Probiotics for management of allergies

Karen Koning, PhD

Vitafoods 2017
Winclowe Probiotics

60+ customers
30+ countries

70+ formulations

Family owned
100% SELF FINANCED

100+ strains
10 prebiotics

110 million
daily dosages sold in 2016

25 years dedicated to PROBIOTIC DEVELOPMENT, research and manufacturing

PhDs +10%

Support staff: 17%
R&D: 15%
Scientific Affairs: 17%
Production & Operations: 35%
RA / QA: 8%
BD & Sales: 8%

Family owned
100% SELF FINANCED

FOOD supplements, FSMP & MD

100+ strains
10 prebiotics

110 million
daily dosages sold in 2016

25 years dedicated to PROBIOTIC DEVELOPMENT, research and manufacturing

PhDs +10%
Winclove Research Institute

Our Focus Areas

- SPORT
- TRAVEL
- IBD
- CONSTIP.
- WOMEN’S HEALTH
- ANTIBIOTIC-ASSOCIATED SYMPTOMS
- GUT-BRAIN AXIS
- ALLERGIES

- 50 RESEARCH PROJECTS started, ongoing, or finished in 2015
- 70% of research in 2016 were in HUMANS
- >40 External research partners worldwide
- >50 peer-reviewed PUBLICATIONS over the last 10 years
- 10 MANUSCRIPTS ACCEPTED for publication in the 2016
How do we sell?

Business to business
Private label (Co-branding)
Medical endorsed
Research driven, large pipeline
Extensive sales support
Flexible
The microbiota

The gut contains approx. **1000** different individual species of **MICROORGANISMS**

**60-80 %** of **IMMUNE SYSTEM** is in the gut

Our bodies are **MORE MICROBE THAN HUMAN**.

Our microbes have **360X more protein DNA** than us.

Gut microbes create **95% of our SEROTONIN**
Winclove’s view on the mode of action

1. **Microbe – Microbe**
   - Compete for colonization space and receptors
   - Resistance and inhibition of pathogens (e.g. H$_2$O$_2$)
   - Modify metabolic environment (e.g. SCFA production)
   - Communicate with commensals (e.g. quorum sensing)

2. **Microbe – Mucosal Layer**
   - Improve barrier function (e.g. claudins)
   - Induce cyto-protective compounds (e.g. defensins)
   - Stimulate mucus production

3. **Microbe – Immune System**
   - Enhance signaling response (e.g. Ig and cytokines)
   - Induce immune cell migration (e.g. T and B cells)
   - Moderate responsiveness (e.g. to food antigens)
Types of Probiotics

• **Monostrain probiotics:**
  • Contain 1 strain of one species
  • **Example:**
    • *Lactobacillus acidophilus*

• **Multistrain probiotics:**
  • Contain >1 strains of one species
  • **Example:**
    • *Lactobacillus acidophilus*
    • *Lactobacillus casei*

• **Multispecies probiotics:**
  • Contain different strains of different species
  • **Example:**
    • *Lactobacillus acidophilus*
    • *Bifidobacterium bifidum*
    • *Enterococcus faecium*
Differences between bacterial strains

Properties bacterium X ≠ Properties bacterium Y

- Multispecies
  Combination of different properties increases efficacy
- Indication specific
  Right strains (properties) for each indication
Our Portfolio

Winclove has three distinct lines:

1. The **Ecologic®** line
   - Clinically proven (*in vivo*)
   - Indication-specific

2. The **Winclove** line
   - Evidence based (*in vitro*)
   - Indication-specific and broad spectrum

3. Tailor made formulations
Ecologic® Formulations

Brain
- Ecologic® BARRIER

Oral
- WINCLOVE SMILE

ENT
- WINCLOVE ENT RESPIRATORY

Allergy
- Ecologic® PANDA
- Ecologic® ALLERGycare TOLERANCE

Gut
- Ecologic® 825
- Ecologic® AAD
- Ecologic® BARRIER
- Ecologic® PERFORMANCE RELIEF
- Ecologic® RESILIENCE TRAVEL

Urogenital
- Ecologic® FEMI+
- WINCLOVE CLEAR
ProbioAct Technology

- Carrier material
- Stability
- Enzymes
- Metabolic activity
- Prebiotics
- Vegetable protein
- Minerals
- G1-survival
- Vegetable protein
Prevalence of allergy

- Prevalence of allergy: up to 40% in Western countries suffer from some form of allergy
- Enormous rise since last 25 years
- Allergic march: allergy follows allergy
Why rise of allergy?

Lack of early childhood exposure to infection → increased susceptibility to allergic diseases by suppressing the natural development of the immune system

Early life pertubations of the microbiota disrupt immune development
Microbiota management

Can Probiotics help with Allergies?
Probiotics for prevention of AD

Probiotics and allergy in infants

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Probiotics Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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<td>1.41 [0.83, 2.39]</td>
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<td>Ou 2012 (16)</td>
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<td>Taylor 2007 (21)</td>
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<td>Taylor 2007 (22)</td>
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<td>88</td>
<td>34</td>
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<td>4.5%</td>
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<td>23</td>
<td>157</td>
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<td>49</td>
<td>146</td>
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<td>0.86 [0.63, 1.16]</td>
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<td>Total (95% CI)</td>
<td>2381</td>
<td>2374</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.78 [0.69, 0.89]</td>
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</table>

Total events: 672
Heterogeneity: Tau^2 = 0.07; Chi^2 = 64.73, df = 28 (P < 0.0001); I^2 = 57%
Test for overall effect: Z = 3.65 (P = 0.0003)
Management allergies

Boyle et al, Cochrane reviews

Zajac et al, Int Forum Allergy Rhinol
Ecologic® Allergycare: *In vitro* characteristics

- *Bifidobacterium bifidum* W23
- *Lactobacillus acidophilus* W55
- *Lactobacillus casei* W56
- *Lactobacillus salivarius* W57
- *Lactococcus lactis* W58

**Dosage:** 2x 2 grams (4.0 x $10^9$ CFU)
40 children (1-13 years) with atopic eczema (moderate – severe SCORAD)

- Double-Blind Randomized Placebo-Controlled Study:
  - 20 children: Ecologic® ALLERGYCARE (probiotic)
  - 20 children: skimmed milk powder + dextrine (placebo)
Ecologic® Allergycare: management of AR

- Does Ecologic® Allergycare have promise as a therapeutic intervention in AR?
- Does this warrant a large RCT?
- Estimation of effect size – avoid underpowered clinical studies.
Ecologic® Allergycare: study design

Simon two stage design: response rate of AR patients to Ecologic Allergycare

- P0; non effective treatment < 15%
- P1; effective treatment >33%
- 40 patients (17-65 years) with more than two year history of AR and positive allergic response to Bermuda grass.

• Mini Rhinocconjunctivitis Quality of Life Questionnaire (≥0.7 clinically beneficial)
• Bi-weekly symptom and medication diary
Conclusion

• Role of microbiota in allergy

• Probiotics are studied with respect to prevention and treatment/management of eczema

  • Prevention: stronger evidence
  • Treatment: more heterogeneous results
Winclove probiotics

Goal

Indication specific probiotics that improve quality of life

• High quality
• Safe to use, no side effects!
• Development in collaboration with universities, academic hospitals and research institutes
• Evidence based
• Shelf life of up to 2 years @ room temperature (25°C)
• Survival through GI-tract and active (ProBioAct)
• User friendly
Thank you for your attention

Please visit us at booth G92