Digestive Health: A Strong Innovation Platform in Asia

Speaker: Robin Wyers, Chief Editor, Innova Market Insights, Netherlands
Digestive health: A strong innovation platform in Asian NPD

Robin Wyers, Chief Editor
Tracking trends since 1994...

Gaio
Fiber and prebiotics are now positioned as ingredients that can differentiate a product.

LC1
Joins Yakult and Actimel as a single shot that delivers functional ingredients (cultures + fiber) for gut health.

Probiotics in Europe
The Japanese pioneered gut health with Yakult. European companies are now actively launching products that deliver functional health benefits. Gut health has mainstream potential.
275,000 products tracked annually across 85 countries
From technology to new products to consumers & markets
Trends of F&B for digestive health in Asia

TOPICS FOR TODAY

• Overview of digestive health NPD in Asian market

• Digestive health NPD targeting different life stages

• Categories to watch in Asia

• Key learnings

ABOUT INNOVA MARKET INSIGHTS

Innova Market Insights is a leading market research company, serving our customers with our unique and powerful Innova Database: the world’s largest database for the food industry, used by leading companies in food ingredients and manufacturing for future success in the dynamic FMCG/CPG industry

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Visit Booth F18

Vitafoods Asia
Overview of digestive health NPD in Asian markets
The gut is often top of mind

Consumers increasingly self-diagnose and experiment with diets that they believe will improve gut health.

These personalized diets are creating new opportunities for free from and fortification.
Manufacturers more focus on digestive health F&B NPD

- The number of product launches of F&B tracked with digestive health claims has doubled in 2016 compared to 2012.
- The mainly growth comes from the baby foods, which has increased three times in number of launches from 2012 to 2016.

Indexed number of new F&B launches tracked with digestive health claims (Asia, 2012=100)

CAGR
2012-2016
+20%

Nestle Lactogen Gold Stage 1 Infant Milk Formula Suitable From 0-6 Months (China, Jul 2017)

Claims: … With added galacto-oligosaccharides (GOS) and fructo-oligosaccharides (FOS). Dietary fiber can help to maintain normal bowel function…
Dairy and Baby Foods dominate the digestive health market

- More than 70% of new Asian product launches with digestive health claims are from Dairy and Baby Foods.
- Other active categories include Hot Drinks, Sauces & Seasonings and Soft Drinks.

Top 5 market categories (in %) of new product launches tracked with digestive health claims (Asia, 2012-2016)

- **Dairy** and **Baby Foods** dominate the market.
  - More than 70% of new Asian product launches with digestive health claims are from **Dairy** and **Baby Foods**.
  - Other active categories include **Hot Drinks**, **Sauces & Seasonings** and **Soft Drinks**.

**Gold Kili Double Shot White Coffee** (Singapore, Feb 2017)
- Claims: **Added inulin**... promote the growth of good **Bifidus bacteria** to help maintain a good digestive health...

**Organic Wellness Ow Zeal Turmeric Powder** (India, Mar 2017)
- Claims: **Turmeric** is helpful in treating flatulence...

**Yuanqi Senlin Sugar Free Oolong Tea** (China, Jul 2017)
- Claims: **Dietary fiber** helps maintain normal function of intestinal tract...
Drinking yogurt/fermented beverages has been the mainstream

Percentage of product launches tracked with digestive health claims per top sub-category (Asia, 2012 vs 2016)

- Drinking Yogurt/Fermented Beverages: 71% in 2016, 58% in 2012, CAGR 2012-2016 +13%
- Spoonable Dairy Yogurt: 63% in 2016, 56% in 2012, CAGR 2012-2016 +9%
- Baby Formula/Milk: 50% in 2016, 40% in 2012, CAGR 2012-2016 +46%
- Baby Cereals & Biscuits: 21% in 2016, 31% in 2012, CAGR 2012-2016 +25%
- Pickled Condiments/Chutney: 10% in 2016, 2% in 2012, CAGR 2012-2016 +51%
China is the key country in Asian market

1/4 OF DIGESTIVE PRODUCTS TRACKED IN CHINA

- China accounts for 27% of total product tracked with digestive health from 2012 to 2016.
- Within the top 5 countries, the fastest growing markets are India and Malaysia. Both of them are growing at a CAGR of 37% for recent five years.

**Top 5 countries for new product launches tracked with digestive health claims (Asia, 2012-2016)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Product Tracking</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>27%</td>
</tr>
<tr>
<td>India</td>
<td>13%</td>
</tr>
<tr>
<td>Malaysia</td>
<td>11%</td>
</tr>
<tr>
<td>Indonesia</td>
<td>10%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>6%</td>
</tr>
<tr>
<td>Others</td>
<td>34%</td>
</tr>
</tbody>
</table>

**TOP 3 COMPANIES ACTIVE IN DIGESTIVE HEALTH**

- **Yili**
- **Mengniu**
- **Bright Dairy**

Local giants dominate: 36% market share
Tackle digestion issues by ingredient in Asian market

**PROBIOTICS**

CAGR Asia 2012-2016
Probiotics  +19%

**PREBIOTICS**

CAGR Asia 2012-2016
Prebiotics  +27%

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**BENEFITS OF PROBIOTICS**

**DID YOU KNOW?**
Probiotics are a culture of good bacteria that can be found in supplements, dairy products and fermented foods like sauerkraut, kimchi and kombucha.

1. **DIGESTIVE HEALTH**
Probiotics have been shown to help with IBS, abdominal pain, cramps, bloating & more.

2. **IMMUNE HEALTH**
One of the main functions of healthy bacteria is to increase the function & effectiveness of our immune system.

3. **SKIN HEALTH**
The skin is the largest organ of the body, so it’s not surprising that gut bacteria affects it.

4. **WOMEN’S HEALTH**
Women are especially at risk for unhealthy gut bacteria, which can lead to pesky infections.
Strong growth of digestive health related claims

- Strong growth in product launches tracked with digestive health related claims in Asia.
- Broader claims of added fiber and high/source of fiber being seen.
Baby foods: The leading Asian probiotic category

Happy Baby Happy Bellies Organic Baby Cereals With Dha Plus Probiotic: Organic Oatmeal Cereal (Indonesia, Jan 2017)

Claims: DHA plus probiotic for immunity support. DHA for eye and brain development. Vitamin and mineral fortified. Dr. Sears recommended. BPA free. Certified organic by California Certified Organic Farmers (CCOF). This container is made from 60% recycled materials. No dairy. No soy. The first baby cereals with probiotics for digestive system health and the only organic cereal with DHA and choline to support brain and eye health...

Probiotic protection: good bacteria specially formulated to help strengthen your baby’s digestive system which can protect against the development of allergies. Dr Sears agrees: “Baby foods with probiotics are a great way to make sure your baby’s system has plenty of “good bowel bugs.” The gastrointestinal (GI) tract is the body’s largest immune organ. The better you feed baby’s GI tract, the better you feed baby’s immune system.” 100% natural: Happy Baby support sustainable agriculture. No pesticides, no chemical fertilizers, no genetically engineered ingredients (GEIs). Life's DHA for healthy brain, eye and heart.
Around ¼ of products with fiber claims are cereals

- Cereals, Bakery and Snacks account for 54% of total products tracked with fiber claims in the last five years.
- 23% of the total F&B products launches with fiber claims are tracked in India.

**Percentage of F&B product launches tracked with fiber claims by category (Asia, 2012-2016)**

- Cereals: 25%
- Bakery: 23%
- Snacks: 17%
- Baby foods: 14%
- Ready Meals: 12%
- Others: 9%
- Others: 9%

Bagrrys Crunchy Muesli: Fruit And Nut With Cranberries (India, Jul 2017)

Radiant Chias Cookies With Oats (Malaysia, Jun 2017)
Gluten free: the growing “better for you” claim

<table>
<thead>
<tr>
<th>SNACK</th>
<th>BABY FOODS</th>
<th>BAKERY</th>
<th>CONFECTIONERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>15%</td>
<td>13%</td>
<td>11%</td>
<td>10%</td>
</tr>
</tbody>
</table>

- **Snapz Organic Apple and Pineapple Crunch** (Hong Kong, Jul 2017)
- **Organics Happy Tot Super Foods Puffed Ancient Grain Dino Snack With Tomato, Basil And Cheddar** (Philippines, Jul 2017)
- **Hidden Garden Red Velvet Cookies** (Japan, Apr 2017)
- **Members Mark Gourmet Jelly Beans Made With Real Fruit Juice** (China, Jun 2017)

Percentage represents market share per top category for launches with gluten free claims tracked 2012-2016.
Lactose free for easier digestion

Lactose breakdown

Only one-third of adults can digest milk. The rest stop making the enzyme needed to process milk sugar.

Nutricia Hi-Q Lactose Free Powdered Infant Formula (Thailand, Mar 2017)
Stable growth of supplements with digestive health claims

**ASIA IS CATCHING UP WITH THE GLOBAL TREND**

Percentage of supplements new product launches tracked with digestive health claims
(Asia vs Global, 2012 vs 2016)

**CHINA ACCOUNTS FOR 1/3 OF TOTAL LAUNCHES IN ASIA**

Top 5 countries of supplements new product launches tracked with digestive health claims
(Asia, 2012-2016)

- China: 34% (CAGR: +112%)
- Others: 14% (CAGR: +69%)
- Philippines: 11% (CAGR: +82%)
- Singapore: 6% (CAGR: +79%)
- Malaysia: 7% (CAGR: +50%)
- India: 6%
89% of Asian probiotics supplements are claimed to benefit digestive health

Percentage of product launches of supplements featuring digestive health claims by sub-category (Asia, 2012 vs 2016)

- **Probiotics**: 89% (2016), 83% (2012)
- **Dietary Fiber**: 54% (2016), 57% (2012)
- **Meal Replacements**: 37% (2016), 14% (2012)
- **Miscellaneous Softgels Capsules**: 23% (2016), 24% (2012)
- **Tablets Powders**: 23% (2016), 18% (2012)
- **Botanical/Herbal Supplements**: 23% (2016), 18% (2012)
- **Fruit And Vegetable Concentrates**: 18% (2016), 13% (2012)

Pn Kids Prebiotics Plus Veggie Dietary Supplement With Mango Flavor (Vietnam, Feb 2017)
Strong growth across supplements sub-categories for digestive health

**MEAL REPLACEMENT**
- **+68%**
  
  **Besunyen Bishengyouyou**
  **Nutri-Diet Milk Shake Solid Drink With Juicy Peach Flavor**
  (China, Jun 2017)


**BOTANICAL/HERBAL SUPPLEMENT**
- **+70%**
  
  **GNC Herbal Plus Ginger Root Herbal Supplement: 550Mg, 100 Capsules**
  (Malaysia, Dec 2016)

  Claims:…Supports digestive health, relieves upset stomach, indigestion and stomach cramps… Traditionally used to improve digestion, take one capsule daily…

**FRUIT & VEGETABLE CONCENTRATES**
- **+100%**
  
  **Swisse Digestion Clean Green Superfood Powder**
  (China, Jan 2016)

  Claims: Helps support digestive health … 2 billion probiotics. 100% natural. No added sugar or dairy. Low KJ. Suitable for vegetarians. Great tasting..
Digestive health NPD targets at different stages
Asian consumers are concerned about digestive problems at high level

How concerned are you about the gastrointestinal/digestive problems? Extremely/Very concerned.

