

Defending the barrier

Effects of probiotics on endogenous defence mechanisms
Thesis of Femke Lutgendorff, 2009

Chapter 9. Role of mast cells and PPAR-γ: Effects of probiotics on chronic stress-induced intestinal permeability in rats.

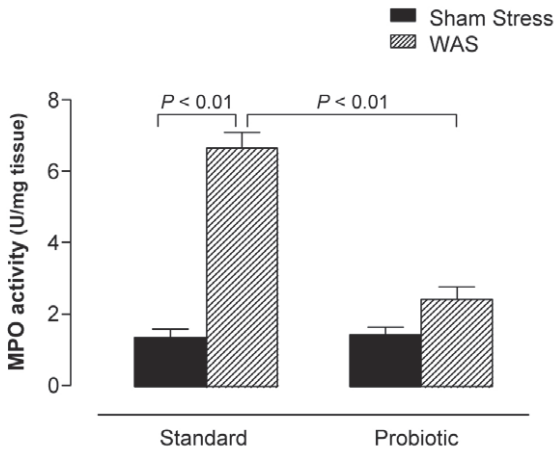
Probiotics; the role of mast cells and PPAR-γ

What is the mechanistic effect of Ecologic® 825? Can this explain an extension of remission time in IBD patients?

Stress is a common experience in daily life. Chronic stress can lead to disruption of the barrier in the gut and to mucosal inflammation. In this way stress can trigger several gastrointestinal disorders. In IBD patients, stress can have an effect on inflammatory activity. It can trigger the disease and increase the number of relapsed in ulcerative colitis patients¹⁻².

In this study rats were given Ecologic® 825 seven days before being stressed. The result shows that pre-treatment with Ecologic® 825 helps to maintain the barrier function and reduced bacterial translocation, compared to placebo.

Short summary of the study results:



Chronic stress, as is induced by water avoidance stress (WAS), causes an enhanced mucosal inflammatory response, measured by MPO activity. Mucosal cells that were pretreated with Ecologic® 825 did not show this inflammatory activity in response to stress, as is shown in the figure on the left.

As a response to chronic stress, the body initiates a defense mechanism to overcome stressful stimuli. Via mast cells the expression PPARγ is upregulated. Activation of the PPARγ pathway has been shown to down-regulate colonic inflammation³⁻⁴.

For this study wild type rats and mast cell deficient rats were used. In the mast cell deficient rats the PPARγ pathway was blocked. Intestinal inflammation was induced by chronic stress. Seven days prior to stress the probiotic treatment was started in half of the rats

Ecologic® 825 treatment prevented stress-induced effects in wild type rats and not in mast cell deficient rats, from which we can conclude that the protective effects of Ecologic® 825 on gut barrier function and mucosal inflammation are dependent on mast cells.

The mast cells contribute, via the PPARγ pathway, to the beneficial effects of Ecologic® 825 treatment of intestinal disorders.

From this study it can be concluded that pretreatment with Ecologic® 825 is effective in protecting the gut against stress-induced intestinal barrier dysfunction and mucosal inflammation. This mechanism could explain why Ecologic 825® can support in the extension of the remission time of IBD patients.

References:

- 1 Duffy, L. C. *et al.* Relevance of major stress events as an indicator of disease activity prevalence in inflammatory bowel disease. *Behav Med* **17**, 101-110 (1991).
- 2 Levenstein, S. *et al.* Stress and exacerbation in ulcerative colitis: a prospective study of patients enrolled in remission. *Am J Gastroenterol* **95**, 1213-1220, doi:S0002927000008042 [pii] 10.1111/j.1572-0241.2000.02012.x (2000).
- 3 Su, C. G. *et al.* A novel therapy for colitis utilizing PPAR-gamma ligands to inhibit the epithelial inflammatory response. *J Clin Invest* **104**, 383-389, doi:10.1172/JCI7145 (1999).
- 4 Desreumaux, P. *et al.* Attenuation of colon inflammation through activators of the retinoid X receptor (RXR)/peroxisome proliferator-activated receptor gamma (PPARgamma) heterodimer. A basis for new therapeutic strategies. *J Exp Med* **193**, 827-838 (2001).