WINCLOVE PROBIOTICS

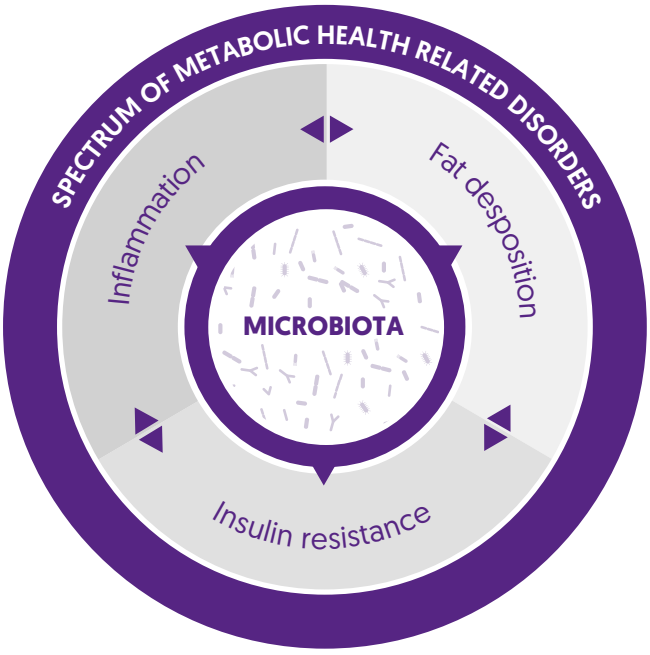
# Probiotics for Metabolic Health

**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.**

## The microbiota and metabolic disorders

Currently there is no strict definition for metabolic health. Often it is referred to as the absence of metabolic disease. Rising levels of blood sugar, triglycerides, low-density lipoprotein (HDL) cholesterol, blood pressure, and waist circumference are generally associated with loss of metabolic health and an increased risk for metabolic diseases ranging from mild insulin resistance all the way to pre-diabetes and type-2 diabetes and cardiovascular disease[2]. Both insulin resistance and systemic low-grade inflammation seem to be at the core of metabolic disorders[3–5].

Insulin resistance is a condition in which cells are less sensitive to the action of insulin. Thus, the pancreas needs to produce even more insulin to lower blood glucose levels. Over time, the pancreas may no longer be able to cope with the high demand, and prediabetes can progress to diabetes[3,4].




Recent research has indicated that the gut microbiota plays an important role in managing metabolic health[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[7–9]. (see figure 1).

## Is there a role for probiotics?

Given the role of the microbiota on metabolic disorders, targeted probiotic formulations may be clinically relevant for optimizing metabolic health, benefiting from the management of insulin resistance and inflammation associated with early- and late-stage metabolic disease, 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 responses[10–14].

## Ecologic BARRIER® for metabolic health

The probiotic formulation Ecologic® BARRIER has been developed by Winclove Probiotics already in 2012. Ecologic® BARRIER is a multispecies probiotic developed to optimize barrier function and to reduce systemic low-grade inflammation[15], making it a suitable choice for research in insulin resistance and metabolic health. The probiotic contains the following bacterial strains: B. bifidum W23, B. lactis W51, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L.salivarius W24, Lc. lactis W19, Lc. Lactis W58 with a viable cell count of $2.5x10^9$ cfu/gram.

**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.**

The probiotic strains were selected based on the following criteria: *in vitro* strengthening of the epithelial barrier, inhibition of mast cell activation, inhibition of pro-inflammatory cytokines and decreasing lipopolysaccharide load. In preclinical research Ecologic® BARRIER has shown to strengthen the epithelial barrier and inhibit pro-inflammatory activation of the immune system[16].