(Selected countries, 2016)

- Philippines 62%
- China 58%
- Japan 48%
- India 47%
- Indonesia 41%
Top companies for launches with digestive health claims in Asian market

<table>
<thead>
<tr>
<th>Company</th>
<th>Product Description</th>
<th>Date/Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nestle</td>
<td>Nestle Cerelac Infant Cereal Rice And Mixed Vegetables With Milk</td>
<td>Malaysia, Sep 2016</td>
</tr>
<tr>
<td>Mead Johnson</td>
<td>Mead Johnson Nutrition Enfagrow A+ Nutritional Milk Powder With Chocolate Flavor For Stage 4 Children From 2 Years And Above</td>
<td>India, May 2017</td>
</tr>
<tr>
<td>Abbott</td>
<td>Abbott Similac Gain Iq Pre-School Milk For Stage 4 Kids From 3 Years Onwards</td>
<td>Singapore, Jun 2017</td>
</tr>
<tr>
<td>Nutricia</td>
<td>Nutricia Fortini Toddler Formula With Vanilla Flavor From 12 To 36 Months</td>
<td>China, Jun 2016</td>
</tr>
</tbody>
</table>
Different stages = different needs, but all cover digestive health

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description/Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy &amp; Newborn (stage 1)</td>
<td>Supports digestive health (whey protein and 100% lactose)</td>
</tr>
<tr>
<td>Breast Feeding (0-6 months)</td>
<td>Supports digestive health (whey protein and 100% lactose)</td>
</tr>
<tr>
<td>Follow on (stage 2)</td>
<td>Contains exclusive patent Bbi beneficial bacteria+ natural dietary fiber...</td>
</tr>
<tr>
<td>6-12 months</td>
<td>Synbiotics are a combination of probiotics (good bacteria) and prebiotic FOS that helps probiotics thrive...</td>
</tr>
<tr>
<td>Growing up (1-3 years)</td>
<td>Contains choline and dietary fiber. Dietary fiber can maintain normal bowel function...</td>
</tr>
<tr>
<td>Children (3-12 years)</td>
<td></td>
</tr>
</tbody>
</table>

Anmum Materna Milk Powder For Pregnant Woman (Taiwan, Dec 2016)
Nutricia Aptamil Infant Formula For Stage 1 Babies From Birth To 6 Months (India, Mar 2017)
Abbott Similac Stage 2 Powdered Follow On Formula For Babies After 6 Months (Singapore, Nov 2016)
Pro Kido Stage 3 Growing-Up Formula Milk Powder For Young Children From 12 To 36 Months (China, Jun 2017)
Abbott Pediasure Plus Milk Drink With Classic Vanilla Flavor For Children Of Preschool Age Above 3 Years Old (Philippines, Sep 2016)
Stages are not always fixed: more options in Asian markets

Dumex Mamil All In One Growing Up Formula For Children From 1 to 6 Years (Singapore, Mar 2017)

Claims:...Prebiotics promote the growth of good Bifidus bacteria to help maintain a healthy digestive system...

Friso Prestige 4 Toddler Formula From 36 To 72 Months (China, Mar 2017)

Claims:...Dietary fiber maintains normal bowel function...

Mead Johnson Nutrition Enfalac A+ 360 Degrees DHA Plus 1 Instant Milk Formula From Birth To 1 Year (Thailand, Mar 2017)

Claims:...2 fibers mixed (PDX and GOS) to help improve the condition of baby's stools...

Special Nutrition for Stunted Malnourished Children from 3 to 10 Years (Vietnam, Aug 2016)

Claims:...Contains L-lysine which stimulates appetite, MCT which helps in nutrient absorption, digestion and weight gain...
Penetration of digestive health claims differs in stages

- Digestive health claims are tracked in more than half of the formula products that target at infant/baby.
- The highest penetration is tracked in the products for kids aged up to 12 years, reaching to 62%.

**Digestive health claims as percentage of new formula milk launches tracked (Asia, 2015-2016)**

- Pregnancy & breastfeeding: 43%
- New born (0-6 months): 54%
- Follow on (6-12 months): 51%
- Growing up (1-3 years): 55%
- Kids (up to 12 years): 62%
High use of prebiotic fibers across all stages

- For all the infant formula products tracked with digestive health claims, more than 80% of them contain prebiotic fibers. And the application of probiotics is increasing with the ages of babies, while the application of hydrolyzed protein is mainly in the products for new born infants and decreasing with the ages of babies.

### Ingredient penetration of new infant formula launches tracked with a digestive health claim (Asia, 2015-2016)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Prebiotic fibers</th>
<th>Probiotics</th>
<th>Hydrolyzed protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy &amp; breastfeeding</td>
<td>88%</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>New born (0-6 months)</td>
<td>79%</td>
<td>21%</td>
<td>16%</td>
</tr>
<tr>
<td>Follow on (6-12 months)</td>
<td>82%</td>
<td>24%</td>
<td>12%</td>
</tr>
<tr>
<td>Growing up (1-3 years)</td>
<td>89%</td>
<td>29%</td>
<td>6%</td>
</tr>
<tr>
<td>Kids (up to 12 years)</td>
<td>82%</td>
<td>39%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Prebiotic fibers for a healthy intestinal flora

- Prebiotic fibers mainly claimed to promote the growth of good bacteria and therefore healthy gut flora.

Mead Johnson Nutrition
Enfagrow A+ Growing Up Milk For Stage 4 Babies From 3-6 Years Old (Singapore, Apr 2017)
Claims: ...Choline helps support overall mental functioning prebiotics (inulin and FOS) promote the growth of good Bifidus bacteria to help maintain a healthy digestive system. Made with a unique blend of dietary fibers (PDX and GOS) and beta-glucan...

Humana Gold 2 Follow Up Formula For Babies (Vietnam, Oct 2016)
Claims: ...GOS: Galactooligosaccharides are prebiotic dietary fibers as they occur in breast milk. They help the development of healthy intestinal flora...

Ai Ni Ke Stage 2 Organic Follow-On Formula For Babies From 6 To 12 Months (China, Apr 2017)
Claims: ...Dietary fiber (FOS plus GOS) is a kinds of low energy, it can help maintain normal bowel function.
Hydrolyzed proteins for easy digestion and preventing milk allergy

**PREVENTING MILK ALLERGY**

- 45% of all comfort pediatric launches new infant formula launches tracked with hydrolyzed proteins carry a preventing (milk) allergy claim.

**EASY TO DIGEST**

- 1 in 2 new infant formula launches tracked with hydrolyzed proteins are claiming to be easy to digest.

Nutricia Nutrilon Pepti Stage 2 Hydrolyzed Milk Protein Formula For Babies From 6 Months (Hong Kong, Jun 2016)

Claims: ... Pepti is a deeply hydrolyzed (fully hydrolyzed) protein formula for the dietary therapy for mild to moderate allergy of babies..

Mead Johnson Enfagrow A Plus Gentle Care 3 Susu Pertumbuhan: Growing Up Milk Formula For Toddlers (Indonesia, Sep 2016)

Description: ..Enfagrow A+ Gentle Care 3 with partially hydrolyzed protein which is easily digested. Completed with macro and micronutrients to help the children growth.
Prebiotic fibers increasingly blended with probiotics and hydrolyzed protein

**FIBER + PROBIOTICS**

- Prebiotic fibers and probiotics are both known for their beneficial effect on the gut flora and are therefore a promising ingredient combination.

**PREBIOTIC + HYDROLYZED PROTEIN**

- Hydrolyzed protein are used in products developed for infants with a cow’s milk allergy and/or lactose intolerance.

Friso Prestige 4 Toddler Formula From 36 to 72 Months (China, Mar 2017)

Claims: Made by nature. Nature Guard formulation. Contains DHA, choline, **added probiotics** *(Bifidobacterium Lactis HN019)* and LockNutri system. Zinc is an essential element for baby’s growth. Vitamin B1 helps maintain the normal neurological function for nervous system. **Dietary fiber maintains normal bowel function.**

Dumex Mamil Gold 1 Extra Care Ha Hypoallergenic Infant Formula From 0 To 6 Months (Singapore, Nov 2016)

Claims: …formula containing **partially hydrolyzed cow’s milk protein.** Contains Preci Nutri+ composed of: partially hydrolyzed protein: gentle protein for **sensitive babies**...Prebiotics (GOS, lcFOS): promote the growth of good Bifidus bacteria to help maintain a healthy digestive system…Hypoallergenic…
Baby cereals & biscuits is another key platform for digestive health claim.

### Share of Baby Cereals & Biscuits Increases for Three Years

<table>
<thead>
<tr>
<th>Year</th>
<th>Baby Cereals &amp; Biscuits</th>
<th>Baby Drinks</th>
<th>Baby Formula/Milk</th>
<th>Baby Meals</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>76%</td>
<td>2%</td>
<td>17%</td>
<td>5%</td>
</tr>
<tr>
<td>2015</td>
<td>75%</td>
<td>1%</td>
<td>18%</td>
<td>5%</td>
</tr>
<tr>
<td>2016</td>
<td>71%</td>
<td>1%</td>
<td>23%</td>
<td>5%</td>
</tr>
</tbody>
</table>

### Indexed Number of Baby Cereals & Biscuits New Product Launches Tracked with Digestive Health Claims (Asia, 2012-2016)

<table>
<thead>
<tr>
<th>Year</th>
<th>Indexed Number of Product Launches</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>100</td>
</tr>
<tr>
<td>2013</td>
<td>177</td>
</tr>
<tr>
<td>2014</td>
<td>259</td>
</tr>
<tr>
<td>2015</td>
<td>252</td>
</tr>
<tr>
<td>2016</td>
<td>243</td>
</tr>
</tbody>
</table>

**CAGR 2012-2016: +25%**
## Ingredients promoted as “good for digestive health” in Baby Cereals & Biscuits

<table>
<thead>
<tr>
<th>Dietary Fiber Maintain Digestive Function</th>
<th>Probiotics To Maintain Digestive Health</th>
<th>Prebiotics To Support Healthy Digestion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Great Food Nutrition Millet Powder With Prebiotics For Babies From 6-36 Months</strong> <em>(China, Jun 2017)</em></td>
<td><strong>Happy Baby Organic Yogis Freeze-Dried Yogurt And Fruit Snacks For Crawling Babies: Strawberry</strong> <em>(Indonesia, May 2017)</em></td>
<td><strong>Heinz Farleys Sunrise Banana Cereal Breakfast For Babies From 4 Months Onwards</strong> <em>(India, Feb 2017)</em></td>
</tr>
</tbody>
</table>

**Claims:**
- Dietary fiber help maintain normal intestinal tract function. With prebiotics...
- Probiotics to help maintain digestive health...
- With prebiotics to support healthy digestion...
China is the most active market for digestive health NPD for seniors

**Synutra Nutritional Goat Milk Powder For Middle Age And Seniors (China, Nov 2016)**

Claims: …Probiotics and dietary fiber in particular add bifidobacteria, beneficial intestinal health. Dietary fiber helps to maintain normal intestinal function…

**Wondersun High Calcium Low Fat Milk Powder For Seniors (China, Jul 2016)**

Claims: High calcium. Low fat. Contains calcium, iron, zinc, vitamin A, vitamin D, vitamin E, multiple vitamins and minerals, and dietary fiber…Dietary fiber can help with the normal bowel function.

