Monograph
The Health benefits of NUTRIOSE® soluble fiber

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Nutrition & Health R&D

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NUTRIOSE® soluble fiber

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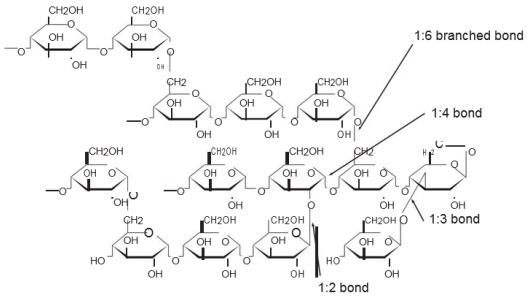
THE HEALTH BENEFITS OF NUTRIOSE® SOLUBLE FIBER

NUTRIOSE® SOLUBLE FIBER

► The production process

NUTRIOSE® can be made from wheat starch (NUTRIOSE® FB range) or maize starch (NUTRIOSE® FM range) or pea starch (NUTRIOSE® pea range), using a highly controlled process of heating of the starch followed by a fractionation step. During the heating step, new glycosidic linkages are formed that converts the starch to fiber. In addition to the typical starch (1,4) and (1,6) digestible linkages, non-digestible glycosidic bonds such as (1,2) or (1,3) are formed, which cannot be cleaved by enzymes in the digestive tract (Roturier *et al.*, 2003; Roturier *et al.* 2006); *Figure 1* and *Table 1*.



Type of glycosidic linkages	NUTRIOSE®	Starch
(1,4)	41	95
(1,6)	32	5
(1,2)	13	0
(1,3)	14	0

Figure 1 and Table 1: Structural formula of NUTRIOSE® and repartition of the glycosidic linkages

The fractionation step decreases the polydispersity of molecular weight distribution, and ensures a high fiber content and expected molecular weight distribution, which in turn, relates to the desired biological and rheological behaviour of the product. Further purification and spray drying steps yield a content of mono- and disaccharides below 0.5% on dry substance with a fiber ratio of 85% for NUTRIOSE® 06 according to the AOAC method 2001-03 (Gordon *et al.*, 2002).

Therefore, NUTRIOSE® is a glucose polymer of natural origin, totally soluble in cold water without inducing either viscosity or taste alteration. NUTRIOSE® 06 may thus be considered a sugar-free soluble fiber.

► Classification of dietary fibers based on physiochemical characteristics

NUTRIOSE® is a soluble, non-viscous, fermentable fiber according to the following *Figure 2* (Lefranc-Millot *et al.*, 2011a).

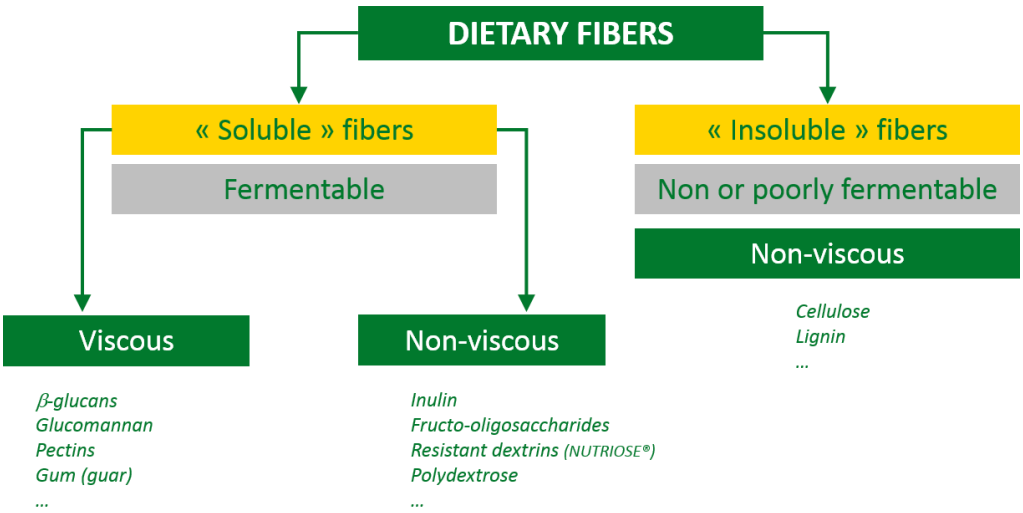


Figure 2: Classification of dietary fibers

► The metabolic fate of NUTRIOSE®

Unlike standard starch, NUTRIOSE® is partially hydrolysed in the upper part of the digestive tract. Only 15% is enzymatically digested in the small intestine, while the rest passes to the colon, where 75% of the initial amount is slowly and progressively fermented in the large intestine and 10% is excreted (van den Heuvel *et al.*, 2004 and 2005); *Figure 3*.

