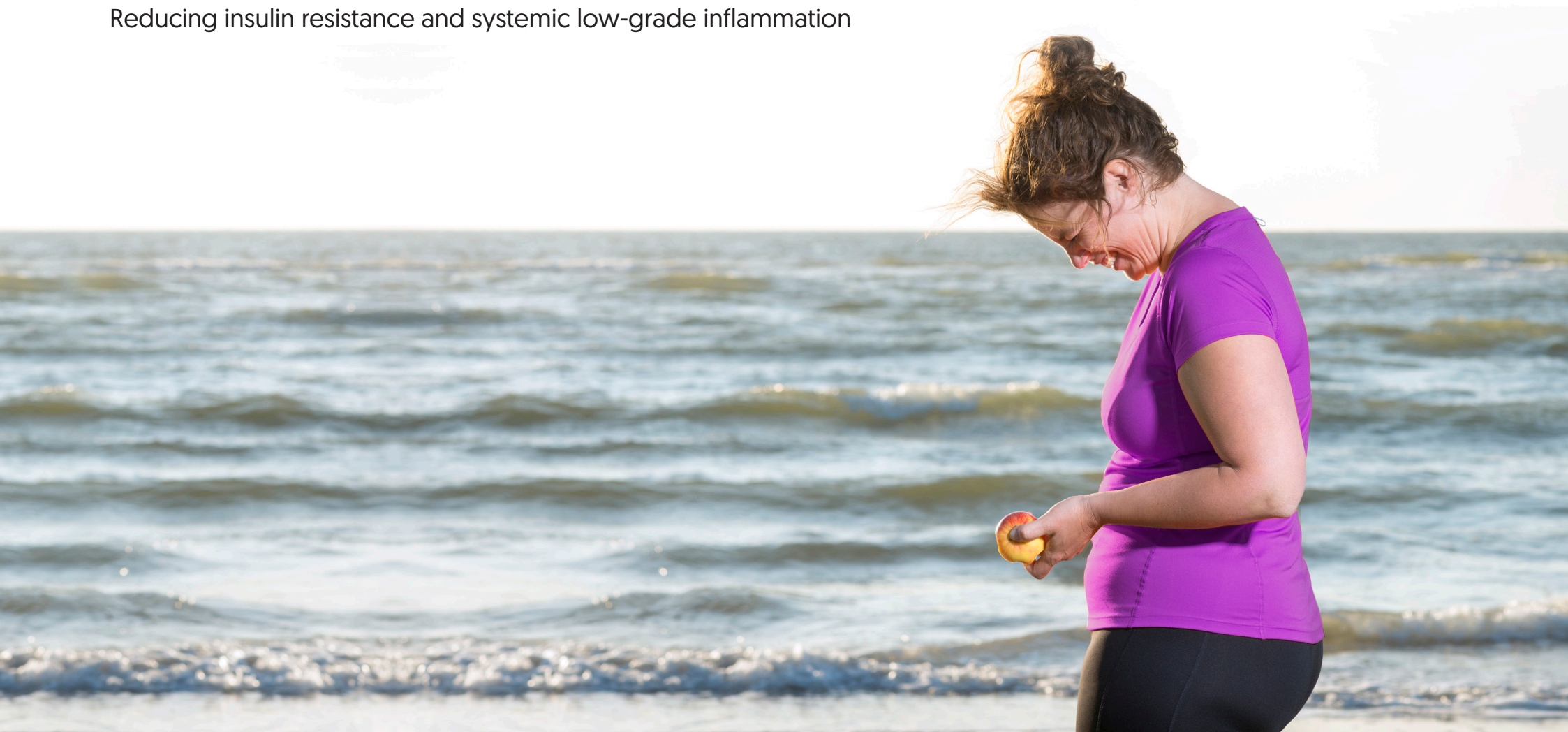


Ecologic[®] BARRIER for Metabolic Health

Reducing insulin resistance and systemic low-grade inflammation

Ecologic[®] BARRIER
inside



Medical Background

Today, a record number of patients worldwide suffer from metabolic disorders, including obesity, non-alcoholic fatty liver disease (NAFLD), type 2 diabetes mellitus (T2DM) and cardio-metabolic disease (CMD)¹. As poor diets, lack of exercise, and other stressors continue to negatively impact millions of people around the globe, we must look for new ways to improve metabolic health, delay disease progression, and foster a better quality of life where possible.

