

# Patented Fish collagen peptides for Intestinal Inflammation

Inflammatory bowel diseases (IBD) comprising Crohn's disease and ulcerative colitis, are chronic inflammatory diseases affecting the gastrointestinal tract. They are associated, among others, with weight loss, abdominal pain, mucosa ulceration, dysbiosis, diarrhea and bloody stools and affect the quality of life.

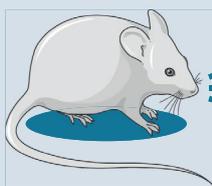
The emergence of IBD involves a complex interaction between genetics, environmental or microbial factors, and the immune responses. It is now established that diet is engaged in the increase of the disease incidence as it can influence intestinal inflammation.

**Naticol<sup>®</sup> Gut, patented fish collagen peptides developed by WEISHARDT, acts as a protective agent against colonic inflammation appearing as a new functional food and an innovative and complementary approach in gut health\*.**

*Publication: M. Rahabi et al. (2022) Bioactive fish collagen peptides weaken intestinal inflammation by orienting colonic macrophages phenotype through mannose receptor activation. European Journal of Nutrition*



## In vivo on mice colitis model METHODS



Control (only water)

DSS

DSS + Naticol<sup>®</sup> Gut

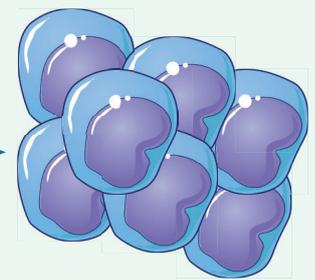
### Experimental model

In this study, C57BL/6 mice were orally administered with a chemical colitogen, Dextran Sodium Sulfate (DSS), for colitis induction. This model is widely used for IBD simulation and allows a great overview of the immune system and microbiota fluctuations. We compared different parameters for the following groups: DSS, Naticol<sup>®</sup> Gut, DSS and Naticol<sup>®</sup> Gut or only water. We characterized the inflammatory profile of an important immune population: macrophages as well as we investigated the role of one of the macrophage receptors known to recognize collagen peptides: mannose receptor. Furthermore, we assessed microbiota composition depending on the addition of DSS and/or Naticol<sup>®</sup> Gut.

## Ex vivo on human blood monocytes METHOD



Human blood

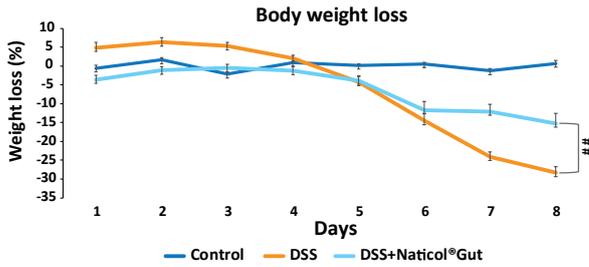


Blood cells

We isolated the monocytes from blood of subjects suffering from inflammatory bowel diseases. Inflammatory profiles of the isolated monocytes were evaluated after stimulation with Naticol<sup>®</sup> Gut.



## › General state and colonic inflammation



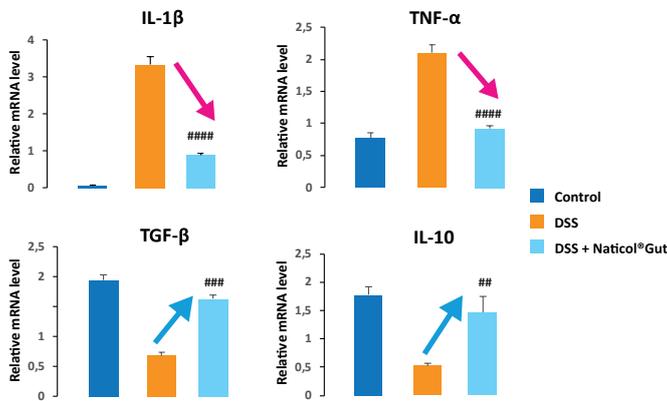
**Figure 1.A: Body weight evolution**  
##p ≤ 0.01, compared to DSS-exposed mice



**Figure 1.B: Histological sections of the colon**

Mice treated with DSS 1,5% lost more weight than the group in which DSS was co-administered with Naticol<sup>®</sup> Gut (Fig 1.A). Naticol<sup>®</sup> Gut-treated DSS mice also displayed a lower degree of colonic inflammation compared to DSS-treated mice (Fig 1.B).