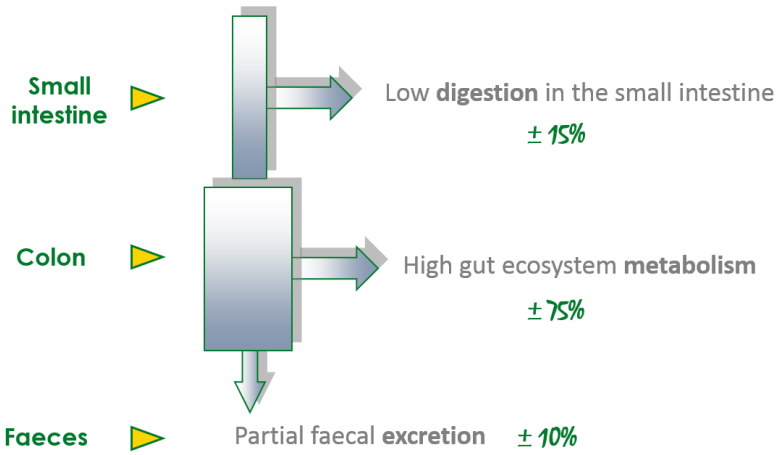


Figure 3: NUTRIOSE® digestion pattern

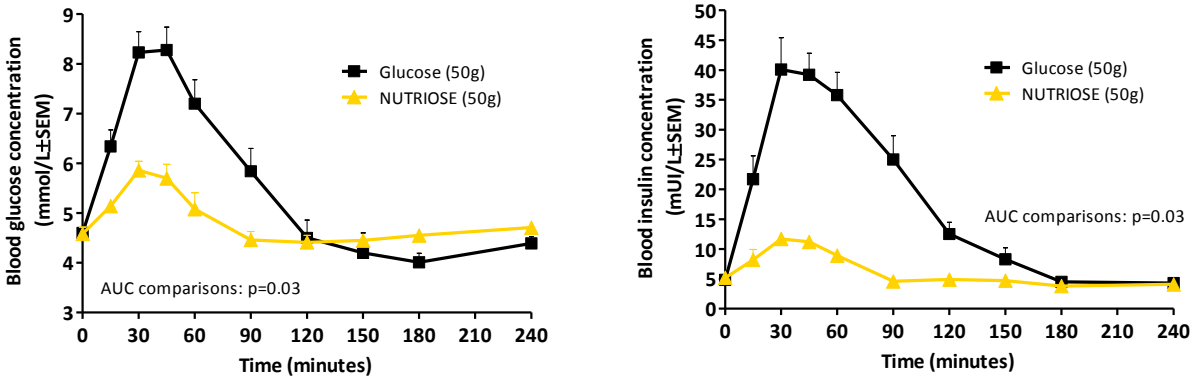
Conclusion: NUTRIOSE® is a **sugar-free soluble non-viscous** dietary fiber, **slightly digested** in the small intestine and **highly fermented** in the colon.

NUTRIOSE® AND BLOOD GLUCOSE MANAGEMENT

▸ The glycaemic and insulinemic responses of NUTRIOSE®

To evaluate the glycaemic and insulinemic responses of NUTRIOSE®, 6 different cross-over trials were conducted in 5 countries (France, UK, Canada, China, India). Six to 24 healthy human volunteers randomly consumed either 50g NUTRIOSE® or 50g glucose (control), at the start of experimental sessions of 120 to 240 minutes. Blood glucose and insulin responses were measured by continual sampling, either from capillary or venous blood. Depending on the methodologies used, glucose responses for NUTRIOSE® ranged from 25 to 48%, insulin responses from 13 to 20%. Both measures showed lower responses with NUTRIOSE®; *Figures 4 and 5*.

Another consequence of this weakly insulinogenic effect is the absence of post-prandial hypoglycaemia after 120 minutes, as compared with glucose ingestion (Lefranc-Millot *et al*., 2008; Lefranc-Millot *et al*., 2015; Guérin-Deremaux *et al*., 2018a; Guérin-Deremaux *et al*., 2018b; Guérin-Deremaux *et al*., 2018c). *Figure 4*.



Figures 4 and 5: Evolution of blood glucose and insulin after ingestion of 50g of NUTRIOSE® or 50g of dextrose

According to the standardized classification, NUTRIOSE® is a low digestibility carbohydrate, inducing low glycaemic and insulinemic responses; *Figure 6*.