Insulin resistance and systemic low-grade inflammation seem to be at the core of metabolic disorders²⁻⁴. Recent research has indicated that the gut microbiota plays an important role in managing metabolic health^{5,6}. Disturbance of gut microbiota by a typical western lifestyle leads to changes in serum lipopolysaccharides (LPS), short-chain fatty acids (SCFAs) and bile acid, resulting in systemic low-grade inflammation and insulin resistance^{5,7,8}. [see figure 1] Given the role the microbiota on metabolic

disorders, targeted probiotic formulations may be clinically relevant for optimizing metabolic health, influencing insulin resistance and systemic low-grade inflammation associated in early- and late-stage metabolic disorder, specifically T2DM. Recent literature has supported the efficacy of probiotics for improving a range of metabolic markers, including HOMA-IR, a measure of insulin resistance, and serum LPS, a measure of gut permeability and a trigger of inflammatory responses⁹⁻¹³.

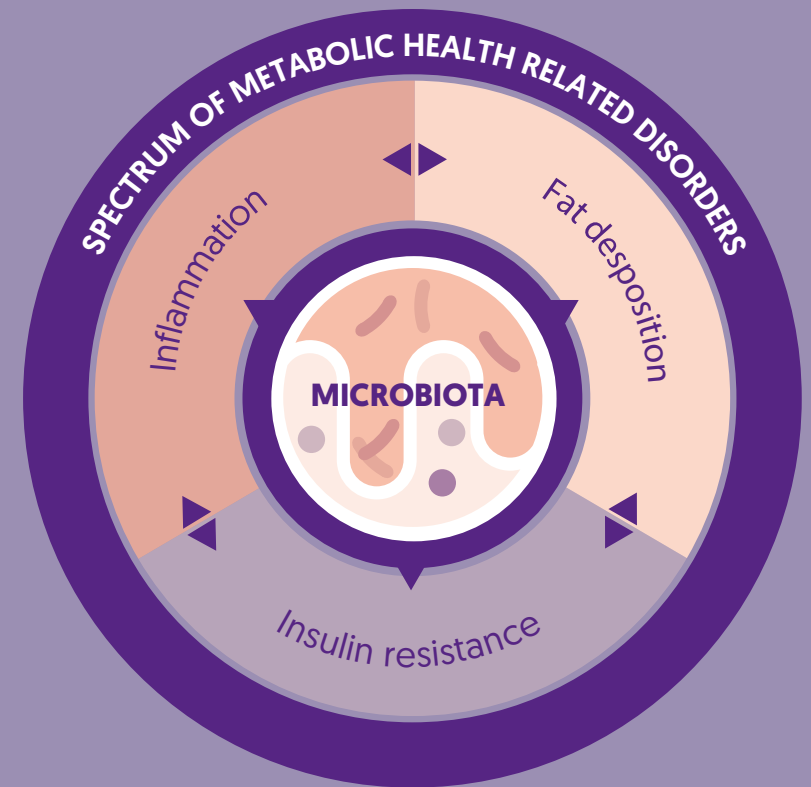


FIGURE 1

Crosstalk between gut microbiota and host's system in terms of inflammation and metabolism. The gut microbiota, through a range of molecular interactions, contribute to host insulin resistance, systemic low-grade inflammation, and fat deposition and therefore, indirectly participate in the onset and progress of (metabolic) diseases.





Product Development

Ecologic® BARRIER is a multispecies probiotic formulation consisting of 9 specifically selected probiotic strains. Probiotics strains can exert health effects at different levels in the gut [figure 2, 3-levels of action]. These strains were selected based on their ability to strengthen the intestinal barrier function [level 2] and reduce low-grade inflammation [level 3]¹⁴, making it a suitable choice for research in insulin resistance and metabolic health.

These strains have been screened for their capacity to:

- Improve the intestinal barrier function
- Inhibit mast cell activation
- Stimulate IL-10 production
- Break down lipopolysaccharides (LPS)

