin (mg/kg)</th>
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<tbody>
<tr>
<td>Wort</td>
<td>2967.5 ± 28.0</td>
</tr>
<tr>
<td>Beer with 2.5g/hl BC</td>
<td>&lt;3.0 ± 1.5</td>
</tr>
<tr>
<td>Beer with no BC</td>
<td>131.1 ± 1.0</td>
</tr>
</tbody>
</table>

Adapted from Guerdrum and Bamforth, 2012
Sensitive LC-MS/MS confirms Brewers Clarex® treated beer is gluten free

LC-MS/MS:
C18 chromatography
Accela LTQ Orbitrap
MS: 300-1500 m/z

97ppm
143

MS: n° of peptides containing possible T-cell epitopes
ELISA score

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Summary

- Healthy digestion is a growing consumer concern due to societal changes in diet and lifestyle.

- Food category with healthy digestion claims is growing rapidly;
  - adding beneficial ingredients (pre/probiotics and fibers)
  - removing ingredients of concern (intolerance)

- DSM has a wide range of ingredients supporting healthy digestion.

- For example, we recently launched an enzyme capable of specific digestion of gluten to support consumers with gluten intolerance:
  - Dietary supplement to digest gluten in the stomach
  - Food processing enzyme to digest gluten in the food (beer, bakery)
Thank you for your attention!

Visit us at the FiE and experience the launch of the Digestive Health Platform

DSM
Bright Science.
Brighter Living

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