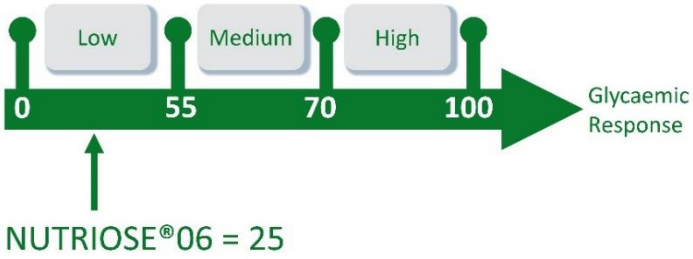


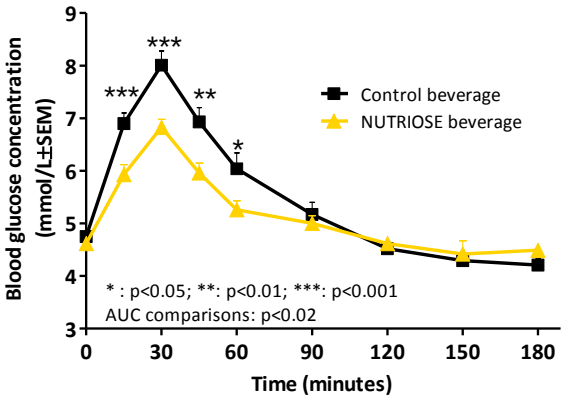
Figure 6: Glycaemic response classification

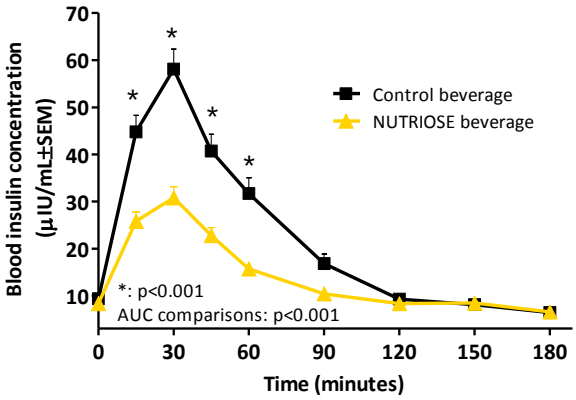
▸ NUTRIOSE®, a good candidate for digestible carbohydrate substitution

Incorporation of NUTRIOSE® as an ingredient of a foodstuff can induce a lower glycaemic response of a meal. To evaluate this benefit, different studies were conducted by substituting digestible carboydrates with NUTRIOSE®.

The three most recent trials were conducted in the US. Healthy volunteers (n=30) participated in a glycaemic and insulinemic responses test. Blood glucose and insulin responses were measured over 180 minutes after intake of either a food matrix containing NUTRIOSE® in place of a fraction of digestible carbohydrates; or a control food matrix containing digestible and glycaemic carbohydrates. Three different food matrices were tested: a powder mix beverage (*Figures 7* and *8*), a biscuit and extruded breakfast cereals.

NUTRIOSE® significantly reduced the glycaemic and insulinaemic impacts of the three fiber-food matrices compared to the control food matrices (Guérin-Deremaux *et al*., 2018a; Guérin-Deremaux *et al*., 2018c).





Figures 7 and 8: Evolution of blood glucose and insulin after ingestion of 30g of powder mix beverage

NUTRIOSE® soluble fiber is a good candidate for sugar and energy substitution or reduction, and for fiber content improvement of a food. This can help consumers reach dietary recommendations worldwide and can contribute to the prevention of obesity and diabetes.

▸ NUTRIOSE®, a longer-term impact on glucose homeostasis

- In a UK-based study, 20 normal weight and 16 overweight volunteers consumed 14g/day of either NUTRIOSE®, or an energy-matched placebo as a mid-morning and mid-afternoon drinks for 28 days. At baseline, day 14 and day 28, NUTRIOSE® intake significantly suppressed the postprandial glucose rise after a carbohydrate- preload administered in the morning. Indeed 30 minutes after the preload intake, the maximal blood glucose concentration was significantly lower at day 14 and day 28

compared to day 0 within the NUTRIOSE® group and was significantly lower at day 28 in the NUTRIOSE® group compared to the control group (Hobden *et al*., 2018, publication pending; Guérin-Deremaux *et al*., 2018a; Guérin-Deremaux *et al*., 2018b; Guérin-Deremaux *et al*., 2018c; Guérin-Deremaux *et al*., 2018e); *Figure 9*.