## Clinical evidence

Since 2017, a series of randomized, double-blind, placebo-controlled studies have established the value of Ecologic® BARRIER for the improvement of metabolic health. 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[10,11]. Ninety-six adult T2DM patients (treatment-naïve and without co-morbidities) were randomized to receive 2 grams of Ecologic® BARRIER ($1.0\times10^{10}$ cfu/day) or placebo twice daily 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 2). 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 barrier function, and improved inflammation markers such as CRP (see figure 3), TNF-α, IL-6. The positive effect of Ecologic® BARRIER on the gut barrier function was also observed in a study performed by researchers from the Medical University of Graz, Austria[14]. This randomized, double-blind, placebo-controlled pilot study investigated the effect of Ecologic® BARRIER combined with a prebiotic on glucose metabolism, gut microbiota, and gut permeability in obese patients with T2DM. For this study, twenty-six treatment-experienced obese T2DM patients were randomized to daily receive 6 grams of Ecologic® BARRIER ($1.5\times10^{10}$ cfu/day) plus a prebiotic or a placebo for 6 months. After 3 months patients in the placebo group showed a worsened 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 women[12]. Eighty-one obese postmenopausal women were randomly assigned to receive placebo, a low dose of Ecologic® BARRIER (LD) ($2.5\times10^{9}$ cfu/day), plus a high dose of Ecologic® BARRIER (HD) (1x1010 cfu/day) divided in two equal doses for 12 weeks. Both LD and HD Ecologic® BARRIER intake resulted in significantly reduced HOMA-IR

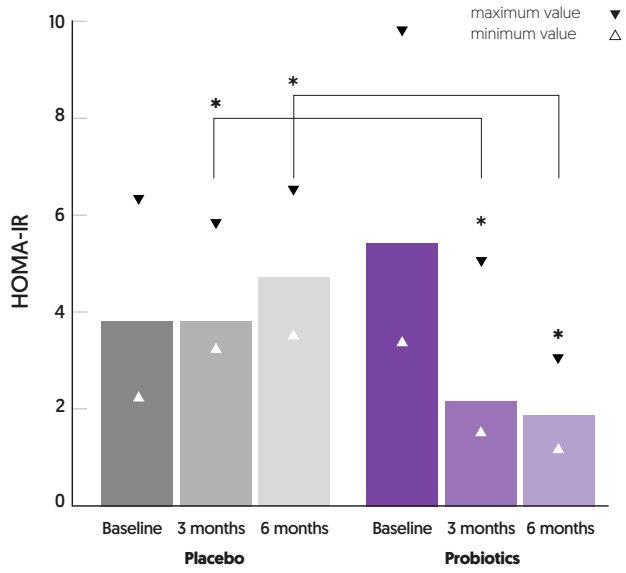



**FIGURE 2: HOMA-IR levels (Median (range)) before and after 3 months and 6 months supplementation with Ecologic® BARRIER.**
* Significant decrease, p<0.05

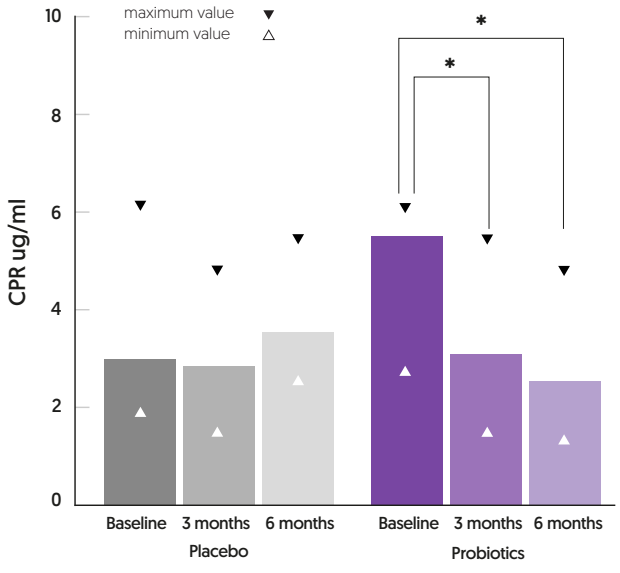



**FIGURE 3: C-reactive protein (CRP) (Median (range)) before and after 3 months and 6 months supplementation with Ecologic® BARRIER.** * Significant decrease, p<0.05

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 (see figure 5).
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 well[13].

