ROQUETTE

WWW.NUTRIOSE.COM

Effects of a soluble fiber, with excellent tolerance, NUTRIOSE® 06, on the gut ecosystem : a review

LEFRANC-MILLOT C[1], WILS D[1], NEUT C[2], SANIEZ-DEGRAVE MH[1] • [1] ROQUETTE Frères, F-62080 Lestrem • [2] Faculté des Sciences pharmaceutiques et biologiques, F-59008 Lille

INTRODUCTION

Soluble dietary fibers reach almost unchanged the colon where they can induce "prebiotic effects", characterized by: (1) an increase in "beneficial bacteria" and/or a decrease in "harmful bacteria", (2) a decrease in intestinal pH, (3) production of short chain fatty acids (SCFAs) and (4) changes in bacterial enzymes concentrations (Woods and Gorbach, 2001).

NUTRIOSE® 06, a resistant dextrin, is mostly resistant to digestion in the small intestine and largely fermented in the colon: it is a soluble dietary fiber (Roberfroid 2005). It also shows (5) an outstanding digestive tolerance, allowing its consumption in amounts fully compatible with beneficial changes in the gut ecosystem, described hereafter.

RESULTS

1. NUTRIOSE® 06 induced an increase of the colonic saccharolytic flora and a decrease in potentially harmful *Clostridium perfringens* in human faeces (Pasman *et al.*, 2006)

These effects were noticed in 2 different clinical studies. In study 1, 48 volunteers were randomly included and distributed into 4 parallel groups. During the 14-day study, the first group consumed 20 g/day glucose (placebo) and the 3 others respectively 10, 15 or 20 g/day NUTRIOSE® 06. At the end of the experiment, an increase in the saccharolytic flora was observed with 10 g/d NUTRIOSE® 06 consumption ($p < 0.05$; ***figure 1***). A decrease of the genus *Clostridium perfringens* was seen following 15 g/d NUTRIOSE® 06 consumption ($p < 0.05$; ***figure 2***). In study 2 (Pasman *et al.*, 2006), 43 volunteers randomly assigned to 3 parallel groups (Placebo, 30 and 45 g/day NUTRIOSE® 06) completed the clinical trial. A significant increase in the mean *Lactobacilli* numbers was observed after a 35-day consumption of 45 g/d NUTRIOSE® 06 ($p < 0.05$; ***figure 3***). During the study, a decrease in the genus *Clostridium perfringens* was observed again, confirming the beneficial effect previously described on potentially harmful bacteria.

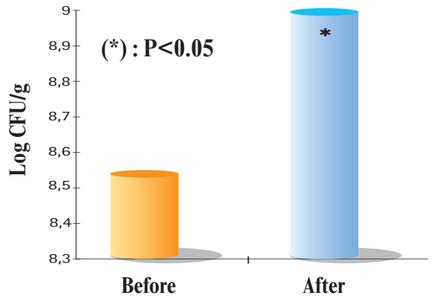

Figure 1: Saccharolytic flora (Bacteroides) in human feces before and after a 14-day administration of 10 g/d NUTRIOSE® 06

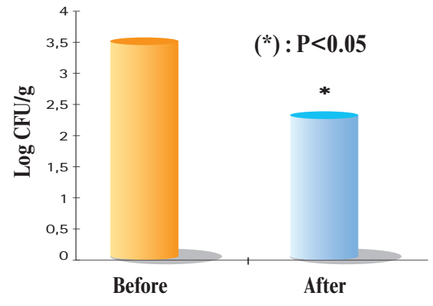

Figure 2 : Clostridium perfringens number in human feces before and after a 14-day administration of 15 g/d NUTRIOSE® 06

2. NUTRIOSE® 06 induced a decrease in the fecal pH of human volunteers

In the two previously described trials, pH measurements were performed at the end of the administration period. We noticed a significant decrease of the fecal pH following either the short or the long period of NUTRIOSE® 06 consumption. In study 1, fecal pH was 6.67 before the intervention phase and 5.99 after a 14-day administration period of 20 g/d ($p < 0.05$; ***figure 4***). In the long-term study (study 2, Pasman *et al.*, 2006), fecal pH decreased at a nearly dose-dependent rate with treatment duration in both treated groups (30 and 45 g/d) unlike what happened in the placebo one, with a significant difference for the pH at day 21 of the 45 g/d NUTRIOSE® 06 group compared to the placebo group ($p < 0.05$).