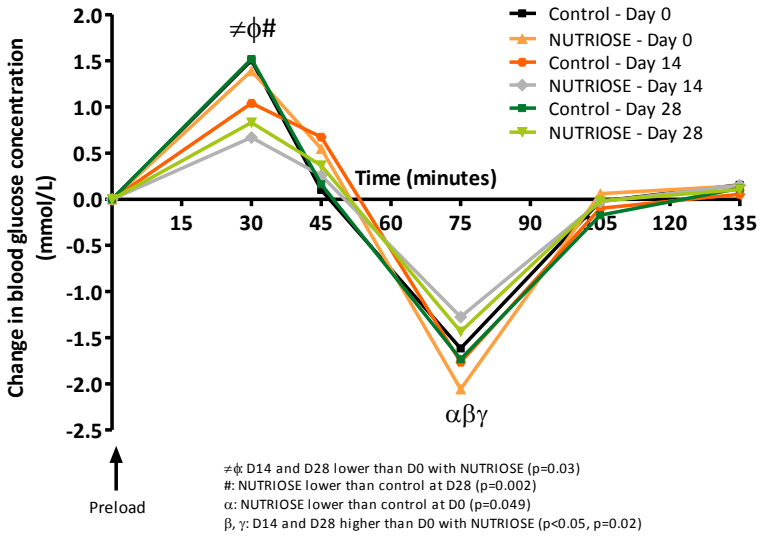
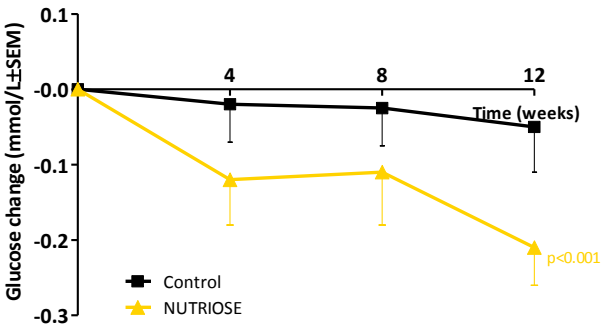
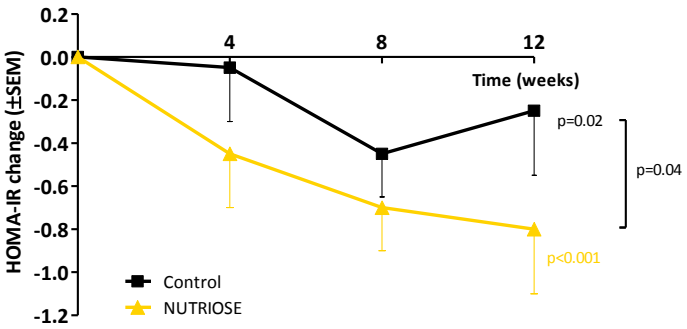


Figure 9: Changes in blood glucose concentrations following intake of a carbohydrate- preload

- A 12-week supplementation with NUTRIOSE® had previously demonstrated its ability to lower insulin resistance, improve determinants of metabolic syndrome and induce improvements in body composition and weight, energy intake and hunger in Chinese overweight men. Volunteers were supplemented with an orange juice containing 17g of NUTRIOSE® twice daily compared to an isocaloric orange juice. Blood parameters were evaluated every 4 weeks during the trial. All markers of glucose metabolism improved in the fiber group, with increases in adiponectin and reductions in glucose, insulin, homeostasis model assessment (HOMA) estimated insulin resistance, glycosylated hemoglobin and glycated albumin (Li *et al*., 2010; Guérin-Deremaux *et al*., 2011a); *Figures 10* and *11*.





Figures 10 and 11: Changes in blood glucose concentrations over the study, Changes in homeostasis model assessment of insulin resistance (HOMA-IR)

- A clinical study conducted in type 2 diabetic women evaluated the impact of an 8-week supplementation period of 10g/day of NUTRIOSE® compared to a similar amount of maltodextrin as placebo. In the first study (Aliasgharzadeh *et al.*, 2015), volunteers supplemented with NUTRIOSE® exhibited a significant decrease in fasting insulin, homeostasis model assessment- (HOMA) estimated insulin resistance, quantitative insulin sensitivity check index, IL-6, TNF-α, and endotoxin. Decreases in fasting blood glucose, HbA1c and CRP concentrations were not significant.

- In mice, the effects of NUTRIOSE® were evaluated on glucose homeostasis and insulin sensitivity after a 2-week supplementation. Following an oral tolerance test (IPGTT), the evolution of glycaemia was significantly lower in the NUTRIOSE® group compared to an iso-glucose control group. The evolution of insulin was also lower but with no statistical differences. These results suggest an improvement of the insulin sensitivity in mice (Delbes *et al.*, 2018, publication pending); *Figure 12*.