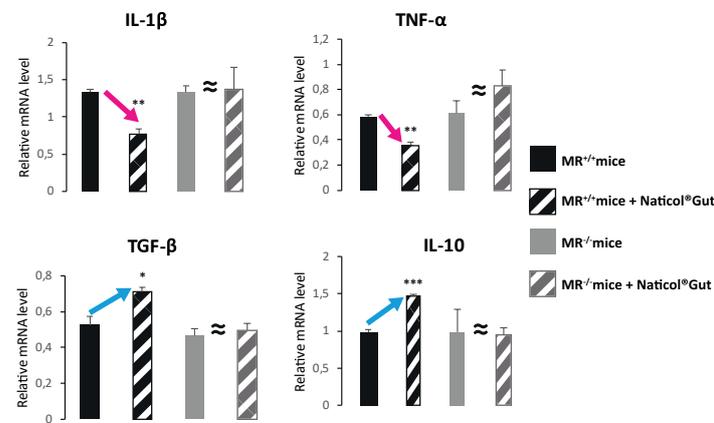
## › Cytokine expression by macrophages



**Figure 2: Cytokine expression by macrophages**  
##p ≤ 0.01, ###p ≤ 0.005, ####p ≤ 0.001, DSS-exposed mice compared to DSS-exposed mice treated with Naticol<sup>®</sup> Gut.

Naticol<sup>®</sup> Gut allowed a decrease of the pro-inflammatory cytokines IL-1β and TNF-α that are highly incriminated in colonic inflammation. Moreover, anti-inflammatory cytokines that attenuate inflammation such as TGF-β and IL-10 are significantly increased by Naticol<sup>®</sup> Gut intake.

## › Role of the mannose receptor of macrophages in the recognition of Naticol<sup>®</sup> Gut

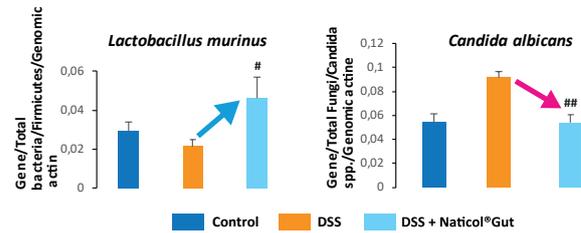


**Figure 3: Cytokine expression of macrophages from normal mice (MR<sup>+/+</sup>) and from mice deficient for the mannose receptor (MR<sup>-/-</sup>)**  
\*p ≤ 0.05, \*\*p ≤ 0.01, \*\*\*p ≤ 0.005, compared to the respective macrophages

Naticol<sup>®</sup> Gut is recognized by the mannose receptor (MR) of macrophages. Indeed, its anti-inflammatory activity on macrophages depends on the MR.

## › Gut microbiota composition

**Figure 4: microbiota fluctuation**

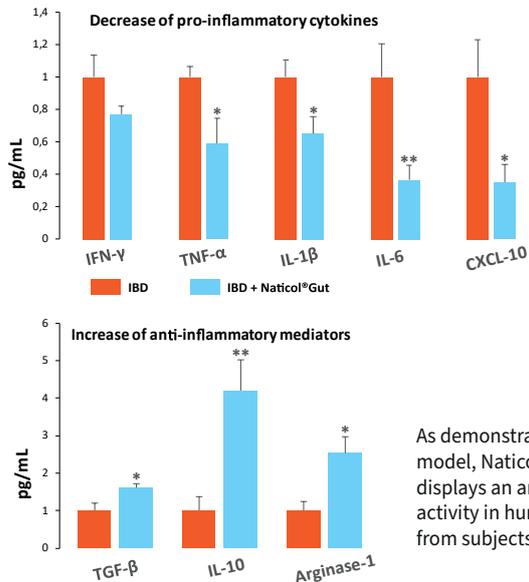


#p ≤ 0.05, ##p ≤ 0.01, DSS-exposed mice compared to DSS-exposed mice treated with Naticol<sup>®</sup> Gut.

Naticol<sup>®</sup> Gut intake in DSS-treated mice increased the proportion of protective bacteria such as *Lactobacillus* in the colon and reduced pathobiontic bacteria and fungi colonization (*Candida albicans*).

# EX VIVO RESULTS

## › Cytokine expression by human blood monocytes



**Figure 5: Mediator expression by human blood monocytes**  
\*p ≤ 0.05, \*\*p ≤ 0.01 compared to the untreated condition.

As demonstrated in the mice model, Naticol<sup>®</sup> Gut also displays an anti-inflammatory activity in human monocytes from subjects with IBD.

**› Conclusion:** Naticol<sup>®</sup> Gut is a **protective agent** against colitis that directly acts on macrophages through the mannose receptor. It orients the **immune response** towards an anti-inflammatory activity. Through this, it indirectly contributes to maintain a healthy **microbiota**. The results with human blood support the use of Naticol<sup>®</sup> Gut as a new functional food and an innovative and complementary approach in **gut health**.