**Nestle Milk Powder With Activated Probiotics For Middle And Old Aged People (China, Apr 2016)**

Description: Milk powder with activated probiotics, for middle and old aged people…
Female consumers are also being targeted

Beimmate Nursing Mommy Formula (China, Jun 2016)

Description: Milk powder-based maternity formula for lactating and pregnant women…

Claims:…Contains dietary fiber…

Wondersun Ms. Milk With Calcium And Vitamin E (China, Jun 2016)

Claims: …Dietary fiber can help with the normal bowel function. Contains calcium, vitamin E, iron, zinc, vitamin A, vitamin D, multiple vitamins and minerals, and dietary fiber…
Products with digestive benefits for all adults have tradition

Acti Life Chocolate Flavored Drink Mix Nutrition for Adults (India, Feb 2012)

Description: Low fat. With prebiotic actifibers. Help reduced cholesterol. Helps improve digestion...

Calpis L 92 Lactic Acid Bacteria Based Drink (Japan, May 2014)

Claims: A unique L-92 lactic acid bacteria and three vitamins based drink for adult health.

Easiyo Real Base & Culture Yogurt Mix: Reduced Fat And Unsweetened (Hong Kong, Sep 2015)

Claims: Reduced fat and unsweetened yogurt mix… ideal for adults.

Anlene Gold Chocolate Flavored Milk Powder (Vietnam, Apr 2016)

Claims: Skimmed milk powder …for adults...

Ingredients: …mixed FOS (fructooligosaccharides) (inulin)…
Digestive health supplements for kids present in many countries

**Lifestream Afc King Chlorella Dietary Supplement: 1,000 Caplets**
(Singapore, Mar 2016)

Claims: …and in weight loss regime. **Aids in detoxification and promotes regular bowel movements**…

**Seven SeasKids Probiotic Multivitamin For 3 Years Old Above With Raspberry Flavor: 30 Chewable Tablets**
(Malaysia, Jan 2016)

Claims: …**Contains …a unique combination of three probiotics that improves your kid’s intestinal microflora** and strengthens their natural immune defenses.

**Hys Colostrum Milk Supplement: 120 Tablets**
(China, Mar 2016)

Claims: …**Colostrum milk is not only rich in nutrients, …lactoferrin, lactoperoxidase, lysozyme, immune regulation, improved digestion**…
Various formats of supplements with digestive health for women

Nutrition Now Omega 3 Adult Gummy Vitamins Dietary Supplement, 60 Gummy Vitamins (Philippines, Sep 2016)

Description: …from award-winning gummy vitamins to digestive health, seasonal care, women’s health and adult gummy products

YGCG Eucheuma Natural Red Dates, Goji And Birds Nest (Singapore, Mar 2016)

Claims:…Promotes a healthy digestive system. Power-packed with nutrients and vitamins. Great natural source of antioxidants. Excellent source of antioxidants…

Natures Way Alive Once DailyWomen’S Ultra Potency Multivitamin Supplement: 60 Tablets (China, May 2016)

Claims:…Supports multiple body system which includes skeletal, cell, digestion, eye, heart, hair/skin/nails, immunity and metabolism…
Emerging markets to watch in Asia
**Digestive health emerge in non-traditional categories**

<table>
<thead>
<tr>
<th>SNACKS</th>
<th>SPREADS</th>
<th>SAUCES &amp; SEASONINGS</th>
</tr>
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<tbody>
<tr>
<td>+83%</td>
<td>+40%</td>
<td>+47%</td>
</tr>
</tbody>
</table>

**Planters Nut-Rition Digestive Health Mix:**
Almonds, Cranberries, Granola, Pistachios (Philippines, Nov 2016)

Claims: Excellent source of fiber. Contains 9g of total fat per serving. Digestive health mix.

**Skippy Creamy Peanut Butter**
(Singapore, May 2017)

Claims: Source of dietary fiber improves digestive efficiency...

**Chongga Kimchi**
(Taiwan, Sep 2016)

Claims: Fermentation of kimchi is carried out by various microorganisms, especially lactic acid bacteria that are already present in the ingredients. ...

Percentage represents CAGR 2012-2016
Sports nutrition provides digestive benefits as well

Pro Athlete Whey Protein Shred Series With Royal Strawberry Ice Cream Flavor (India, Feb 2017)

Claims: Most clean and purest form of protein combined with healthy digestive enzymes packed with highly bio available and easily digested proteins… It is the most clean and purest form of protein combined with healthy digestive enzymes packed with highly bio available and easily digested proteins…

Supreme Protein High Protein Bar With Cookies N Cream Flavor (Thailand, Apr 2016)

Claims: …It contains 30 grams of high quality protein, with virtually no sugar. New look. Fiber is good for digestion and absorption of nutrients. Rich in vitamins, minerals and nutrients that are beneficial.
Can beer be good for your gut?

**Lulu Sour Craft Beer**
With Blackcurrant Juice
(Poland, Jun 2017)

Ingredients: Water, barley malt (pilznenski, munich), oat flakes, hop: sybilla, yeast belle saison, additives: black currant pulp, bacteria: *lactobacillus helveticus*..

**Paramo Brauhaus Cerveza**
Artesanal Altbier: Craft Beer
(Ecuador, Oct 2016)

Ingredients: Water, barley malt, hops, *brewer's yeast* (*saccharomyces cerevisiae)*.

**Beaus Oak Skal Beer**
(Canada, Jun 2016)

Ingredients: Local spring water, organic barley malts, organic dates, organic maple syrup, organic hops, organic cane sugar, brewers yeast, *brettanomyces*, *lactobacillus*. 
The answer is yes!

This New Beer Claims It’ll Boost Your Immunity and Improve Your Gut Health

It’s all thanks to an infusion of probiotics

BY CHRISTA SOHBA  July 5, 2017
Fiber added to Coke’s latest diet drink: Coca-Cola Plus

Coca-Cola now sells a soda with added fiber in Japan:

- 0 sugar or calories and
- 5 grams of dietary fiber (indigestible dextrin)
Key learnings
Key learnings

• Strong growth of F&B products tracked with digestive health claims in Asia.
  • Dairy and baby foods are the top categories for digestive health claims in Asia.
  • 1/3 of total supplements products with digestive health claims are tracked in the Chinese market.
  • Both probiotics and prebiotics are trending.
  • Gluten free, lactose free claims are all showing significant growth for recent five years.

• Digestive health products targeting at all ages.
  • Opportunities for NPD specifically for different consumer groups, from early stage to seniors.
  • Baby formula is the most active platform of baby foods tracked with digestive health.

• Innovation on digestive health has started in non-traditional categories.
  • Growing NPD in mainstream categories, such as snacks, spreads and sauces & seasonings.
  • Sports nutrition is another potential segment with digestive benefits.
Keynote Panel Discussion

Identifying the commercial opportunities within the microbiome and realizing the next generation of digestive health product development

Speaker 1: Prof Yuan Kun Lee, Asian Microbiome Program, c/o Department of Microbiology & Immunology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Speaker 2: Chin-Kun Wang, President, International Society of Nutraceuticals and Functional Foods, Taiwan

Speaker 3: Dr Anders Henriksson, Principal Application Specialist, DuPont Nutrition & Health

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
Lactobacillus plantarum PS128, a novel psychobiotics

Speaker: Prof Ying-Chieh Tsai, Professor, Institute of Biochemistry and Molecular Biology, National Yang-Ming University, Director, Microbiome Research Center, National Yang-Ming University, Taiwan

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
Lactobacillus plantarum PS128: a novel psychobiotics

Ying-Chieh Tsai
National Yang-Ming University, Taipei, Taiwan

Microbiota-Gut-Brain Axis
Microbiota in our intestines have a major impact on our state of mind. The microbiome may yield a new class of psychobiotics for the treatment of anxiety, depression and other mood disorders.
**Lactobacillus plantarum PS128: a novel psychobiotic strain**

1. A novel strain isolated from **Fu-Tsai**, a traditional fermented mustard in Taiwan.
2. High **Immuno-modulatory** and **anti-inflammatory** activities as evaluated using PBMC and macrophage cell models, and DSS-induced colitic animal model.
3. It increased the **locomotor** activity of mice in open field test.

**Psalm 128**

Blessed are all who fear the **LORD**, who walk in obedience to him. You will eat the fruit of your labor; **blessings** and prosperity will be yours.

**P45**: Hypnotic effects of PS150 on pentobarbital induced sleep mice model
Maternal separation protocol (Early life stress model)

Mice: C57BL/6J

Random grouping

maternal separation (3 h / day)

born

weaning

PS128 feeding: $10^9$ CFU/day

EPM

TST

OFT

FST

SPT

Day 0 2 14 28 36 40 56

Pups are isolated from their dams and littermates

Pups are isolated from their dams and littermates

EPM: Elevated plus maze

OFT: open field test

FST: forced swimming test

SPT: sugar preference test

TST: tail suspension test

Brain, blood...

Behavioral tests
**Immunity time in FST**

**Forced swimming test**

**Immobility (s)**

- **NS**
- **MS**
- **128**

**Germ Free**

**Immobility (s)**

- **Saline 128**

**MS+PS128**

**MS**
Elevated Plus Maize

Closed arm

Open arm

MS+PS128

MS
Dopamine

Serotonin

**DA** (ng/g)

**5-HT** (ng/g)

Saline 128

Saline 128

Reward System

Prefrontal Cortex
Corticosterone: Stress hormone
Fight or flight response

Elevated levels will interfere with learning, memory, lower immune function and bone density, increase weight gain, blood pressure, heart disease, depression, mental illness…….
Irritable Bowel Syndrome: 5-HTP induced visceral hypersensitivity without chronic inflammation

5 week old male SD rats, n=12/group

Day1
EMG Electrode implantation

Day10
Recovery from surgery

Day24
10⁹ CFU/Rat/Day

Oral administration of PS128 for 14 days

5-HTP (5 mg/Kg)

After 30 mins

Colorectal distension

CRD test for the effects on probiotics
PS128 ameliorating 5-HTP induced visceral hypersensitivity

**5-HTP:** 5 mg/kg; Values are expressed as mean ± SD (n = 6 in each group).

* $p < 0.05$ versus basal line group by one-way ANOVA with Turkey’s post test.
**PS128 inhibited GR decrease & MR increase induced by 5-HTP injection in amygdala**

Exposure of the **amygdala** to CORT increases the sensitivity to visceral stimuli through **glucocorticoid receptors** (GR) and **mineralocorticoid receptors** (MR).
Summary

Amygdala GR & MR unbalance

PS128

5-HTP induced visceral sensitivity → CRD

Restored!

Visceral hypersensitivity

Cortex

Serotonin

Restored!

BDNF

Restored!

SP CGRP

Restored!

5-HTP

CORT

IL-6

DRG

Spinal cord

Restored!
MPTP-induced Parkinson’s disease-like mice model

Control group: Saline (200 ul)
PS128 group: PS128 $10^9$ CFU/200 ul
Total 28 days

MPTP injection: 30mg/kg, ip

- Narrow beam test
- Rotarod test
- Pole test

L-dopa group: 100 mg/kg L-DOPA + 25 mg/kg benserazide

Substantial nigra
Tyrosine hydroxylase stain in substantial nigra

Control

MPTP

MPTP+PS128

MPTP+L-Dopa

Percent TH positive cell in SN

Control + Saline

Control + PS128

MPTP + Saline

MPTP + PS128

MPTP + L-Dopa

PS128

PS128/M

MPTP

#
Tourette Syndrome

DOI: Serotonin receptor agonist
Haloperidol: Dopamine receptor antagonist

DOI, ip

back muscle contraction

BMC in 35 min

PS128

Day
1
14
15

PS128
Haldol

DOI - + + + +
Prepulse inhibition (PPI) deficit

PPI: a weaker prestimulus (prepulse) inhibits the reaction to a subsequent strong startling stimulus. PPI deficits have been noted in TS, ADHD, OCD & Schizophrenia patients.