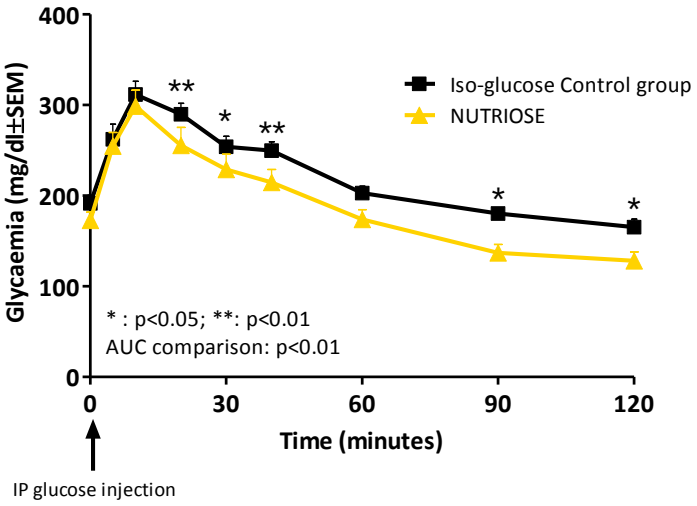


Figure 12: Evolution of glycaemia following a glucose tolerance test

▸ The health benefits recognized by EFSA and the European Commission

Roquette submitted a successful claim application to EFSA related to NUTRIOSE®. The accepted claim has been published in Regulation (EU) no. 2016/854 in 2016. This claim states that NUTRIOSE® induces a lower postprandial glycaemic response. It is supported by the 6 clinical studies conducted in 5 countries. The favorable claim is: "Consumption of foods/drinks containing NUTRIOSE®*

instead of sugars induces a lower blood glucose rise after their consumption compared to sugar-containing foods/drinks". (*: recommended wordings are: "NUTRIOSE®", "non-digestible carbohydrates", "non-digestible carbohydrates (such as NUTRIOSE®", "NUTRIOSE®(soluble fiber)", "NUTRIOSE®, soluble fiber").

In accordance with Article 10(3) of the European Regulation (EC) No 1924/2006, the health benefits of NUTRIOSE® soluble fiber can be indicated on end product packaging provided that it respects the usage conditions and includes the authorized health benefit claim, as well as a statement indicating the importance of a varied and balanced diet and a healthy lifestyle. For example, in the case of a biscuit with reduced sugars obtained with NUTRIOSE®, the package may indicate: "Reduced blood glucose impact" or "Helps reduce glycaemic response" or "Helps maintain healthy blood glucose levels" or include pictograms (*Figure 13*). The package may also provide that 30% of the sugars usually used in these biscuits are substituted with NUTRIOSE®, that the total energy value is equal or less than the total energy of a similar product, and that the official claim on a balanced diet described above are quoted.

Figure 13: Proposition of pictograms to be used on packaging

Conclusion: NUTRIOSE® soluble fiber is a good candidate for dietary **sugar reduction** and improvement of the **fiber content** of food. More importantly, this fiber may be used as an integrated solution for better **blood glucose management** as NUTRIOSE® helps to **maintain healthy blood glucose** levels and **controls fluctuations** in blood glucose after a preload rich in carbohydrates; *Figure 14*.

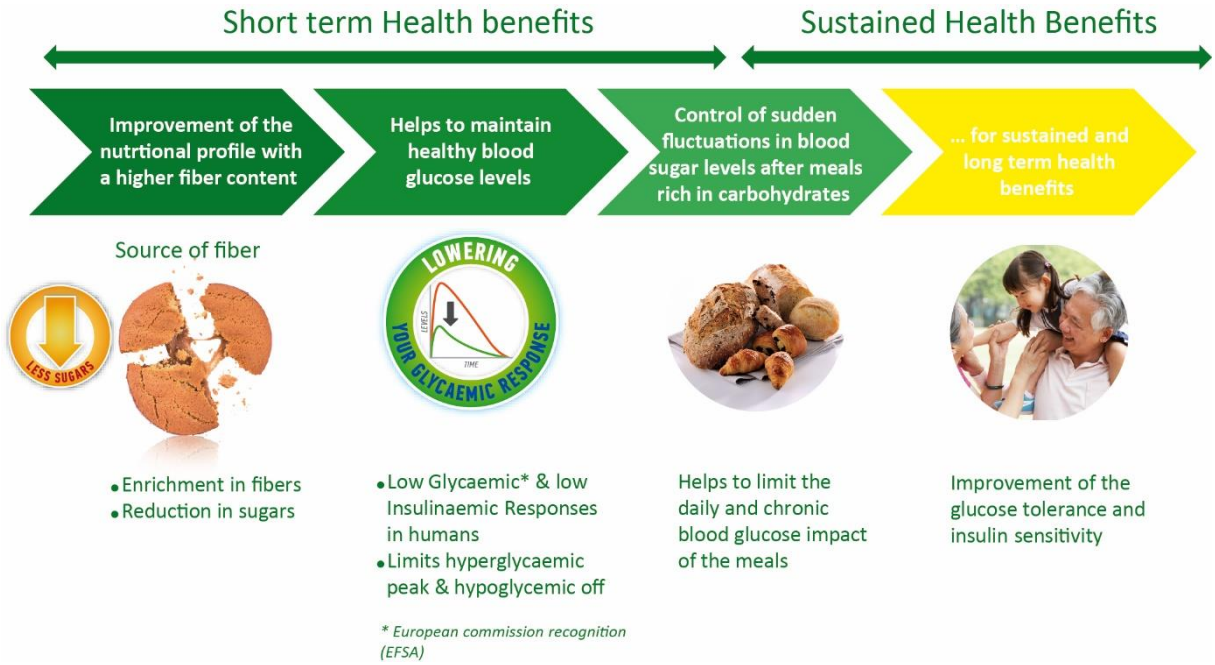


Figure 14: NUTRIOSE®, an integrated solution for a better blood glucose management