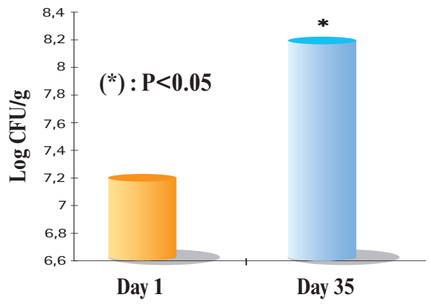

Figure 3 : Mean Lactobacilli number in human feces after a 35-day administration of 45 g/d NUTRIOSE® 06

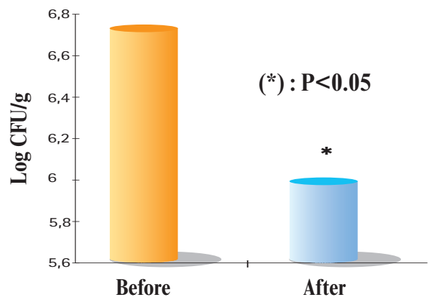

Figure 4 : pH of human feces before and after a 14-day administration of 20 g/d NUTRIOSE® 06

3. NUTRIOSE® 06 increased production of short chain fatty acids (SCFAs) in rats

Animal models are described as the only way to study production of colonic SCFAs because they are likely absorbed by the gut mucosa essentially to produce energy after metabolism (Roberfroid and Slavin, 2001). NUTRIOSE® 06 was administered during 36 days to Sprague-Dawley laboratory rats. The total amount of caecal SCFAs (acetic, propionic and butyric acids) after 14 days was 36.04, 38.63, 51.10 and 62.39 mg/caecum for respectively the control group, the rats treated with 2.5 %, with 5 % and with 10 % NUTRIOSE® 06 in feed ***(figure 5)***. In the group receiving 10 % NUTRIOSE®, the 108 % increase observed for the propionic acid was significant ($p < 0.005$).

4. NUTRIOSE® 06 induced changes in faecal bacterial enzyme concentration

In study 1, administering NUTRIOSE® 06 to human volunteers promoted changes in faecal bacterial enzyme concentration. Specifically, faecal concentrations of β-glucosidase, an inducible enzyme, were respectively 12.9 for the control group, 24.4, 22.6 and 31.4 UI/min/g for the 10 g/d, 15 g/d and 20 g/d groups after 15 days administration. The concentration was significantly higher for the 10 and 15 g/d groups as compared with the placebo one ($p < 0.05$; ***figure 6***). In a previous short-term tolerance study in 20 humans (Van den Heuvel *et al.*, 2004), where NUTRIOSE® was administered at daily levels of 10 and 15 g up to 60 and 80 g, a similar significant increase of β-glucosidase faecal concentration ($p < 0.05$) had been already observed in all groups (10 to 80 g/d NUTRIOSE® 06) as compared with the Placebo, even at the lowest dose of 10 g/d. This clearly indicates that significant changes of the gut microflora occur early after the beginning of NUTRIOSE® 06 consumption. In study 2 (Pasman *et al.*, 2006), a significant increase of β-glucosidase production ($p < 0.05$) was observed at the first observation (21 days) and still maintained after a 35-day consumption of 30 and 45 g/d ($p < 0.05$), showing a modification and a stabilization of the colonic flora.

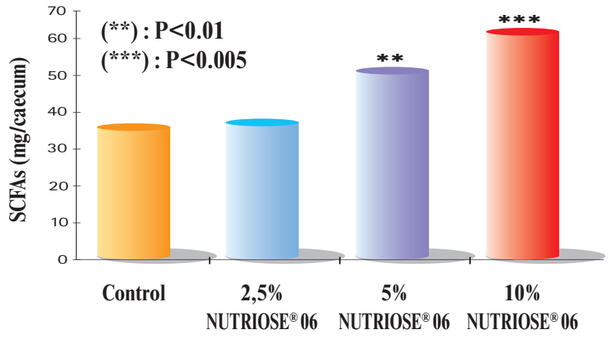

Figure 5 : Total amount of SCFAs in rat's caeca after a 14-day administration of NUTRIOSE® 06 in feed

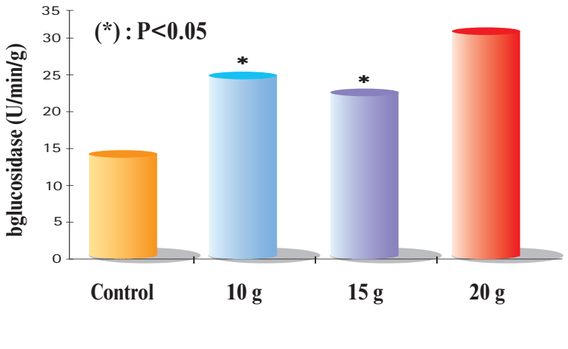

Figure 6 : Fecal β-glucosidase production after a 14-day administration of NUTRIOSE® 06