Weaker stimulus

Higher PPI

Lower PPI

Sensorimotor gating deficit

120 db

70 db

4 sec

120 db Pulse

100

100

10

50

Prepulse inhibition (%)

Saline

PS128

Saline

Hal

PS128

Prepulse Inhibition Deficit

DOI(+)
PS128 suppressed the expression of DOI-induced dopamine transporter (DAT) in the cortex of Tourette rats dose-dependently.
Principal component analysis of cecal microbiota component through 16S RNA pyro-sequencing

N ≥ 6
Clinical research of P128

1. PS128 on autism boys; 80 subjects
2. PS128 on geriatric: depression amelioration and improvement of quality of life. 200 subjects
3. Major depression disorder (escitalorlpam)
   (Kai-Syuan Psychiatric H.) 60 subjects
4. Parkinson’s diseases (Chang Gung H.) (80 subjects)
5. Tourette syndrome and Rett syndrome
   (80 TS, 40RS, Taiwan U Children H)
6. Panic, Headache, Sleep disorder
   (8 private clinics) (400 subjects)
Founded in Apr, 2015, as a spin-off company from a research grant of Ministry of Economic Affairs. Focused on Psycobiotics.

Capital: USD 5.5 M, Employee: 30

IPO at 2019-2020

Our Psycobiotics strains

PS128, PS150, PS23

www.benedbiomed.com
Microbiota-brain axis could be a powerful target for influencing mood and behaviour, e.g. in anxiety, depression, Parkinson’s disease, Alzheimer’s disease, and autism.

Bridging the gap between animal studies and application for treatment in humans will be the next big challenge.
Exercise, the Microbiome and Probiotics

Speaker: Jin-Seng Ling, Director, Culture, Collection & Research Institute, Synbio Tech Inc, Taiwan
Exercise, the Microbiome and Probiotics

Speaker: Jin-Seng Ling, Director, Culture, Collection & Research Institute, Synbio Tech Inc, Taiwan

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
Exercise, Microbiome and Probiotics

Jin-Seng Lin
SYNBIOTECH INC.
2017/9/5
What is the Microbiome

“the ecological community of commensal, symbiotic, and pathogenic microorganisms literally share our body space”

-Joshua Lederberg
Factors Influencing Gut Microbiota

- Genetics
- Stress
- Pregnancy
- Type of Birth
- Nutrition
- Age
- Exercise
- Antibiotic

Factors influencing gut microbiota

doi: 10.3389/fphys.2016.00051
Exercise and Microbiota

MICROBIAL COMMUNITIES DIFFER AMONG ELITE RUGBY ATHLETES AND NON-ATHLETES

<table>
<thead>
<tr>
<th></th>
<th>Elite athletes (n=40)</th>
<th>Low BMI controls (n=23)</th>
<th>High BMI controls (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.8±3.8</td>
<td>28.1±5.1</td>
<td>30.8±5.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.1±3.0*</td>
<td>22.7±1.8**</td>
<td>31.2±3.0†</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>101.3±13.8</td>
<td>74.3±6.3</td>
<td>103.1±13.8</td>
</tr>
<tr>
<td>Body fat % (kg)</td>
<td>16.9±6.1++</td>
<td>15±4.6*</td>
<td>33.9±8.8†</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>80±8.9***</td>
<td>55.4±5.6**</td>
<td>65±8†</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.8±0.04++</td>
<td>0.8±0.05</td>
<td>0.9±0.07*</td>
</tr>
</tbody>
</table>

Gut Microbiota Effect on Exercise Performance

Hsu YJ et al. 2015

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SPF</th>
<th>GF</th>
<th>BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>UA (U·L⁻¹)</td>
<td>2.32 ± 0.4ᵃ</td>
<td>2.94 ± 0.5ᵇ</td>
<td>2.18 ± 0.4ᵃ</td>
</tr>
<tr>
<td>BUN (mg·dl⁻¹)</td>
<td>32.3 ± 1.3ᵇ</td>
<td>32.6 ± 1.2ᵇ</td>
<td>26.5 ± 1.4ᵃ</td>
</tr>
<tr>
<td>TC (mg·dl⁻¹)</td>
<td>98.0 ± 2.3ᵇ</td>
<td>96.9 ± 8.5ᵃᵇ</td>
<td>87.1 ± 9.6ᵃ</td>
</tr>
<tr>
<td>TG (mg·dl⁻¹)</td>
<td>81.0 ± 20.5</td>
<td>80.2 ± 19.5</td>
<td>72.3 ± 7.9</td>
</tr>
<tr>
<td>LDH (U·L⁻¹)</td>
<td>232 ± 60</td>
<td>289 ± 63</td>
<td>279 ± 64</td>
</tr>
<tr>
<td>Lactate (mmol·ml⁻¹)</td>
<td>1.35 ± 0.06</td>
<td>1.39 ± 0.03</td>
<td>1.41 ± 0.05</td>
</tr>
<tr>
<td>Glucose (mg·dl⁻¹)</td>
<td>262 ± 29</td>
<td>265 ± 27</td>
<td>284 ± 16</td>
</tr>
<tr>
<td>Liver glycogen (μg·mg⁻¹)</td>
<td>6.34 ± 1.0ᵃ</td>
<td>7.74 ± 0.8ᵇ</td>
<td>7.56 ± 0.4ᵇ</td>
</tr>
<tr>
<td>Muscle glycogen (μg·mg⁻¹)</td>
<td>0.11 ± 0.03</td>
<td>0.10 ± 0.03</td>
<td>0.09 ± 0.02</td>
</tr>
</tbody>
</table>

*Data are mean ± SEM for n = 8 mice in each group. Data in the same line followed by different letters (a, b, c) differ significantly at p ≤ 0.05 by 1-way analysis of variance. SPF = specific pathogen free; GF = germ free; BF = Bacteroides fragilis; UA = uric acid; BUN = blood urea nitrogen; TC = total cholesterol; TG = triacylglycerol; LDH = lactate dehydrogenase; CK = creatine kinase.
Could Supplementation of Probiotic Change the Gut Microbiota and Exercise Performance?
TWK10 Profile

Lactobacillus plantarum
Study Design

Oral supplementation for 6 weeks

6-week-old male ICR mice (n=24)

TWK10-5X
(1.03 x 10^9/Kg/Day)

TWK10-1X
(2.05 x 10^8/Kg/Day)

Lactobacillus plantarum TWK10

Forelimb grip strength test

5% weight loading exhaust swimming test

15 min acute exercise challenge

Clinical Biochemical analysis

Histology of Tissues

Immunohistochemical (IHC) Staining of Gastrocnemius Muscles

Lactate

NH3

CK

Glucose
The Change of Body Weight

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle</th>
<th>LP10-1X</th>
<th>LP10-5X</th>
<th>Trend Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food intake (g/day)</td>
<td>6.3 ± 0.1 a</td>
<td>6.2 ± 0.0 a</td>
<td>7.5 ± 0.1 b</td>
<td>&lt;0.0001 (↑)</td>
</tr>
<tr>
<td>Water intake (mL/day)</td>
<td>6.9 ± 0.1 a</td>
<td>6.8 ± 0.2 a</td>
<td>7.6 ± 0.0 b</td>
<td>&lt;0.0001 (↑)</td>
</tr>
</tbody>
</table>
# General Characteristics Of Mice With TWK10 Supplementation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle</th>
<th>LP10-1X</th>
<th>LP10-5X</th>
<th>Trend Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative weight (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>5.29 ± 0.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.65 ± 0.09&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.43 ± 0.06&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.1073</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.70 ± 0.02&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.81 ± 0.02&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.86 ± 0.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.0001 (↑)</td>
</tr>
<tr>
<td>EFP</td>
<td>2.09 ± 0.16&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.48 ± 0.09&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.08 ± 0.15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.0001 (↓)</td>
</tr>
<tr>
<td>Heart</td>
<td>0.49 ± 0.10&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.54 ± 0.07&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.53 ± 0.07&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0018 (↑)</td>
</tr>
<tr>
<td>Lung</td>
<td>0.53 ± 0.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.58 ± 0.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.55 ± 0.01&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>0.2009</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.90 ± 0.02&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.99 ± 0.01&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.96 ± 0.02&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0326 (↑)</td>
</tr>
<tr>
<td>BAT</td>
<td>0.31 ± 0.01</td>
<td>0.31 ± 0.01</td>
<td>0.33 ± 0.02</td>
<td>0.6881</td>
</tr>
</tbody>
</table>

1X and 5X TWK10 group both increased muscle mass and decreased fat mass.

EFP: epididymal fat pad

Measuring EFP relative weight is like a overview of mice’s fat mass.
TWK10 Increased Exercise Performance and Endurance Time

**Forelimb Grip Strength**

**5% Weight-Loaded Swimming Test**

**Grip strength (g)**

- Control: 0
- TWK10-1X: 131
- TWK10-5X: 140

Trend analysis ($p < 0.0001$)

**Swimming time (min)**

- Control: 5
- TWK10-1X: 185
- TWK10-5X: 481

Trend analysis ($p < 0.0001$)
TWK10 Against Fatigue

(a) Trend analysis \((p < 0.0001)\)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TWK10-1X</th>
<th>TWK10-5X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate (mmol/L)</td>
<td>6</td>
<td>8.8</td>
<td>4</td>
</tr>
</tbody>
</table>

(b) Trend analysis \((p < 0.0001)\)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TWK10-1X</th>
<th>TWK10-5X</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/H₂ (μmol/L)</td>
<td>150</td>
<td>120</td>
<td>100</td>
</tr>
</tbody>
</table>

(c) Trend analysis \((p = 0.0018)\)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TWK10-1X</th>
<th>TWK10-5X</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK (U/L)</td>
<td>200</td>
<td>320</td>
<td>350</td>
</tr>
</tbody>
</table>

(d) Trend analysis \((p = 0.0151)\)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TWK10-1X</th>
<th>TWK10-5X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>150</td>
<td>160</td>
<td>170</td>
</tr>
</tbody>
</table>
TWK10 Increased Type I Muscle Fiber in Gastrocnemius Muscle

Type I and Type II Muscle Fibers

- Type I muscle fiber is also known as "slow twitch oxidative" fibers. They are characterized by low force/power/speed production and long-duration aerobic activities such as marathon.
TWK10 Impacts on Intestinal Microbiota

**Phylum**
- Bacteroidetes
- Firmicutes

**Class**
- Bacteroidales
- Clostridiales

**Family**
- Porphyromonadaceae
- Rikenellaceae
- Lachnospraceae

**Genes**
- Barnesiella
- Alistipes

Vehicle
Different Intestinal Microflora

Metagenomic Analysis

6 weeks TWK10 supplementation
TWK10 Impacts on Intestinal Microbiota

**Firmicutes**  
*Clostriaiales*  
Main metabolism is short chain fatty acids, especially butyrate  

**Barnesiella**  
Related with resistance of gastrointestinal diseases  
[Weiss *et al.*, 2014]

**Alistipes**  
Overweight people has higher Alistipes in gut in generally  
[Zhanf *et al.*, 2019; Hugon *et al.*, 2013]
The Mechanism Of TWK10 Impacts On Muscle Tissue

- TWK10 supplementation
  - Firmicutes
  - Before
  - After
  - Effect on gastrointestinal microflora

- Shot-chain fatty acids (SCFAs) ↑
- Glucose utilization ↑
- Energy (ATP)
- Degradation of adipocyte triacylglycerols (TG) ↑
- Protein degradation in muscle tissue ↓
- Muscle protein synthesis ↑
- Muscle mass ↑
- Lactic acid accumulation
- Glycogen
- Reduce fatigue
- Glycogen degradation to energy for muscle use as exercising

ENHANCE EXERCISE PERFORMANCE
Human Trial

- Double blind test
- $N = 16$ male
- Control group: placebo
- TWK10 group: 1 capsule of 100 billion CFU TWK10
- Period: 6 weeks

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TWK10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>176±6</td>
<td>173±8</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>77±13</td>
<td>75±14</td>
</tr>
</tbody>
</table>
Results Of Human Trial

After 6 weeks, subjects are asked to run on the treadmill at 75% VO\textsubscript{2}\text{max} for endurance test until the subjects are exhausted.