NUTRIOSE® AND DIGESTIVE HEALTH

► NUTRIOSE®, a fiber with an excellent digestive tolerance

Some soluble fibers are rapidly fermented and may cause digestive discomfort such as bloating, flatulence and diarrhea. When consumed in the quantity specified in the nutritional benefit claim, NUTRIOSE® is outstandingly well tolerated. The digestive tolerance threshold of NUTRIOSE® has been estimated as being 45g/day: up to this dose, no symptom of non-tolerance occurs. For doses between 45 and 60g/d, occurrence of flatulence has been reported, the symptom decreasing after 7 days of adaptation. The laxative dose has never been reached, even at a dose of 100g/d of NUTRIOSE®, meaning that the mean laxative threshold is over 100g/d, the maximal dose administered to date (van den Heuvel *et al*., 2004; Vermorel *et al*., 2004; Pasman *et al*., 2006); *Figure 15*.

Figure 15: Digestive tolerance of NUTRIOSE®

Different factors may explain this outstanding digestive tolerance. NUTRIOSE® is partially digested (15%) in the upper part of the intestinal tract, allowing better tolerance; the high degree of polymerisation of this resistant glucose polymer induces a lower osmotic pressure and a slower fermentation; and the food dextrin is fermented throughout the colon, allowing the SCFAs produced to be progressively absorbed and thus inducing little osmotic effect.

▸ NUTRIOSE® acts as a prebiotic

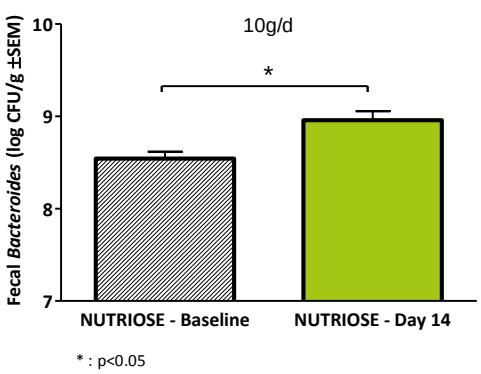
Numerous definitions of prebiotics with more or less subtle variations have been given in the past decades. The prebiotic concept was first defined in 1995 as a "*non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria already resident in the colon*". Most of the first prebiotics assessed in humans were shown to stimulate Lactobacilli and Bifidobacteria specially. Today, the "bifidogenic" effect is a restricted vision of what is a prebiotic.

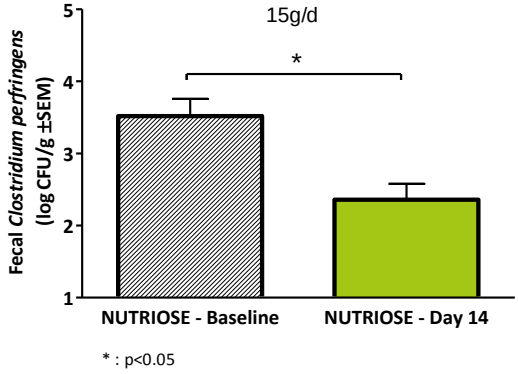
NUTRIOSE® meets the definition of Woods and Gorbach (2001) that prebiotic effects are characterized by an increase in "beneficial bacteria" and/or a decrease in "harmful bacteria", a decrease in intestinal pH, a production of Short Chain Fatty Acids (SCFAs) and changes in bacterial enzymes concentrations. This definition is in accordance with a proposed revised definition of a prebiotic as "*a non-viable food component that confers a health benefit on the host associated with modulation of the microbiota*" (FAO, 2007) and specifying that a prebiotic can be a fiber - but that a fiber need not be a prebiotic. A recent publication (Bindels *et al*., 2015) also considers the composition and activity of the gut microbiota. The last definition was published by the ISAPP (International Scientific Association for Probiotics and Prebiotics) in 2017: "*A substrate that is selectively utilized by host microorganisms conferring a health benefits*". This new definition clarifies that prebiotic targets extend beyond stimulation of Bifidobacteria and Lactobacilli, and recognizes that health benefits can derive from effects on other beneficial bacteria. The health benefits of prebiotic are evolving but currently include benefits to the gastrointestinal tract, cardiometabolism, mental health, bone health… among others.

