

- Reducing vulnerability to depression

- Improving brain functioning under stress

Mental disorders, depression in particular, are becoming a global epidemic. Worldwide, more than 350 million people of all ages suffer from depression¹. A variety of lifestyle and environmental changes may be responsible for the increased prevalence of mental disorders. One specific area of interest is the relationship between the intestinal microbiota and mental health (figure 1).

The gut microbiota is essential for human health by protecting against pathogens and digesting food². However, the influence of the microbiota extends beyond the gastrointestinal (GI) tract, playing an important role in the bidirectional communication between the GI tract and the central nervous system (CNS). This connection is also called the gut-brain axis³. The high co-morbidity between psychiatric disorders with GI conditions such as irritable bowel syndrome and inflammatory

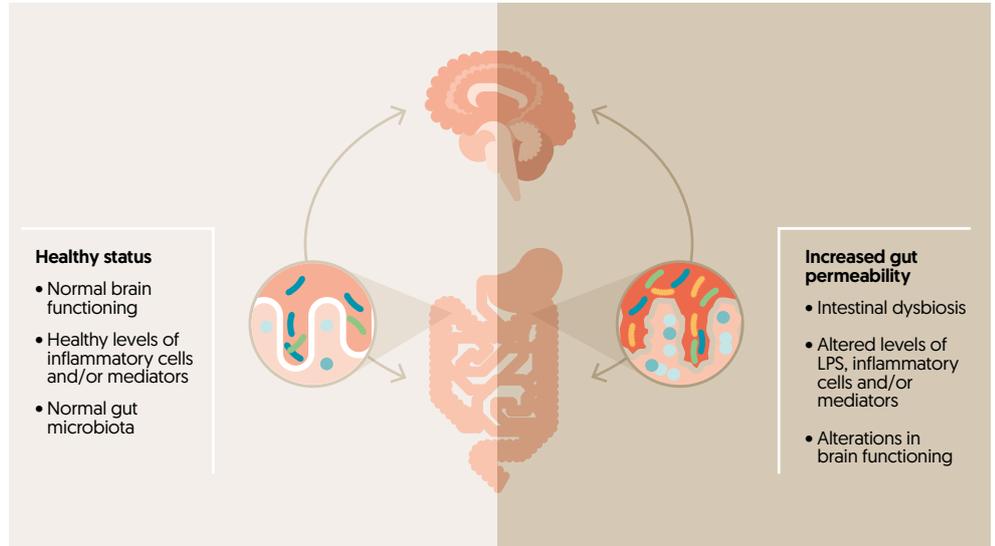


Figure 1: The microbiota-gut-brain axis.

bowel disease supports the evidence of the existence of this axis^{4,5,6}. The intestinal barrier appears to play an important role in the communication between the gut and the brain. An impaired barrier function negatively influences hormones, immune cells, and bacterial metabolites that affect the gut-brain axis⁷. Re-

search has shown that probiotics can positively influence the gut microbiota and intestinal barrier function. This raises the question whether probiotics can influence brain functioning as well. Recent studies have demonstrated the ability of probiotics to influence the gut-brain axis and consequently brain functioning⁸.

Strain selection

Ecologic[®] BARRIER is a multispecies probiotic formulation consisting of 9 specially selected probiotic strains. Probiotic strains can exert health effects at different levels in the gut (see figure 2). The probiotic strains of Ecologic[®] BARRIER have been selected for their capacity to strengthen the intestinal barrier function (level 2) and reduce low grade inflammation⁹ (level 3).

The 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).