- Placebo: 13.62 minutes
- TWK10: 21.53 minutes

\textbf{+58\% (P=0.0475)}
Summary

- It is suggested that continual intake of TWK10 for 6 week to change gastrointestinal microbiota

- TWK10 promotes energy harvest and exercise endurance, specially suitable for athletics with endurance exercise such as marathon and bicycle.

- TWK10 promotes fatty acid utilization and energy consumption to increase muscle mass, thus TWK10 can be a sport nutrition supplement

- Recommended Dosage: at least $1 \times 10^{10}$ CFU/Day
Thank you !
Streaming Live – Your Probiotic

Speaker: Dr Anurag Pande, VP Scientific Affairs, Sabinsa, USA

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
Streaming Live – Your Probiotic

Speaker: Dr Anurag Pande, VP Scientific Affairs, Sabinsa, USA

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
STREAMING LIVE

YOUR PROBIOTICS
PROBIOTICS

Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.

Joint FAO/WHO Working Group on Drafting
Guidelines for the Evaluation of Probiotics in Food
2002
Probiotics is now leading segment of Dietary supplement market

Source - Euromonitor
Characteristic Features of Bacillus coagulans- MTCC5856

✓ Rod-shaped, Gram positive, endospore-forming bacteria
✓ Grow optimally at 37°C & pH in the range 5.5 to 6.2
✓ Facultative aerobic
✓ High tolerance to bile and gastric acidity
✓ Capability of easy proliferation in the gut
✓ Non pathogenic
Probiotic Features of Bacillus coagulans MTCC5856

- After germination, *B. coagulans* is metabolically active as part of facultative anaerobes in the intestine, producing \( L(+) \) Lactic Acid, as primary product of fermentation.

- The acidic environment created by production of \( L(+) \) Lactic Acid prevents the growth of pathogenic microbes and allows growth of *B. coagulans* which ultimately dominate the microflora.

- Production of bacteriocins in the gut
Mechanism of Action

Antimicrobial Activity
- Decrease luminal pH
- Host cell Antimicrobial Peptides
- Probiotic Antimicrobial peptide
- Inhibition of pathogen adhesion
- Inhibit bacterial invasion

Enhancement of Barrier Function
- Increased mucus production
- Epithelial Adherence
- Enhanced barrier integrity
- Immune Modulation
- Interference with Quorum Sensing Signalling

STABILITY

✓ High & Low Temperature Stability

✓ Can undergo the production stress of tableting

✓ Can withstand the heat exposure in making gummies, chocolates, candies.
Sabinsa Biotechnology (FDA Inspected Facility)
Genetic and phenotypic consistency of LactoSpore

Objective- Phenotypic and genotypic techniques including the biochemical profiling, 16S rRNA sequencing, GTG 5”, BOX PCR fingerprinting and MLST (Multi locus Sequence typing) were carried on to evaluate the identity and consistency of B. coagulans MTCC5856, additionally stability was also evaluated for the strain.

Results- All the samples evaluated by biochemical profiling and 16s rRNA sequencing were identified as B. coagulans. Further the samples evaluated over three years by GTG 5”, BOX PCR fingerprints and MLST showed consistency of strain MTCC5856 in the LactoSpore.

Conclusion- MTCC 5856 strain manufactured by Sabinsa at its in-house facility showed phenotypic and genotypic consistency as well as it was also found to be non mutagenic, non cytotoxic, negative for enterotoxin genes and stable for 3 years shelf life.
Uniqueness of Bacillus coagulans MTCC5856

- Free from Dairy Allergens (Lactose free, Casein).
- Gluten free & Non-GMO.
- Free from Antibiotic/preservatives.
- Free from other Bacillus spore which are pathogens such as *Bacillus cereus*.
- Even the excipient used to formulate lower strengths of LactoSpore® (100 Billion spores/g, 15 Billion spores/g and 6 Billion spores/g) is Non-GMO.
- For more information, visit: www.lactospore.com
Objective: LactoSpore was formulated in a variety of functional foods such as baked food items, beverages, vegetable oil, concentrated glucose syrup, and brewed coffee.

Results: LactoSpore was stable during processing and storage of baked foods. LactoSpore retained its viability (87%) during coffee brewing. LactoSpore retained its viability (99%) in apple juice up to 6 months at 4°C and over 90% viability in glucose syrup at 40°C for 2 years.

Conclusion: Bacillus coagulans MTCC spores demonstrated high viability to overcome the adverse processing conditions encountered during the formulations and retained its viability in the functional products during storage, to deliver the probiotic benefits. Ref: International Journal of Food Science and Technology 2016
### LactoSpore Heat Stability Study

**Trial #1**
*Temperature: 90°C (hot air oven)*  
*Duration: 30-150 sec.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>TVSC (billion spores/g)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control G80241 (15bs/g)</td>
<td>16.6</td>
<td>100%</td>
</tr>
<tr>
<td>90°C for 30sec</td>
<td>16.0</td>
<td>96.4%</td>
</tr>
<tr>
<td>90°C for 60sec</td>
<td>16.0</td>
<td>96.4%</td>
</tr>
<tr>
<td>90°C for 90sec</td>
<td>15.4</td>
<td>92.8%</td>
</tr>
<tr>
<td>90°C for 120sec</td>
<td>15.8</td>
<td>95.19%</td>
</tr>
<tr>
<td>90°C for 150sec</td>
<td>15.4</td>
<td>92.8%</td>
</tr>
</tbody>
</table>

**Trial #2**
*Temperature: 90°C (water bath)*  
*Duration: 30-180 sec.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>TVSC (billion spores/g)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control G80241 (15bs/g)</td>
<td>17.4</td>
<td>100%</td>
</tr>
<tr>
<td>90°C for 30sec</td>
<td>16.9</td>
<td>97.1</td>
</tr>
<tr>
<td>90°C for 60sec</td>
<td>13.2</td>
<td>75.86</td>
</tr>
<tr>
<td>90°C for 90sec</td>
<td>13.2</td>
<td>75.86</td>
</tr>
<tr>
<td>90°C for 120sec</td>
<td>14.5</td>
<td>83.33</td>
</tr>
<tr>
<td>90°C for 160sec</td>
<td>14.2</td>
<td>81.60</td>
</tr>
<tr>
<td>90°C for 180sec</td>
<td>14.3</td>
<td>82.10</td>
</tr>
</tbody>
</table>

**Trial #3**
*Temperature: 140°C (hot air oven)*  
*Duration: 30-120 sec.*

<table>
<thead>
<tr>
<th>Sample</th>
<th>TVSC (billion spores/g)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control G80241 (15bs/g)</td>
<td>17.9</td>
<td>100%</td>
</tr>
<tr>
<td>140°C for 30sec</td>
<td>17.4</td>
<td>97.2%</td>
</tr>
<tr>
<td>140°C for 60sec</td>
<td>15.7</td>
<td>87.71%</td>
</tr>
<tr>
<td>140°C for 120sec</td>
<td>13.6</td>
<td>75.98%</td>
</tr>
</tbody>
</table>
Stability Study – Waffles, Chocolate fudge frosting

Waffles - 91% survival of B coagulans during manufacturing process

Banana muffin mix, chocolate fudge frosting, hot fudge topping retained 95% of viability during manufacturing and storage at room temperature
Stability Study - Brewed Coffee

Brewed at 90C and stored at 72C
Stability Study - Brewed Coffee

Retained 87% viability after brewing for 2 minutes

Retained 66% viability at 4Hr holding time
Stability Study: Vegetable oil

98% viability on storage

% Viability

Initial 0 month 1 month 2 month 3 month 6 month 12 month
LIVE IN YOUR STORES...
MYPROTEIN

http://www.myprotein.com/uk/products/hurricane_evo
PROTEIN WITH PROBIOTICS

http://www.affordablesupplements.co.uk/reflex-peptide-fusion-shaker-cup.html
Pea Based protein with Probiotic and Enzymes
Energy Bars with Probiotics

http://www.bulkpowders.co.uk/hi gh-protein-snack-bar.html
Ahora con ProBióticos

PESO NETO: 450 g

INSTRUCCIONES DE USO:
Después de abrirlo, el pan se descompone en seis días. Manténgalo en lugar fresco y seco.

Registro sanitario: R0004-13

Fecha: 19 JUL 12

Ingredientes: Harina de trigo, harina de maíz, sal, azúcar, aceite de girasol, levadura, sal para el pan, sal de mesa.

El sabor de la tradición Desde 1948

PAN TAJADO

Perman

¡Ahora con ProBióticos!

El sabro de la tradición

Desde 1948

PESO NETO: 450 g

INSTRUCCIONES DE USO:
Después de abrirlo, el pan se descompone en seis días. Manténgalo en lugar fresco y seco.

Registro sanitario: R0004-13

Fecha: 19 JUL 12

Ingredientes: Harina de trigo, harina de maíz, sal, azúcar, aceite de girasol, levadura, sal para el pan, sal de mesa.
Self Serve Frozen Yogurt
Shakeology from BeachBody

FINALLY, VEGAN TASTES GREAT!

NOW 100% ANIMAL-PRODUCT-FREE TROPICAL STRAWBERRY

When Olympic athletes break a world record, they start training to do it again. Since we launched the Healthiest Meal of the Day® in 2009, we’ve been working to take Shakeology to the next level by creating a 100% vegan shake. Tropical Strawberry Shakeology contains even more exotic, nutritious whole food ingredients from around the world. And now with RicePro® ultra fine bio-fermented raw sprouted brown rice protein, it’s also 100% animal-product free.

DIRECTIONS: Combine 1 scoop (42 g) of Shakeology with 8 to 12 fl. oz. of cold water or beverage (juice, almond milk, rice milk, etc.) and ice in a blender. Mix well for a refreshing, frosty smoothie. Best consumed within 30 minutes. For more smoothie recipes, go to Shakeology.com.