NUTRIOSE® has been shown to display all mentioned effects through colonic fermentations. A health claim has been obtained by the Korea Food and Drug administration (KFDA). KFDA certifies NUTRIOSE®'s function, which help proliferate intestinal beneficial bacteria and inhibit harmful bacteria. This claims is supported by the data described below, provided that the daily intake is 8 to 20g/day.

- Results have been shown in several human studies with NUTRIOSE® (Van den Heuvel *et al.*, 2005; Lefranc-Millot *et al.*, 2011b; Pasman *et al.*, 2006; Hobden *et al.*, 2018, publication pending; Guérin-Deremaux *et al*., 2018a; Guérin-Deremaux *et al*., 2018b; Guérin-Deremaux *et al*., 2018e):

- An increase in the population of Lactobacilli was observed in human feces after a 35-day administration of 45g/day NUTRIOSE®.
- In two clinical studies, an increase in *Bacteroides* was observed in human feces after a 14-day administration of 8g/day and 10g/day of NUTRIOSE®; *Figure 16*. A decrease in *Clostridium perfringens* was observed after a 14-day administration of 8g/day and 15g/day of NUTRIOSE®; *Figure 17*. A subsequent decrease in colonic pH was also observed from 8g/day of NUTRIOSE®.
- A reduction in faecal microbial diversity (Shannon Index) was observed after a 28-day intake of 14g/day NUTRIOSE®. It may be a result of the dominance and specialization of specific populations with an observed elevation of *Clostridium* cluster IX (a cluster known as propionate producers) and *Parabacteroides* genus counts (a carbohydrate fermenting genus belonging to the Bacteroides subgroup of the phylum *Bacteroidetes*).
- In some studies a change in fecal bacterial enzyme concentrations were observed. Indeed, fecal β-glucosidase concentrations were significantly higher after 14 days of 10 or 15 g/day NUTRIOSE® consumption and after 28 days of 14g/day of NUTRIOSE®.

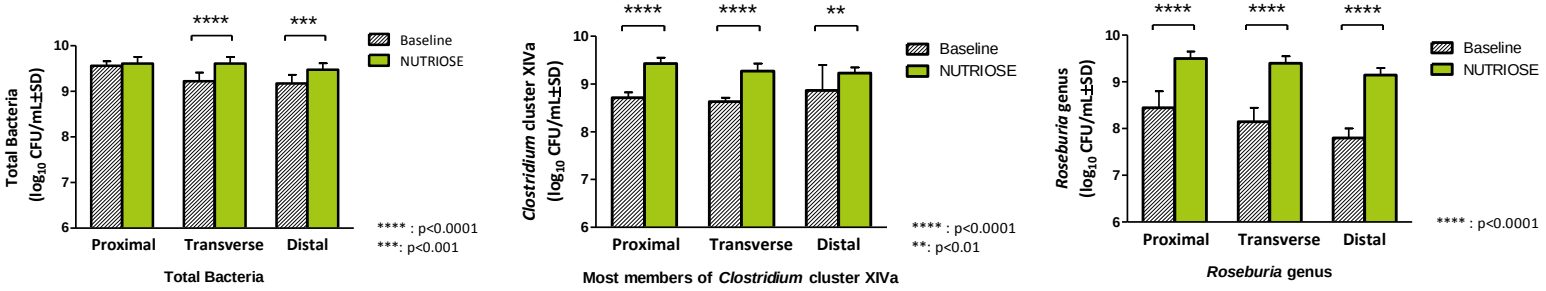




Figures 16 and 17: Fecal Bacteroides and Clostridium perfringens numbers in healthy volunteers

- The impact of NUTRIOSE® on the overall colonic environment was also described in rats (Guérin-Deremaux *et al.*, 2010). This preclinical model emphasized the beneficial impact of NUTRIOSE® administration on SCFAs production, total cecal weight, cecal content, cecal wall weight, cecal pH.

- An *in vitro* model of colonic SCFAs production has been used (Hobden *et al.*, 2013) because in humans SCFAs are absorbed in the colon, making it impossible to quantify their production. Using an *in vitro* three-stage continuous culture human colonic system, NUTRIOSE® induced a significant increase in total bacteria, in key butyrate-producing bacteria *Clostridium* cluster XIVa and *Roseburia* genus; *Figures 18, 19* and *20*. The production of acetate, propionate and butyrate significantly increased in the 3 vessels of the gut model system; *Figure 21*.