Formulation details

Indication	Reducing insulin resistance and systemic low-grade inflammation.			
Colony forming units (CFU)	2,5 x 10 ⁹ CFU/gram.			
Recommended daily dosage	2-4 grams.			
Bacterial strains	<i>B. bifidum</i> W23 <i>B. lactis</i> W51 <i>B. lactis</i> W52	<i>L. acidophilus</i> W37 <i>L. brevis</i> W63	<i>L. casei</i> W56 <i>L. salivarius</i> W24	<i>Lc. lactis</i> W19 <i>Lc. lactis</i> W58
PROBIOACT® Technology	 Protective and nutritional ingredients that improve the stability of the formulation, GI survival and metabolic activity of the bacteria.			
Treatment period	For as long as desired/needed.			
Storage and stability	2 years stable at room temperature, no refrigeration needed.			
Available dosage forms	Dry powder which can be supplied as bulk or sachets and fully packed (with your design).			
Safety and Quality Profile	  All probiotic strains have the Qualified Presumption of Safety (QPS) status ¹⁶ . Winclave is a NSF International Certified GMP Facility for manufacturing dietary supplements and is ISO 22000:2005 certified for the development and production of pre-and probiotics.			
Marketing	 Medically endorsed under private label on a co-branding basis. Co-branding enables our business partners to use the scientific data in their marketing communication.			

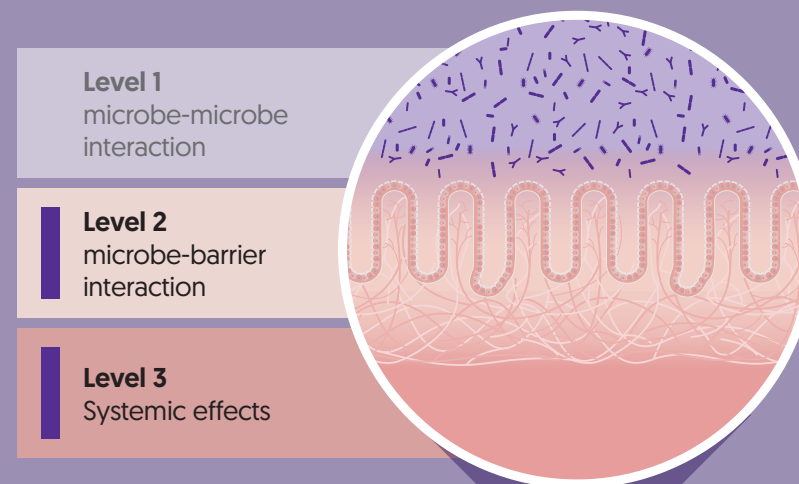
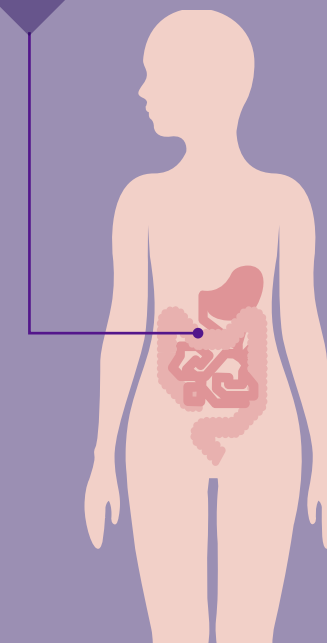


FIGURE 2
Probiotic strains can be active on three levels in the gut. The strains in Ecologic® BARRIER have been proven active at level 2 and 3.



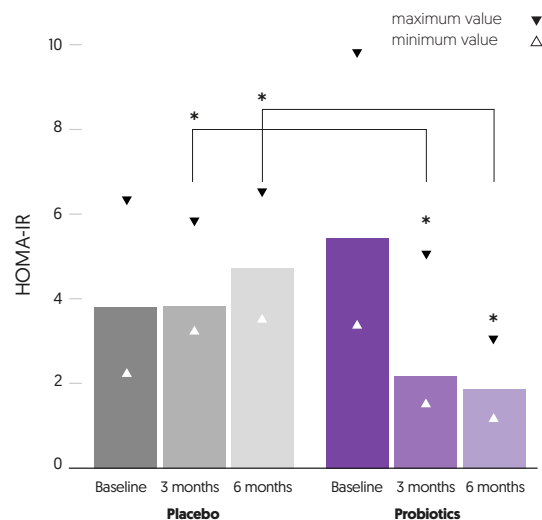
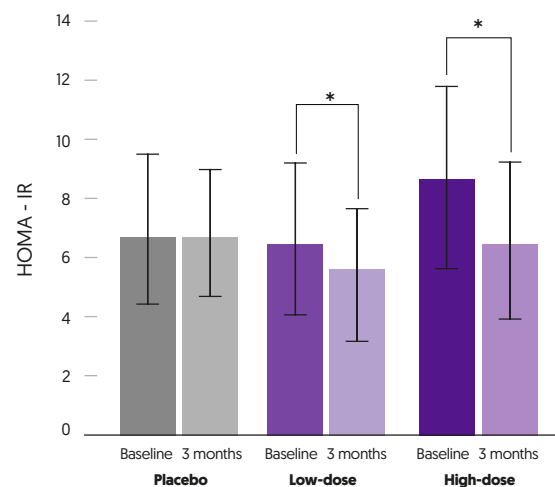