Supplement Facts

Serving Size: 1 scoop (42 g) Servings Per Container: 30

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>160</td>
<td></td>
</tr>
<tr>
<td>Calories from Fat</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Total Fat</td>
<td>1 g</td>
<td>2%</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>0 g</td>
<td></td>
</tr>
<tr>
<td>Trans Fat</td>
<td>0 g</td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0 mg</td>
<td>0%</td>
</tr>
<tr>
<td>Sodium</td>
<td>70 mg</td>
<td>3%</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>20 g</td>
<td>7%</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>4 g</td>
<td>16%</td>
</tr>
<tr>
<td>Sugars</td>
<td>10 g</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>15 g</td>
<td>30%</td>
</tr>
</tbody>
</table>

PROPRIETARY VEGAN PROTEIN BLEND: 9 g
Raw sprouted whole grain brown rice protein, Sacha Inchi (Plukenetia volubilis), seed

PROPRIETARY SUPERFOOD/FIBER BLEND: 8,350 mg
Coconut flower nectar, Sprouted Chia (Salvia hispanica), Sprouted Fava (Vicia faba), Flax (Linum usitatissimum), seed, Pea Fiber (Pisum sativum, seed), Quinoa (Chenopodium quinoa), seed, Amaanthan (Amaranthus hypochondriacus), seed

PROPRIETARY ADAPTOGEN HERB BLEND: 1,675 mg
Maca root (Lepidium meyenii), Astragalus root (Astragalus membranaceus), Ashwagandha root (Withania somnifera), Matata mushroom (Grifola frondosa), Cordyceps (Cordyceps sinensis, long), Reishi mushroom (Ganoderma lucidum), Holy basil (Ocimum sanctum, leaf), Schisandra (Schisandrae ssp. fructus), Ginkgo (Ginkgo biloba, leaf)

OTHER INGREDIENTS: Tapioca, Natural flavors (strawberry, banana, pineapple), Enzyme gum, Beet juice powder, Citric acid, Natural sweetener (proprietary blend of erythritol, oligosaccharides and natural flavors), Cinnamon powder, Himalayan salt, Stevia, and Luo Han Guo.

ALLERGY INFORMATION: This product is manufactured in a plant that processes soy, egg, fish, crustacean shellfish, tree nuts, and wheat (gluten) ingredients.

STORAGE: Store in a cool, dry place. To ensure freshness, consume within 4 to 5 weeks of opening.

WARNING: Consult with a healthcare professional if you are pregnant, breast feeding, or if you have any medical conditions. Keep out of reach of children.

Amino Acid Profile

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Amount Per Serving</th>
<th>Amino Acid</th>
<th>Amount Per Serving</th>
<th>Amino Acid</th>
<th>Amount Per Serving</th>
<th>Amino Acid</th>
<th>Amount Per Serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>850 mg</td>
<td>Arginine</td>
<td>1,261 mg</td>
<td>Aspartic Acid</td>
<td>1,394 mg</td>
<td>Cysteine</td>
<td>287 mg</td>
</tr>
<tr>
<td>Glycine</td>
<td>699 mg</td>
<td>Histidine</td>
<td>364 mg</td>
<td>Isoleucine</td>
<td>658 mg</td>
<td>Leucine</td>
<td>1,322 mg</td>
</tr>
<tr>
<td>Methionine</td>
<td>998 mg</td>
<td>Phenylalanine</td>
<td>671 mg</td>
<td>Proline</td>
<td>754 mg</td>
<td>Serine</td>
<td>791 mg</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>192 mg</td>
<td>Valine</td>
<td>926 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** All statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

**Note:** Although highly nutritious, Shakeology does not meet all of your daily dietary needs and should not be the only meal you consume throughout the day.

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For more information, visit Shakeology.com
Myogenix - ProFiber

http://www.lpsupplements.com/servlet/the-1741/Myogenix-PRO-FIBER-Enzymes/Detail
Contains 1% juice

<table>
<thead>
<tr>
<th>Nutrition Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serving Size: 8 fl oz (240 mL)</td>
</tr>
<tr>
<td>Servings Per Container: About 2</td>
</tr>
<tr>
<td>Amount Per Serving</td>
</tr>
<tr>
<td>Calories 35</td>
</tr>
<tr>
<td>% Daily Value</td>
</tr>
<tr>
<td>Total Fat 0 g</td>
</tr>
<tr>
<td>Sodium 20 mg</td>
</tr>
<tr>
<td>Total Carbohydrate 8 g</td>
</tr>
<tr>
<td>Sugars 8 g</td>
</tr>
<tr>
<td>Protein 0 g</td>
</tr>
<tr>
<td>Thiamin (Vitamin B₁)</td>
</tr>
<tr>
<td>Riboflavin (Vitamin B₂)</td>
</tr>
<tr>
<td>Niacin (Vitamin B₃)</td>
</tr>
<tr>
<td>Vitamin B₆</td>
</tr>
<tr>
<td>Folic Acid (Vitamin B₉)</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
</tr>
</tbody>
</table>

Not a significant source of Calories from Fat, Saturated Fat, Trans fat, Cholesterol, Dietary Fiber, Vitamin A, Vitamin C, Calcium, or Iron.

†Percent Daily Values (DV) are based on a 2,000 calorie diet.

PER BOTTLE: Contains the probiotic cultures B. coagulans MTCC 5856 and L. rhamnosus. (4 billion CFUs at time of manufacture)
Addicted to caffeine?
Bring Your own Straw...

Balanced Berry Probiotic Drink Mix
Supplement Facts

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount per Serving</th>
<th>% Daily Value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>6g</td>
<td>2%*</td>
</tr>
<tr>
<td>Sugars</td>
<td>3g</td>
<td></td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>2g</td>
<td>8%*</td>
</tr>
<tr>
<td>Vitamin A (as Vitamin A Palmitate)</td>
<td>100IU</td>
<td>2%*</td>
</tr>
<tr>
<td>Vitamin C (as Ascorbic Acid)</td>
<td>60mg</td>
<td>100%*</td>
</tr>
</tbody>
</table>

Proprietary Probiotic Complex 10 Billion**

- LactoSpore® (Bacillus coagulans)
- Lactobacillus Bulgaricus
- Lactobacillus Acidophilus
- Fibersol 2.3g

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs. + Daily value not established.

**Over 10 billion probiotics at time of manufacturing

OTHER INGREDIENTS: Evaporated Sugar Cane Juice, Natural Flavors, Vegetable and Fruit Juice (for natural color), and Silica.
Probiotic Chews

- Our fruity chews are a great alternative to other treats and offers the same amount of probiotics as most commercial yogurts without all the sugar and calories.
- 1 billion probiotics per serving
- Sweetened with Stevia
- No refined sugars
- Gluten free
Fruit d’Or Nutraceuticals Launches Choco Cran
World’s First Cranberry Probiotic
Organic Chocolate Peanut Butter Cup

Each Choco Cran contains prebiotic, probiotic, and protein.
A super food for gut health.

Each Cup Contains:
- 50% Fiber
- 25% Protein
- 2 Billion CFU Probiotics Bacillus Coagulans MTCC 5856
- Fatty Acids Omega 3,6,9
- Tocotrienols, Tocopherols, Sterols

For more information contact Stephen Lukawski, Phone: (239) 248-7118 Email: stephen@fruit-dor.ca
LactoCran™ Nutrition Health Chocolate

✓ LactoCran – First of its kind tailored Synbiotic

✓ Using the LactoSpore and cranberry seed powder as a prebiotic.

✓ Sabinsa holds patent for this combination

✓ Probiotic chocolate is a new delivery system
Effect of Cranberry Fiber on the LactoSpore® Viability

Cranberry Fiber alone (% w/v) and MRS media with and without Dextrose

- Cranberry Fiber
- FOS

Initial Count (0h)  | 0.50%  | 1%  | 2%  | MRSD + 0  | MRS + 0

LactoSpore® viable count (Log10 cfu/ml)
- Initial Count (0h) | 5.9
- 0.50% | 6.5 ± 3.1
- 1% | 7.5 ± 3.6
- 2% | 8.1 ± 3.7
- MRSD + 0 | 7.2
- MRS + 0 | 8.5
Cranberry Protein- Ideal Prebiotic for LactoSpore®

LactoSpore® does not require any additional nutrient other than Cranberry Protein powder

LactoSpore® can utilize Cranberry Fiber more efficiently than FOS

Using Cranberry Fibers as a prebiotic, LactoSpore® can provide optimum growth, good intestinal flora and all the probiotic benefits to Gut

Based on In House Study for assessment of growth potential of LactoSpore® when used Konsyl and FOS (Fructo-Oligosaccharides) as growth media.
LactoSpore Gummies

✓ Promising delivery system for probiotics

✓ LactoSpore offers high stability, low overages and 3 years shelf life for gummies

✓ High potency of LactoSpore allows packing of therapeutically effective dosage in gummies

✓ Tasteful with health benefits
FDA GRAS (2016)
Versatile Application in Foods

✓ FDA GRAS : August 2016
✓ 2 Billion CFU spores/person/day is safe

✓ Baked Goods
✓ Breakfast Cereals
✓ Other Grains
✓ Fats & Oils
✓ Milk Products
✓ Cheese
✓ Frozen Dairy
✓ Soft Candy
✓ Confectionery & Frosting
✓ Gelatins & Puddings
✓ Gummies
✓ Snack Foods
✓ Non-alcoholic Beverages
✓ Imitation Dairy Products
✓ Hard Candy
✓ Sugar Substitutes
✓ Instant Coffee & Tea
✓ Soups
Finished products containing LactoSpore has received the Natural Product License to be marketed as Natural Health Product in Canada.

Product License : **NPN 80063390**
Product Name : **LactoSpore- Your Favorite Probiotic**

Product License : **NPN 80071354**
Product Name : **LactoSpore- Balance**
Health Claims - Canada

Probiotic – Bacillus coagulans MTCC 5856
Dosage - 2 Billion per day

a. SOURCE OF PROBIOTIC
b. HELPS SUPPORT INTESTINAL / GASTROINTESTINAL HEALTH
c. COULD PROMOTE A FAVORABLE GUT FLORA

a. HELPS RELIEVE ABDOMINAL PAIN ASSOCIATED WITH IBS
Bacillus coagulans MTCC 5856 brings to probiotic world...

✧ New delivery system providing probiotic benefits in shelf stable foods.

✧ Flexibility to deliver therapeutic dosage in both beverage and solid food format.

✧ Overcome losses in production due to processing requirements.

