

Can depression be treated with probiotics?

Depression is a growing public health concern. The World Health Organization currently estimates that depression affects about 322 million people worldwide, which is a proportion of 4.4% of the total population. [1] Depression can be present in many forms; mild or severe and long lasting or recurrent. It can substantially impair an individual's ability to function at work or school or cope with daily life.

Microbiome-gut-brain-axis

In recent years, the bidirectional link between gut and brain has gained a lot of attention. There is growing evidence that the gut can affect brain function and behavior. For example, there is a clear association between imbalances in the gut microbiota and stress-related disorders such as anxiety and depression. [2] The exact mechanisms are still unknown, but they include neural, endocrine, immune, and metabolic pathways. The vagus nerve is a fundamental neural route of communication between gut and brain. [3]

Researchers have found that the microbial composition in people with depression differs from that of non-depressed people. Depressed people tend to have less Bifidobacteria and Lactobacilli and more Bacteroidetes, Proteobacteria and Actinobacteria. [2] This suggests that modulating the gut microbiome could have an effect on depressive symptoms.

Is there a role for probiotics?

Pre- and probiotics can have a major influence on the bidirectional communication between the gut and the brain. The anti-inflammatory and immune-regulatory properties and the ability of many bacteria to synthesize and release neurotransmitters may help in tackling the underlying causes of depression. [3,4] Initial evidence from clinical research supports the potential of probiotics as a supplementary

treatment strategy for brain-related problems such as; autism, ADHD, depression, Alzheimer's disease and Parkinson's disease. [5]

Ecologic® BARRIER

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 low-grade inflammation. 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, in a carrier matrix of maize starch and maltodextrins with a viable cell count of 2.5×10^9 cfu/gram. 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 can inhibit pro-inflammatory activation of the immune system. [6]

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 of Ecologic® BARRIER or placebo for 4 weeks. The results showed that Ecologic® BARRIER significantly reduced overall cognitive reactivity to sad mood [7], [see figure 1].

Figure 1: LEIDS-r scores before and after 4 weeks of supplementation with Ecologic® BARRIER.
*Significant decrease, $p < 0.001$.

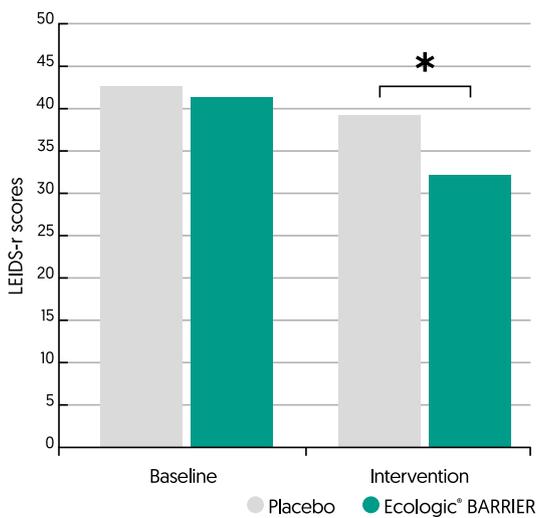
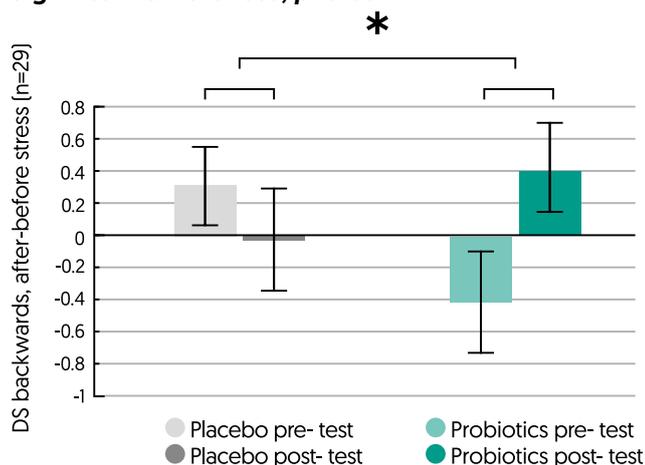


Figure 2: Stress-induced changes in working memory. Calculated as the difference of DS backwards scores after stress minus scores before stress.
*Significant differences, $p < 0.05$.



The effect of Ecologic® BARRIER was also tested in patients with Major Depressive Disorder (MDD). Researchers from University of Technology Sydney, Australia, conducted a randomized, triple-blind, placebo-controlled

trial. Seventy-one MDD patients were randomized 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 to sad mood, particularly in mild to moderate depressed individuals. [8]

Ecologic® BARRIER also showed to buffer against the damaging effects of stress on brain functioning. 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 [9], [see figure 2].

Preclinical evidence

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. [10-13] 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 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.

Clinical practice

Previous studies assessing probiotic effects in participants with at least some degree of depression have reported positive effects on depression scales. [14,15] People suffering from depression are known to exhibit a different gut-microbiome composition relative to healthy individuals. [16,17] The findings of stress-

dependent beneficial effects of Ecologic® BARRIER on cognition in people prone to depression can be of clinical importance for stress-related psychiatric and gastro-intestinal disorders. Ecologic® BARRIER could be a possible adjuvant therapy for patients suffering from depression or gastro-intestinal disorders which are [partly] caused by acute or chronic stress.

In clinical practice, Ecologic® BARRIER may be a useful adjunct to potentiate the effects of therapies, such as cognitive behavioral therapy, which involves changing cognitive patterns. If health care professionals are interested to explore the potential of Ecologic® BARRIER in depressed patients, the mild-to-moderate group is where the best response is expected.

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