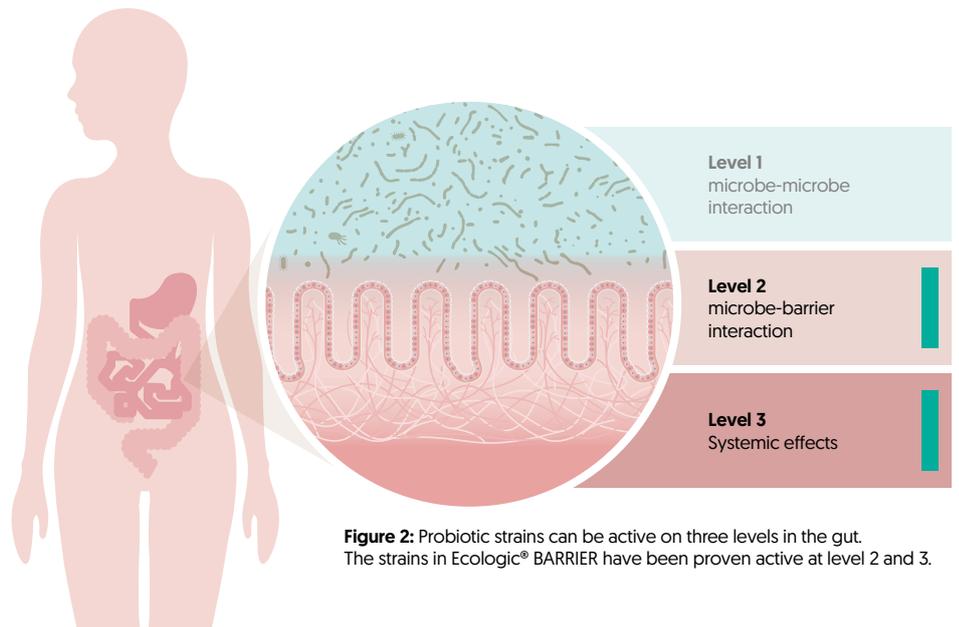


Figure 2: Probiotic strains can be active on three levels in the gut. The strains in Ecologic[®] BARRIER have been proven active at level 2 and 3.

Clinical evidence

The effect of Ecologic® BARRIER on vulnerability for depression was tested in a triple-blind, placebo-controlled, randomized, human trial, performed by Leiden University, The Netherlands. The researchers investigated the effect of Ecologic® BARRIER on cognitive reactivity to sad mood using the Leiden Index of depression sensitivity scale (LEIDS-r). Forty healthy participants received 2 grams Ecologic® BARRIER or placebo for 4 weeks. The results showed that **Ecologic® BARRIER significantly reduced overall cognitive reactivity to sad mood**¹⁰ (see figure 3).

In addition, Researchers from University of Technology Sydney, Australia, conducted a randomised, triple-blind, placebo-controlled trial to determine the effect of Ecologic® BARRIER in patients with Major Depressive Disorder (MDD). Seventy-one participants were randomised to receive 4 grams of Ecologic BARRIER or placebo for 8 weeks. The symptoms severity improved in both groups. **Ecologic® BARRIER significantly reduced cognitive reactivity, particularly in mild to moderate depressed individuals.**¹¹

Multiple, placebo-controlled, rat studies were performed with Ecologic® BARRIER by Aarhus University, Denmark, using wild type rats and a genetic rat model for depression.¹²⁻¹⁵ In the genetic model, Ecologic® BARRIER reduced risk taking behavior and prevented the exacerbation of depressive-like behavior normally induced by a high-fat diet. In the wild-type rats, Ecologic® BARRIER **significantly reduced depressive-like behavior**, measured by a forced swim test (see figure 4), and differences in gut microbiota between responder and non-responder animals were identified. Ecologic® BARRIER influenced gene-expression in the hippocampus and altered immunological and metabolic markers, explaining the positive outcomes.

Moreover, researchers from Radboud University Nijmegen and Donders Institute for Brain Cognition and Behavior, The Netherlands, performed a double-blind, placebo-controlled, randomized, human trial with Ecologic® BARRIER. The researchers investigated the effect on neurocognition, using functional magnetic resonance imaging (fMRI), and stress-induced working memory performance measured by a Digit Span Backwards test. 58 participants received 2 grams of Ecologic® BARRIER or placebo for 4 weeks. **Ecologic® BARRIER significantly increased working memory performance**¹⁶ (see figure 5). Ecologic® BARRIER buffered against the damaging effects of stress on brain functioning.

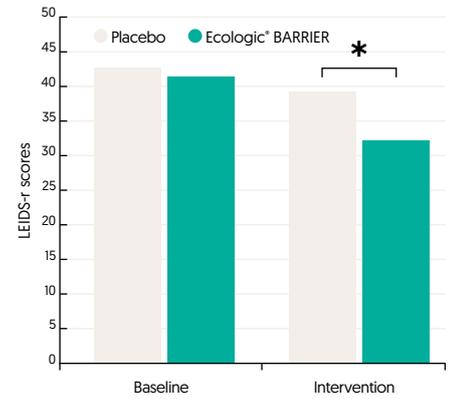


Figure 3: LEIDS-r scores before and after 4 weeks of supplementation with Ecologic® BARRIER. *Significant decrease, $p < 0.001$.

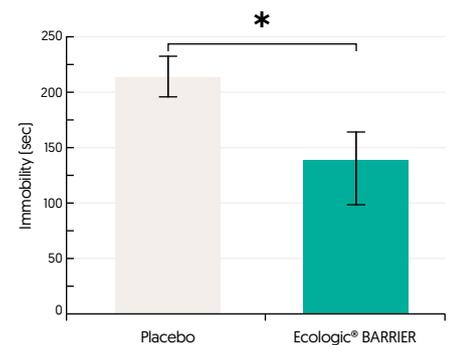


Figure 4: Seconds of immobility during the Forced Swim Test. *Significant decrease, $p < 0.001$.

Formulation details

Indication	Reducing vulnerability to depression and improving brain functioning under stress.			
Colony forming units (CFU)	2,5 x 10 ⁹ CFU/gram.			
Recommended daily dosage	2 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.		

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