✧ Health benefits in gut and beyond.
THANK YOU

www.sabinsa.com

participating members of:

© Sabinsa Corporation | Streaming Live – your Probiotic | www.sabinsa.com
Promising ingredients for GI health beyond probiotics

Speaker: Dr Heike Stier, Senior Consultant, analyze & realize GmbH, Germany
Promising ingredients for GI health beyond probiotics

Dr. Heike Stier
analyze & realize GmbH, (Booth B30 Advice Center)
VitaFoods Asia, Sep. 5th 2017

www.analyze-realize.com
Outline

1. GI - Market
2. Herbal GI-Product Market
3. Alternatives for Probiotic
4. THMP as one option to the EU Market
5. Summary
Claim Situation on Probiotics in Europe
Health Claims Situation on Probiotics - EU

- In the EU it is not allowed to make currently any Health Claims on Probiotic

- WHY?
  - NHCR since 2007: (EC) No 1924/2006
  - Approval by EFSA (European Food Safety Authority) for all health claims is needed
    - All, but one, of > 400 applications have been rejected
  - According to EFSA already the term “probiotic” already implies a health benefit, which falls under the HCR
    ⇒ use of this term is not allowed
    ⇒ Ban of all claims on probiotic despite numerous scientific data
Gastro-Intestinal Product Market - Europe

- Awareness of the link between health & wellbeing and the digestive system is increasing
- Growing demand for natural ingredients for gastrointestinal health
  - Food intolerance => people suffering from digestive problems
  - Ageing population (about 30% above 65 in 2050) suffering digestive problems
  - Prevention instead of curing
- 66% of adults suffered from indigestion, gas, bloating or flatulence in the past year; 58% heartburn/acid reflux; 55% diarrhea; 51% constipation (Mintel, 2016).
- GI Market: the biggest growing segment of herbal drugs in EU
- Euromonitor projections: supplements and OTC/Rx digestive: one of the fastest-growing global healthcare categories from 2015 to 2020
Top 10 herbal medicinal products in Germany (Pharmacy retail values)*

- Respiratory systems: +2.7
- Cough: +0.5
- Circulation: +2.7
- Gastro-intestinal: +7.7
- Urinary tract: +6.8
- Calmatives and sleep aid: +2.1
- Infections / common cold: +4.0
- Muscle and joint pain: -3.7
- Cardio-vascular: -0.9
- Blood vessel (leg): +6.1

*Source: BAH (2016): “DER ARZNEIMITTELMARKT IN DEUTSCHLAND - Zahlen und Fakten”
Herbal Alternatives for Probiotics

Intestinal motility (Constipation, Diarrhea)
- Senna
- Aloe
- Psyllium
- Bilberry

Barrier function / anti-inflammatory
- Rosemary
- Green tea
- Curcuma
- Aloe

Pain, bloating, flatulence
- Fennel
- Ginger
- Parsley
- Anis

Dyspepsia / digestion / mal-absorption
- Artichoke
- Boldo
- Gentiana
- Salvia
Herbal Products for GI in Europe

Commonly used plants for GI disorders

- Peppermint (Mentha piperita)
- Roman camomile (Chamaemelum nobile)
- Green tea (Camellia sinensis)
- Turmeric (Curcuma longa)
- Ginger (Zingiber officinale)
- Boldo leaf (Peumus boldus)
- Fennel (Foeniculum vulgare)
- Black psyllium
- Senna (Senna alexandrana)
- Psyllium (Plantago ovata)
- Aloe vera/ferox (Aloe vera, A. ferox)
- Rosemary (Rosmarinus officinalis)
- Artichoke (Cynaria scolymus)
- Fumitory (Fumaria officinalis)
Herbal Products for GI in Europe

Commonly used plants for GI disorders

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# THMP – Basic Requirements


<table>
<thead>
<tr>
<th>Requirement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proof of 30 year tradition</td>
<td>Replaces clinical trial&lt;br&gt;Replaces pre-clinical safety data</td>
</tr>
<tr>
<td>Ingredients</td>
<td>Herbs only&lt;br&gt;Ancillary: vitamins or minerals&lt;br&gt;Not: isolated (highly enriched) compounds</td>
</tr>
<tr>
<td>Dosage forms</td>
<td>Only oral, topical, or by inhalation applied nonprescription drug use</td>
</tr>
<tr>
<td>Indication</td>
<td>Self diagnosable&lt;br&gt;W/o medical supervision</td>
</tr>
<tr>
<td>Quality</td>
<td>Raw material GACP&lt;br&gt;Production according GMP</td>
</tr>
</tbody>
</table>
Proof of Tradition replaces clinical studies (CTD module 2.5)

**Most important information:**

- **Time** in safe medicinal use (30 years world wide and 15 years of which must be within the EU *(Article 16a(1)d)*)
- Same traditional therapeutic **indication** (self diagnosed, w/o medical supervision)
- Same **strength/type** of preparation
  - **Important:** same (comparable) DER, same extraction solvent
- Same **posology** (dosage) and
- Same **dosage form**

“Proof of traditional use” by detailed reference to

- scientific literature
- best with historically comparable reference product (post-marketing data)
Non-Clinical requirements (CTD module 2.4) = Safety (Article 16a(1)e)

- Necessary: Pharmacological and Toxicological expert statement
  
  - **Pharmacology:**
    - No own data: bibliographic
  
  - **Pharmacokinetics:**
    - No own data: bibliographic
  
  - **Toxicology:**
    - No own data: bibliographic

- A product specific AMES test (genotoxicity) is required
  
  
  - Further safety tests upon authority request is required
THMP – Requirement on Indication

- Indication has to be self diagnosable, without medical supervision, or to refer to the use ‘after exclusion of serious conditions by a medical doctor, for more serious pathologic conditions
- Indication is part of the „Proof of Traditional use“
  => Same traditional therapeutic indication
- The product labeling: “product x is a Traditional Herbal Medicinal Product, traditionally for the use for indication z, exclusively based on longstanding use.“
THMP – Quality Requirements

QUALITY (Directive 2001/83/EC Article 16e(1)e)

- Quality requirements are as high as for any drugs
  - No reduction regarding the production quality
  - No reduction regarding quality documentation
  - GMP for all productions steps (raw material GACP)

- Complete CTD Module 3
  - Drug substance (CTD Module 3.S.)
    - Herbal substance (herbal raw material)
    - Herbal preparation (extract)
  - Drug product (capsules, tablets, etc.; CTD Module 3.P.)
The CTD for THMP

- EMA/HMPC/71049/2007
- Bibliographical, simplified application simplified registration (EMEA/HMPC/32116/2005)

Application form

Regional administrative Information
Module 1

2.3 Quality overall summary
2.4 Non-clinical overview
2.5 Clinical overview

Non-clinical study reports
Clinical study Reports

Non-Clinical Expert Statement

Proof of Tradition

CTD
THMP granted in the EU

- Number of indications granted in TUR for THMP grouped by typical traditional therapeutic areas for monocomponent and combination products in the EU (31 Dec. 2016)

![Bar chart showing indications by typical areas](chart)

- Cough and cold
- Mental stress & mood disorders
- Gastrointestinal disorders
- Urinary tract and genital disorders
- Sleep disorders & temporary insomnia
- Pain and inflammation
- Other*
- Mouth and throat disorders
- Skin disorders & minor wounds
- Circulatory disorders
- Fatigue & weakness
- Loss of appetite
- Constipation
- Eye discomfort

<table>
<thead>
<tr>
<th>Area</th>
<th>Monocomponent Products</th>
<th>Combination Products</th>
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</thead>
<tbody>
<tr>
<td>Cough and cold</td>
<td>282</td>
<td>392</td>
</tr>
<tr>
<td>Mental stress &amp; mood disorders</td>
<td>270</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>267</td>
<td></td>
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<tr>
<td>Urinary tract and genital disorders</td>
<td>209</td>
<td></td>
</tr>
<tr>
<td>Sleep disorders &amp; temporary insomnia</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>Pain and inflammation</td>
<td>152</td>
<td></td>
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<tr>
<td>Other*</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Mouth and throat disorders</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Skin disorders &amp; minor wounds</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Circulatory disorders</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Fatigue &amp; weakness</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

The **Committee on Herbal Medicinal Products (HMPC)** compiles and assesses scientific data on herbal substances, preparations and combinations with a focus on safety and efficacy.

EU monographs provide information about specific herbal substance or preparation, with regard to:

- Indication, patient population
- Strength, dosage
- Safety information (undesirable effects and interactions)

Those can be used for the Proof of Tradition (without individual tradition data)
EMI - HMPC Monographs GI disorders

- Currently 46 HMPC monographs with GI-indication

| A | Absinthii herba, Agrimoniae herba, Althaeae radix, Anisi aetheroleum, Anisi fructus |
| B | Boldi folium |
| C | Carvi aetheroleum, Carvi fructus, Centaurii herba, Chamomillae romanae flos, Cichorii intybi radix, Cinnamomi cortex, Cinnamomi corticis aetheroleum, Curcumae longae rhizome, Curcumae xanthorrhizae rhizoma, Cynarae folium |
| F | Foeniculi amari fructus, Foeniculi dulcis fructus, Fucus vesiculosus thallus, Fumariae herba |
| G | Gentianae radix |
| H | Harpagophyti radix, Hyperici herba, Helichrysi flos |
| J | Juniperi aetheroleum, Juniperi pseudo-fructus |
| L | Lini semen |
| M | Marrubii herba, Matricariae flos, Melissae folium, Menthae piperitae aetheroleum, Menthae piperitae folium, Millefolii flos, Millefolii herba, Myrtilli fructus siccus |
| O | Origani dictamni herba, Origani majorana herba |
| Q | Quercus cortex |
| R | Rosmarini aetheroleum, Rosmarini folium, Rubi idaei folium |
| S | Salviae officinalis folium, Sideritis herba |
| T | Taraxaci radix cum herba, Tormentillae rhizome |
| Z | Zingiberis rhizome TU WEU |

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Successful Herbal Products for GI Health

Iberogast
- Herbal Medicinal Product
- 9 herbal ingredient
- Number one in the GI OTC product market Germany
  - 2015 ≈ 95 mio €
  - 2016 > 100 mio €

Gasteo
- THMP
- 6 herbal ingredients
  - *Potentilla anserina* L
  - Chamomile flowers
  - Licorice root
  - *Angelica* root
  - *Cnicus benedictus*
  - *Artemisia absinthium*

MYRRHINIL-INTEST®
- THMP
- 3 herbal ingredients
  - Chamomile flowers
  - Myrrh
  - Coffeae carbo
Chances: TCM Products for EU

- Traditional herbal registration procedure is open for all herbals
  - Tradition can be based on marketing as Supplement in EU (15 years) + medicinal use in any other country worldwide (30 years)

March 14, 2012
- Frist TCM as THMP in The Netherlands.
- Di’ao Xin Xue Kang (Japanese yam root - *Dioscorea nipponica*)
  - treatment of myocardial ischemia

Febr. 18 2015
- Phynova Joint and Muscle Relief Tablets in UK
- Sigesbeckia (Xi Xian Cao)
Summary

- Probiotics are not the only natural product for gastro-intestinal health.
- In Europe there is a growing demand for natural ingredients for gastrointestinal health.
- The GI category in the OTC market is growing especially for products based on herbals.
- Numerous herbal products as alternatives for probiotics are available.
- One option are THMP, with simplified registration procedure for EU.
- THMP option is a chance for TCM products for the EU-Market.
analyze & realize GmbH

More than 20 years: "The experts in natural health products"
35 professionals from pharmaceutical, nutraceutical, medical device industries, CROs and academic research

Consulting & Strategic Innovation
Scientific Excellence
Regulatory Creativity
In vitro mode-of-action
Process driven Innovation

Clinical Research (CRO)
Full range of clinical trials
Highly specific study designs
Study centre
Thank you for your attention!