## Future clinical applications

Taken together, these studies establish a strong rationale for Ecologic® BARRIER's impact on key metabolic markers, both biochemical and functional. Several other probiotics have been studied for their effect on insulin resistance and type 2 diabetes. Unlike many other formulations, Ecologic® BARRIER has been investigated in several independent studies showing a clear positive effect on HOMA-IR, which was dose-dependent and persisted over a prolonged period of time. This positive effect was also observed on markers of inflammation (e.g. CRP, TNF-α and IL-6), intestinal barrier function (zonulin and LPS) and vascular dysfunction (e.g. blood pressure).
Overall, this indicates that Ecologic® BARRIER can lower both insulin resistance and systemic low-grade inflammation, which are the hallmark symptoms in prediabetes and type 2 diabetes. This may help to either postpone, prevent, or lower the need for medication in prediabetic patients, and might help to lower medication class or dosage in diabetics. In conclusion, these studies show that there is a role to play for Ecologic® BARRIER in improving overall metabolic health, ideally when combined with a comprehensive lifestyle, wellness, and medical plan.

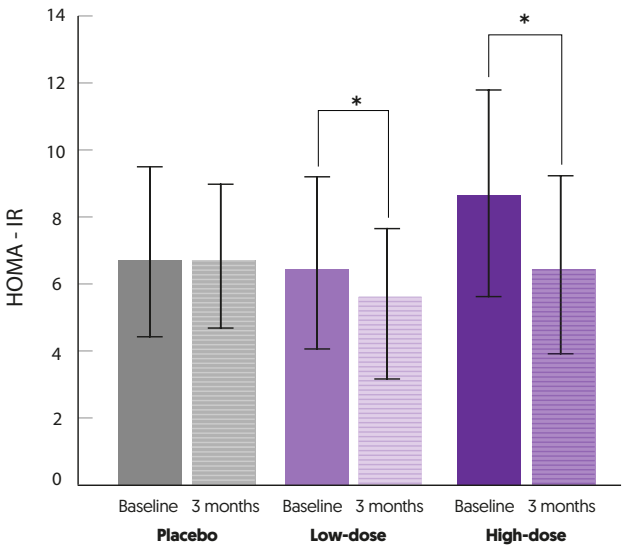



**FIGURE 4: HOMA-IR levels (Mean ± SD) before and after 12 weeks of low or high dose supplementation with Ecologic® BARRIER.**
* Significant decrease, p<0.05

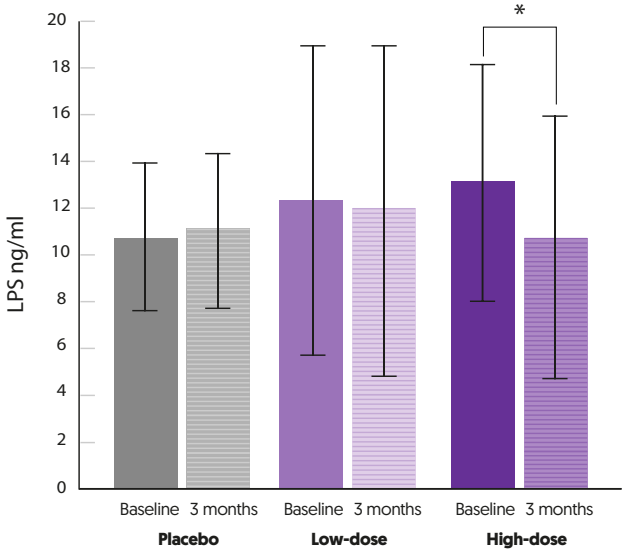



**FIGURE 5: LPS levels (Mean ± SD) before and after 12 weeks of low or high dose supplementation with Ecologic® BARRIER.**
* Significant decrease, p<0.05

**We encourage you to learn more about the Ecologic® BARRIER formulation and its wide-ranging health benefits.
Reach out to the team at Winclove Probiotics.**

# References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