FIGURE 3
HOMA-IR levels (Median [range]) before and after 3 months and 6 months supplementation with Ecologic[®] BARRIER.
*Significant decrease, $p < 0.05$



Clinical evidence

Ecologic[®] BARRIER has been tested in a double-blind, placebo-controlled, randomized study, performed by the Warwick University, UK and King Saud University, Saudi Arabia^{9,10}. Ninety-six adult T2DM patients (treatment-naïve and without co-morbidities) were randomized to receive 2 grams of Ecologic[®] BARRIER twice daily (1.0×10^{10} cfu/day) or placebo for 6 months. In the probiotic group Ecologic[®] BARRIER significantly reduced HOMA-IR levels after 3 months and 6 months, which did not occur in the placebo group (see figure 3). In line with this a significant decrease in fasting glucose and fasting insulin was observed in the probiotic group. In addition, Ecologic[®] BARRIER intake reduced circulating endotoxin levels (LPS), a trigger of inflammation and a marker for gut barrier function, and improved inflammation markers such as CRP, TNF- α , IL-6.

The positive effect of Ecologic[®] BARRIER on the gut barrier function was also observed randomized, double-blind, placebo-controlled pilot study performed by researchers from the Medical University of Graz, Austria¹³. In this study, twenty-six treatment-experienced obese T2DM patients were randomized to receive 6 grams of Ecologic[®] BARRIER (1.5×10^{10} cfu/day) and a prebiotic or a placebo daily for 6 months. After 3 months patients in the placebo group showed a degraded gut permeability (increase in serum zonuline) which was not observed in the Ecologic[®] BARRIER plus prebiotic group. Another double-blind, placebo-controlled randomized study performed by the University of Medical Sciences in Poznan, Poland studied the effects of Ecologic[®] BARRIER on the metabolic health of obese postmenopausal women¹¹. Eighty-one obese postmenopausal

women were randomly assigned to receive placebo, a low dose of Ecologic[®] BARRIER (LD) (2.5×10^9 cfu/day), or a high dose of Ecologic[®] BARRIER (HD) (1×10^{10} cfu/day) divided in two equal doses for 12 weeks. Both LD and HD Ecologic[®] BARRIER intake resulted in significantly reduced HOMA-IR levels compared to baseline, which was not observed in the placebo group. A dose-response effect was observed as a significant larger reduction of HOMA-IR occurred in the HD group (see figure 4). Moreover, Ecologic[®] BARRIER improved circulating endotoxin (LPS) levels. A second publication of the same clinical trial showed that inflammation makers such as TNF- α , IL-6 and functional and biochemical markers of vascular dysfunction such as blood pressure improved as well¹².

Product - Market Perspective

By lowering insulin resistance and reducing systemic low-grade inflammation, Ecologic[®] BARRIER can positively impact metabolic health, delay disease progression and help to live a healthier & fulfilling life.

Ecologic[®] BARRIER can make a meaningful difference in lives during the different stages of the diabetes journey by supporting efforts in maintaining a balanced diet and lifestyle and ultimately helping keeping blood glucose levels under control.

MARKET OPPORTUNITIES

Two opportunities to bring Ecologic[®] BARRIER to the market, depending on the target groups;

1. Opportunity to position Ecologic[®] BARRIER as part of a healthful living regimen (including a high-nutrition, low-inflammation diet, and regular exercise) for the conscious consumer in a more wellness orientated campaign.
2. Opportunity to position Ecologic[®] BARRIER as a treatment option to prevent or delay disease progression in a more healthcare professional orientated campaign.

CONTACT US

We are deeply committed to your product's success and offer our scientific, commercial and broad knowledge bases to contribute in making this success a reality. We look very much forward to explore this new indication with you. Please reach out to us to discuss any questions and/or ideas that come to mind.

Contact us via sales@winclove.com



CONCERNS & DRIVERS

Diet and weight management as well as keeping blood glycemia under control are the main concerns shared by all groups. Other than controlling blood glucose levels, living a healthy life is the main driver shared by all groups and is discussed positively, with an optimistic tone of voice.

During the different stages of the journey the focus shifts from more wellness orientated topics to more disease orientated topics¹⁵.

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