- Please visit us at Vitafood on **Booth B30** - Advice Center

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Novel biomarkers and therapeutic targets to help restore microbial symbiosis

Speaker: Niranjan Nagarajan, Associate Director and Group Leader, Genome Institute of Singapore (A*STAR); Adjunct Associate Professor, National University of Singapore

Join the conversation on Twitter at: @VitafoodsAsia #VFA17
Novel biomarkers and therapeutics to help restore microbial symbiosis

Niranjan Nagarajan
Associate Director and Senior Group Leader
GIS, A*STAR
Adjunct Associate Professor, National University of Singapore
Antibiotics and the Gut Microbiome

Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation

Les Dethlefsen* and David A. Relman*a,b,1

Antibiotic treatment expands the resistance reservoir and ecological network of the phage metagenome

Sheetal R. Modi1, Henry H. Lee1‡, Catherine S. Spina1,2,3 & James J. Collins1,2,3

The initial state of the human gut microbiome determines its reshaping by antibiotics

Frédéric Raymond1, Amin A Ouameur1, Maxime Déraspe1, Naeem Iqbal1, Hélène Gingras1, Bédis Dridi1, Philippe Leprohon1, Pier-Luc Plante1, Richard Giroux1, Éve Bérubé1, Johanne Frenette1, Dominique K Boudreau1, Jean-Luc Simard1, Isabelle Chabot1, Marc-Christian Domingo2, Sylvie Trottier1, Maurice Boissinot1, Ann Huletsky1, Paul H Roy1, Marc Ouellette1, Michel G Bergeron1,3 and Jacques Corbeil1,3

1Centre de Recherche en Infectiologie, CHU de Québec–Université Laval, Québec, Canada and 2Institut National de Santé Publique du Québec, Laboratoire de Santé Publique du Québec, Montréal, Québec, Canada
If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine” – David Cameron
Healthcare-associated Infections in Asia

Multi-drug Resistant Enterobacteriaceae

- *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*
- Resistance to extended-spectrum β-lactams, Carbapenems

**Sepsis** (~50% mortality rate) and *Klebsiella* liver abscess

Asymptomatic colonization of gut
Gut microbiome is a reservoir for resistance

- How can we prevent transfer of resistance?
- How can we stop colonization/persistence and promote decolonization?
Antibiotic Usage & Colonization

**Selective Digestive Decontamination**
- Topical non-absorbable antibiotics
- Short course of intravenous antibiotics

Antibiotic usage is a risk factor for pathogen colonization (>3x)

What enables microbiome recovery?

Genome Med. 2016; 8: 39
Understanding Gut Microbiome Recovery

Confidence intervals:
- 0 - 25%
- 25 - 50%
- 50 - 75%
- 75 - 95%

- Four Cohorts: Singapore* (WGS), Canada (WGS), England (16S), Sweden (16S)

- >300 samples from 96 subjects
- 1 week treatment, 3 months post abx
Identification of Recovery Associated Bacteria (RAB)

Methodology
• FDR < 0.1 (Mann-Whitney Test)
• Validated (seen in 2 cohorts)
• Consistent Trends

Results
• 20 Species
• 6 in 3/4 cohorts
• 6 Bacteroides, 2 Parabacteroides, 2 Alistipes, 2 Eubacteria, 2 Bifidobacteria

<table>
<thead>
<tr>
<th>Species</th>
<th>Cohort-specific FDR-corrected p-value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Canada</td>
<td>England</td>
</tr>
<tr>
<td>Alistipes spp. A</td>
<td>0.046</td>
<td>0.083</td>
</tr>
<tr>
<td>Bacteroides spp. A</td>
<td>0.082</td>
<td>0.008</td>
</tr>
<tr>
<td>Alistipes spp. B</td>
<td>0.033</td>
<td>0.069</td>
</tr>
<tr>
<td>Bacteroides spp. B</td>
<td>0.001</td>
<td>0.697</td>
</tr>
<tr>
<td>Bacteroides spp. C</td>
<td>0.003</td>
<td>0.917</td>
</tr>
<tr>
<td>Parabacteroides spp. A</td>
<td>0.027</td>
<td>0.877</td>
</tr>
<tr>
<td>Bifidobacterium spp. A</td>
<td>0.012</td>
<td>0.054</td>
</tr>
<tr>
<td>Bacteroides spp. D</td>
<td>0.009</td>
<td>0.777</td>
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<tr>
<td>Bacteroides spp. E</td>
<td>0.012</td>
<td>0.370</td>
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<tr>
<td>Bacteroides spp. F</td>
<td>0.248</td>
<td>0.425</td>
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<tr>
<td>Parabacteroides spp. A</td>
<td>0.245</td>
<td>0.509</td>
</tr>
<tr>
<td>Pseudoflavonifract or spp. A</td>
<td>0.013</td>
<td>0.054</td>
</tr>
<tr>
<td>Roseburia spp. A</td>
<td>0.560</td>
<td>0.054</td>
</tr>
</tbody>
</table>
**Bacteroides spp. A**
- Commensal Anaerobe
- Negatively associated with IBD, Obesity
- Counteracts High-Fat-Diet in Mice

**Bacteroides spp. B**
- Promotes gut angiogenesis and development of mucosal barrier
- Digests complex plant materials

**Parabacteroides spp.**
- Anaerobic, Non-sporulating
- Smaller genome, having fewer environmental sensing and carbohydrate-degrading genes
**Bifidobacterium spp.**

- Common Probiotic
- Early colonizer
- Marker of healthy microbiota
- Breakdown of conjugated bile acids
- ...

**Alistipes spp.**

Strict anaerobes, Bile resistant

---

**Alistipes spp. A**

- Canada
- England
- Sweden
- Singapore

**Alistipes spp. B**

- Canada
- England
- Sweden
- Singapore
Enriched Functions in Recovering Microbiomes

Amino acid Biosynthesis

- L-lysine biosynthesis
- Superpathway arginine polyamine biosynthesis
- Superpathway L-aspartate/L-asparagine biosynthesis
- Superpathway aspartate biosynthesis
- L-arginine biosynthesis
- L-methionine biosynthesis
- L-methionine biosynthesis II

Nucleotide Biosynthesis

- Guanosine ribonucleotides de novo biosynthesis
- Pyridoxal-5-Phosphate synthesis and salvage
- Thiamine diphosphate biosynthesis
- Purine nucleotides biosynthesis
- Tetrahydrofolate biosynthesis and salvage

Co-factor Biosynthesis

- Phosphopantothenate biosynthesis
- NAD biosynthesis from aspartate
- Flavin biosynthesis (bacteria and plants)
- Biotin biosynthesis
- Pyridoxal phosphate superpathway
- Thiamin salvage

Energy Production

- TCA cycle
- Glycolysis: Entner-Doudoroff Pathway
- Glycolysis: TCA / Glyoxylate bypass

Cell wall Biosynthesis

- Peptidoglycan biosynthesis pathway: Diaminopimelate
- N-acetylmuramoyl-pentapeptide biosynthesis
- Enterobactin biosynthesis
- Keto-3-deoxy-D-manno-octulosonate biosynthesis

Carbohydrate degradation

- N-acetylneuraminate degradation
- Rhamnose and fucose degradation

GDP-mannose biosynthesis

Sucrose degradation: Invertase

LDA SCORE (log 10)
RABs have more CAZymes

Recoverers are enriched for CAZyme families

Model for Mechanism

RABs → CAZyme → CGR → Recovery

Not Recovered

Recovered

P < 0.002

P < 0.04

RABs

Non RABs

RABs → CAZyme → CGR → Recovery

P < 1e-11

Canada

Singapore

Number of CAZyme families

Fraction

Number of CAZyme families

Recoverers are enriched for CAZyme families

RABs → CAZyme → CGR → Recovery

Not Recovered

Recovered

RABs

Non RABs

P < 0.002

P < 0.04

RABs → CAZyme → CGR → Recovery

P < 1e-11

Canada

Singapore

Number of CAZyme families

Fraction
Growth Rate from Genomic Coverage Skew

MICROBIOME

Growth dynamics of gut microbiota in health and disease inferred from single metagenomic samples

Tal Korem,1,2* David Zeevi,1,2* Jotham Suez,3* Adina Weinberger,1,3* Tali Avnit-Sagi,1,2 Maya Pompan-Lotan,1,2 Elad Matot,1,2 Ghil Jona,4 Alon Harmelin,5 Nadav Cohen,1,2 Alexandra Sirota-Madi,6 Christoph A. Thaiss,3 Meirav Pevsner-Fischer,3 Rotem Sorek,7 Ramnik J. Xavier,6 Eran Elinav,3* Eran Segal1,2*

CGR is higher in Recoverers

P < 0.02
P < 0.003

CGR is associated with CAZyme diversity

R = 0.636
R = 0.675

Canada

Singapore

*Corresponding authors.
Clustering of Carbohydrate Degraders (125 species)

RABs in Cluster 1 (P < 0.038)
Food Webs and Dependency Relationships

Association Rule Mining

- 782 Microbiome Profiles (MEDUSA)
- Binary Relationships (A \(\Rightarrow\) B), Remove transitive edges
  - Confidence = 0.95
Bacterial Food Web

Primary Colonizers
Secondary Colonizers
Tertiary Colonizers

Bacteroides
Eubacterium
Bifidobacterium
Ruminococcus
Faecalibacterium

Degradation Profile:
- Cluster 1' (Plant Cell Wall + Animal Carbohydrates + Mucin)
- Cluster 2' (Plant Cell Wall + Animal Carbohydrates)
- Cluster 3' (Low Plant + Animal Carbohydrate + High Starch)

Abundance Profile:
1 = Cluster 1' (High in all stages)
Primary Colonizers

Mucin

Colonocytes for growth

SCFA

Simple sugars

Other Bacteria

Other Carbohydrate Degraders

Dietary carbohydrate

Primary Colonizer

Increased mucin production

Lamina propria
Promoting microbiome recovery in a mouse model

Extensive Metagenomic Profiling
- Samples taken every 3 days (11 timepoints)
- 6 conditions, 6 replicates per condition
- 396 shotgun metagenomic libraries
RABs promote accelerated microbiome recovery
Degradation of Host and Diet-derived Carbohydrates

![Graphs showing degradation of Plant/Animal cell wall and Mucin over days since start of experiment for different treatments: Bif, BacX, BacX+Bif, Bac, Bac+Bif, Vehicle. Asterisks indicate significant differences.]

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Legend Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bif</td>
<td>Light blue</td>
</tr>
<tr>
<td>BacX</td>
<td>Beige</td>
</tr>
<tr>
<td>BacX+Bif</td>
<td>Green</td>
</tr>
<tr>
<td>Bac</td>
<td>Blue</td>
</tr>
<tr>
<td>Bac+Bif</td>
<td>Red</td>
</tr>
<tr>
<td>Vehicle</td>
<td>Gray</td>
</tr>
</tbody>
</table>
Reducing risk of Enterobacteriaceae colonization

![Graph showing proteobacteria abundance over days since start of experiment for different treatments: Bif, BacX, BacX+Bif, Bac, Bac+Bif, and Vehicle.](image)
Results Summary

- **Microbiome Recovery**
  - Multi-cohort association analysis
  - Taxa and functions associated with it

- **Mechanistic Model**
  
  | RABs | CAZyme | CGR | Recovery |

- **Microbial Food Web**

- **In vivo Models**
  - 100× enhanced recovery
  - Reducing risk of Enterobacteriacea colonization
Future Work

Predict
Microbiome recovery (host, antibiotic, diet dependence)

Model
Microbial community dynamics (gLVMs)
Antibiotics, probiotics & pathogens
Lisa Tucker-Kellog (Duke-NUS), Gan Yunn Hwen (NUHS)

Engineer
Synergistic effects
Henning Seedorf (TLL), Matthew Chang (NUS)
>$15B market for HAIs
>$35B probiotics market