

Metabolic Health: Reducing insulin resistance and systemic low-grade inflammation

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.

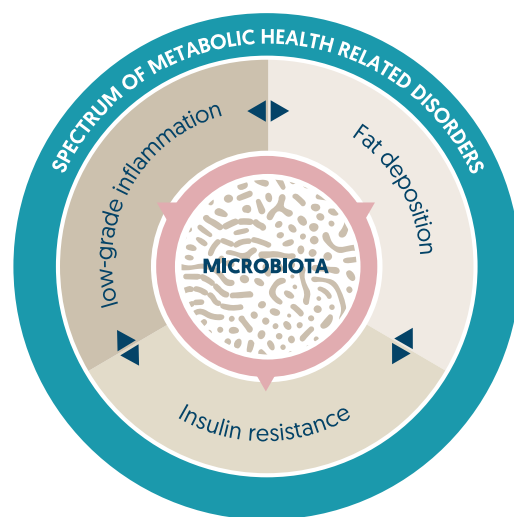


Figure 1: Crosstalk between gut microbiota and host's system in terms of inflammation and metabolism. The gut microbiota, through a range of molecular interactions, contribute to host insulin resistance, systemic low-grade inflammation, and fat deposition and therefore, indirectly participate in the onset and progress of [metabolic] diseases.

Strain selection

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)

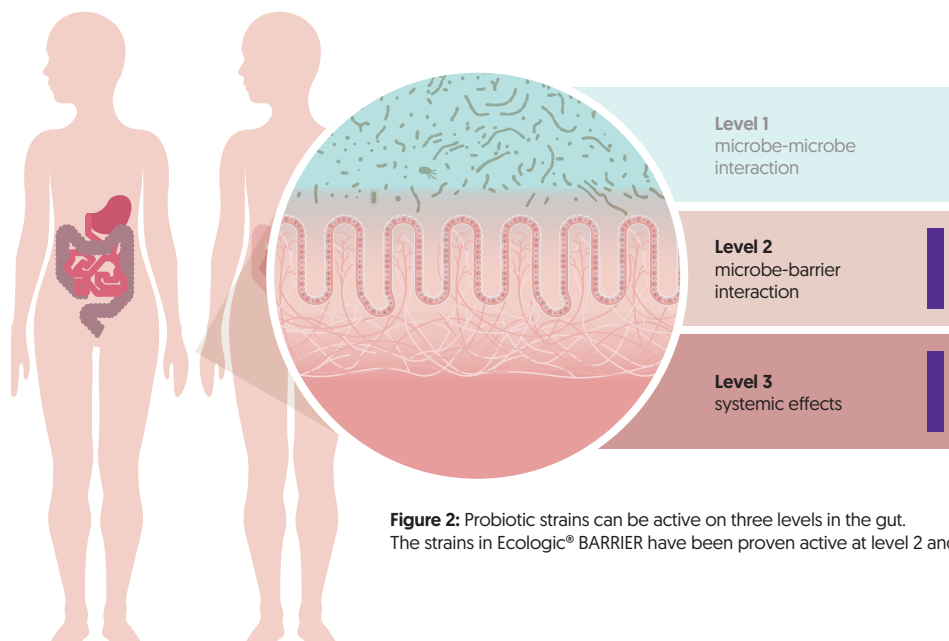


Figure 2: Probiotic strains can be active on three levels in the gut. The strains in Ecologic[®] BARRIER have been proven active at level 2 and 3.

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.

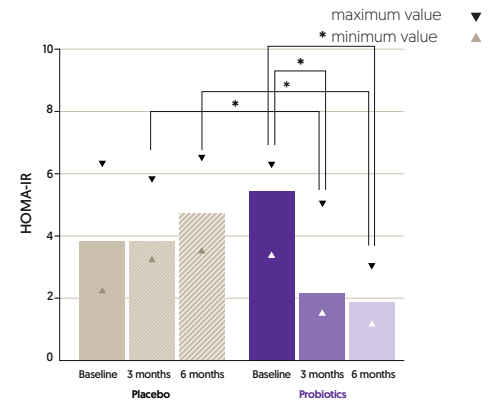


Figure 3: HOMA-IR levels [Median (range)] before and after 3 months and 6 months supplementation with Ecologic® BARRIER. *Significant decrease, $p < 0.05$