5. NUTRIOSE® 06 exhibits an outstanding digestive tolerance

In study 1, the digestive tolerance of NUTRIOSE® 06 was very good: only flatulence occurred more frequently but at a mild intensity in the NUTRIOSE® 06 groups compared to the placebo one. Abdominal pain, at a mild intensity, was more important in the placebo group, and bloating, with a similar incidence in all groups, remained unmodified by the product consumption. In the short-term human tolerance study (Van den Heuvel *et al.*, 2004), a similar result was observed: more frequently occurring flatulence in 30, 60 and 80 g/d NUTRIOSE® 06 groups ($p < 0.05$), bloating occurring more often during the last day with 80 g/d NUTRIOSE® 06 ($p < 0.05$), with none of the doses resulting in diarrhoea, even at more than 80 g/d. Adaptation was observed with a decrease in the symptom intensity after 20 days. In the long term tolerance study (study 2, Pasman *et al.*, 2006), both dosages of 30 and 45 g/d were well tolerated, with no diarrhoea occurring ***(figure 7)***.

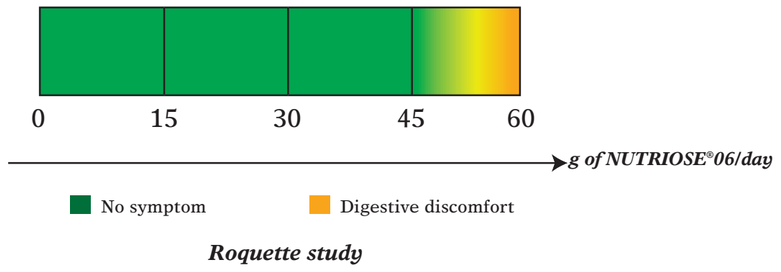

Figure 7 : Schematic representation of the tolerance scale of NUTRIOSE®

DISCUSSION

Results presented above show the specific fermentation pattern of NUTRIOSE® 06 in humans. It is related to the molecular structure of the dietary fiber and to its specific physico-chemical characteristics. As a glucose polymer, NUTRIOSE® 06 likely stimulates the proliferation of colonic bacteria able to adapt to non-digestible carbohydrates (Marteau *et al.*, 1990), among which the genus *Bacteroides*. This is a well-known producer of glycosidases, which is seen through the production of β-glucosidase in the above described experiments. Firstly, this enzyme (Marteau *et al.*, 1990) clearly indicates that oral consumption of as little as 10 g/d NUTRIOSE® 06 induces deep changes in the metabolic activity of the colonic flora. Secondly, this enzyme can act in the gut on residual polysaccharides coming from diet and remaining undigested, as for example vegetables residues. As a result, end products as minerals and other micronutrients can become available for the colon and the body (Vermorel *et al.*, 2004). An increase in *Lactobacilli* was also observed. These bacteria are classified as desirable colonic bacteria. They contribute to maintaining a healthy colon. SCFAs production is difficult to monitor in human clinical studies mainly for technical reasons. Animal models are usually used in this context for studying SCFAs production following dietary fiber consumption. In all animal studies conducted, an increase in SCFAs production was observed. SCFAs and gases were indicators of the fermentation processes occurring after NUTRIOSE® 06 consumption. As a result of these colonic fermentations, a pH decrease of the colonic content is visible through the fall in the faecal pH. This point is very interesting in terms of colonic health as a weak decrease in gut pH, coupled with propionic acid production (powerfully inhibiting enterobacteria in acidic conditions) is associated with a decrease in potentially harmful gram-negative bacteria. This is the case with a 15 g/d NUTRIOSE® 06 consumption as displayed by a decrease of the species *Clostridium perfringens*.

CONCLUSION

The results presented show that the consumption of 10 g and above per day of NUTRIOSE® 06 produce positive observable changes in the gut microflora. Bacteria that may ferment NUTRIOSE® 06 are likely bacteria from the glucidolytic flora. These bacteria are thus increasing in number to the detriment of proteolytic species such as *Clostridium perfringens* because of the promotion of acidic conditions in the gut. The enzymes produced by the saccharolytic flora are enzymes that can play an ultimate role in the production of end products of interest in terms of colonic health, like vitamins, minerals, and antioxidants. Moreover, NUTRIOSE® 06 is outstandingly well-tolerated, even at high dosages. According to all these observations, and based on the definition given above, the changes in the colonic environment suggest that NUTRIOSE® 06 can be considered as a prebiotic.