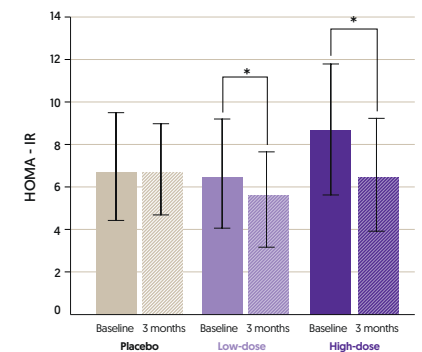






Figure 4: HOMA-IR levels (Mean \pm SD) before and after 12 weeks of low or high dose supplementation with Ecologic® BARRIER. *Significant decrease, $p < 0.05$

Formulation details

Indication	Reducing insulin resistance and systemic low-grade inflammation.			
Colony forming units (cfu)	2.5×10^9 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	 Carefully selected ingredients that contribute to stability (shelf-life), GI-survival and metabolic activity of the probiotic strains.			
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 . Winclove 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.		

References

- Bennett JE, Stevens GA, Mathers CD, et al. NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. *The Lancet* 2018; **392**: 1072–88.
- Ighbariya A, Weiss R. Insulin Resistance, Prediabetes, Metabolic Syndrome: What Should Every Pediatrician Know? *J Clin Res Pediatr Endocrinol* 2018; : 49–57.
- Petersen MC, Shulman GI. Mechanisms of Insulin Action and Insulin Resistance. *Physiol Rev* 2018; **98**: 2133–223.
- Kumari R, Kumar S, Kant R. An update on metabolic syndrome: Metabolic risk markers and adipokines in the development of metabolic syndrome. *Diabetes Metab Syndr Clin Res Rev* 2019; **13**: 2409–17.
- Dabke K, Hendrick G, Devkota S. The gut microbiome and metabolic syndrome. *J Clin Invest* 2019; **129**: 4050–7.
- Parekh PI, Balart LA, Johnson DA. The Influence of the Gut Microbiome on Obesity, Metabolic Syndrome and Gastrointestinal Disease. *Clin Transl Gastroenterol* 2015; **6**: e91.
- Janssen AWF, Kersten S. The role of the gut microbiota in metabolic health. *FASEB J Off Publ Fed Am Soc Exp Biol* 2015; **29**: 3111–23.
- Jayashree B, Bibin YS, Prabhu D, et al. Increased circulatory levels of lipopolysaccharide (LPS) and zonulin signify novel biomarkers of proinflammation in patients with type 2 diabetes. *Mol Cell Biochem* 2014; **388**: 203–10.
- Sabico S, Al-Mashharawi A, Al-Daghri NM, et al. Effects of a multi-strain probiotic supplement for 12 weeks in circulating endotoxin levels and cardiometabolic profiles of medication naïve T2DM patients: a randomized clinical trial. *J Transl Med* 2017; **15**: 249.
- Sabico S, Al-Mashharawi A, Al-Daghri NM, et al. Effects of a 6-month multi-strain probiotics supplementation in endotoxemic, inflammatory and cardiometabolic status of T2DM patients: A randomized, double-blind, placebo-controlled trial. *Clin Nutr* 2018; published online Aug 17. DOI:10.1016/j.clnu.2018.08.009.
- Szulińska M, Loniewski I, van Hemert S, Sobieska M, Bogdański P. Dose-Dependent Effects of Multispecies Probiotic Supplementation on the Lipopolysaccharide (LPS) Level and Cardiometabolic Profile in Obese Postmenopausal Women: A 12-Week Randomized Clinical Trial. *Nutrients* 2018; **10**: 773.
- Szulińska M, Loniewski I, Skrypnik K, et al. Multispecies Probiotic Supplementation Favorably Affects Vascular Function and Reduces Arterial Stiffness in Obese Postmenopausal Women—A 12-Week Placebo-Controlled and Randomized Clinical Study. *Nutrients* 2018; **10**: 1672.
- Horvath A, Leber B, Feldbacher N, et al. Effects of a multispecies synbiotic on glucose metabolism, lipid marker, gut microbiome composition, gut permeability, and quality of life in diabetes: a randomized, double-blind, placebo-controlled pilot study. *Eur J Nutr* 2019; published online Nov 15. DOI:10.1007/s00394-019-02135-w.
- Van Hemert S. Design of a multispecies probiotic product improving the intestinal barrier. San Antonio, USA, 2012.

This information is intended for business professionals only, not for consumers.
The formulations contained herein are concepts, not commercially available and not intended to diagnose, cure or prevent any diseases.