Figures 18, 19, 20: Total bacteria, Most members of Clostridium cluster XIVa and Roseburia genus

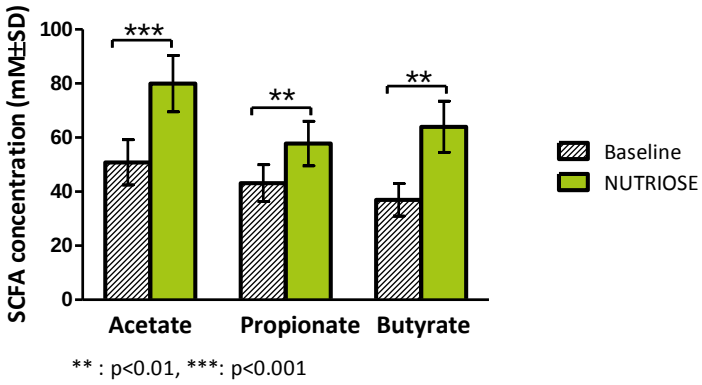


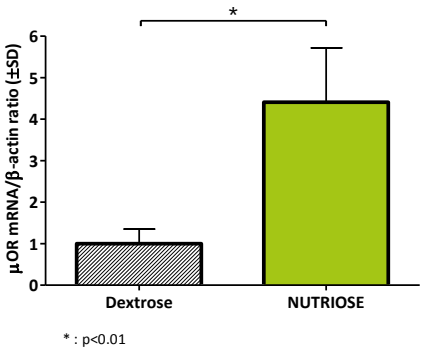
Figure 21: SCFAs production in the distal compartment of the in vitro system

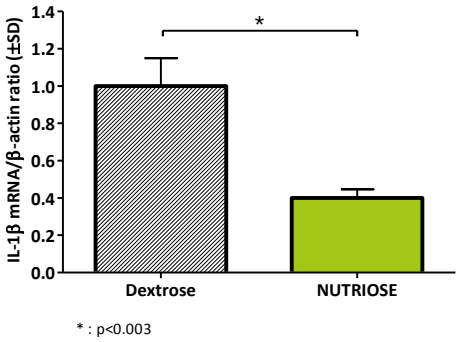
- Preclinical studies conducted in rats demonstrated a synergic effect of NUTRIOSE® and ginseng extracts suggesting beneficial interactions with introduction of NUTRIOSE® in food matrix. Indeed, in rats, colonic microbiota modulation from NUTRIOSE® fermentation promoted metabolic conversion of ginsenosides and ginseng extract and promoted its absorption into the bloodstream (Kim *et al*. 2014; Kim *et al.*, 2015).

▸ NUTRIOSE® promotes intestinal well-being

Preclinical data suggest that NUTRIOSE® may improve colon well-being through blunting of inflammation and reinforcement of intestinal immunity:

- The impact of a 4-week supplementation study with NUTRIOSE® ingestion in healthy mice was evaluated for effects on colonic mediators involved in the regulation of pain (μ-OR) and inflammation (PPARγ, IL-1β, TNFα). Results showed (Lefranc-Millot *et al*., 2007):
    - a significantly increased colonic expression of the analgesic receptor μ-OR and of the anti-inflammatory nuclear receptor PPARγ ; *Figure 22*,
    - a significantly decreased concentration of the pro-inflammatory IL-1β ; *Figure 23*,
    - a trend of decreased levels of mRNAs of the pro-inflammatory mediator TNFα.





Figures 22 and 23: MOR and IL-1β mRNA expression

- In a pre-clinical trial in piglets, the impact of NUTRIOSE® ingestion was evaluated on the inflammatory status of the colon following a TNBS-induced colitis (2,4,6-trinitrobenzene sulphonic acid). NUTRIOSE® supplementation alleviated the symptoms of colitis (body weight loss, bloody stools) induced by TNBS. There was also an improvement in endoscopic and histological scores of inflammation. In addition, NUTRIOSE® has shown to selectively downregulate some of the proinflammatory factors like IL-1β and TNFα. NUTRIOSE® also stimulated butyrogenic bacterial strains (Pouillart *et al*., 2010).

- The protective effects of NUTRIOSE® ingestion on colonic inflammation was investigated. A decrease in macroscopic and histological scores of colons was observed in rats with TNBS-induced colonic inflammation, after consuming NUTRIOSE®. This was also associated with an improvement of the cognitive assessments (Rozan *et al*., 2009).

- Finally, in an IBS model in rats NUTRIOSE® ingestion decreased colonic hypersensitivity (trend to significance) induced by intracolonic injection of butyrate (internal data).

All these results obtained on preclinical models support the position that NUTRIOSE® beneficially influences the regulation of local immunity, including visceral pain and colonic inflammation.

► NUTRIOSE®, its impact on microbiota explains the beneficial effects on physiological endpoints

A possible mechanism of action was determined in the UK-based clinical study described above (Hobden *et al*., 2018, publication pending), whose results are elaborated in *Figure 24*.

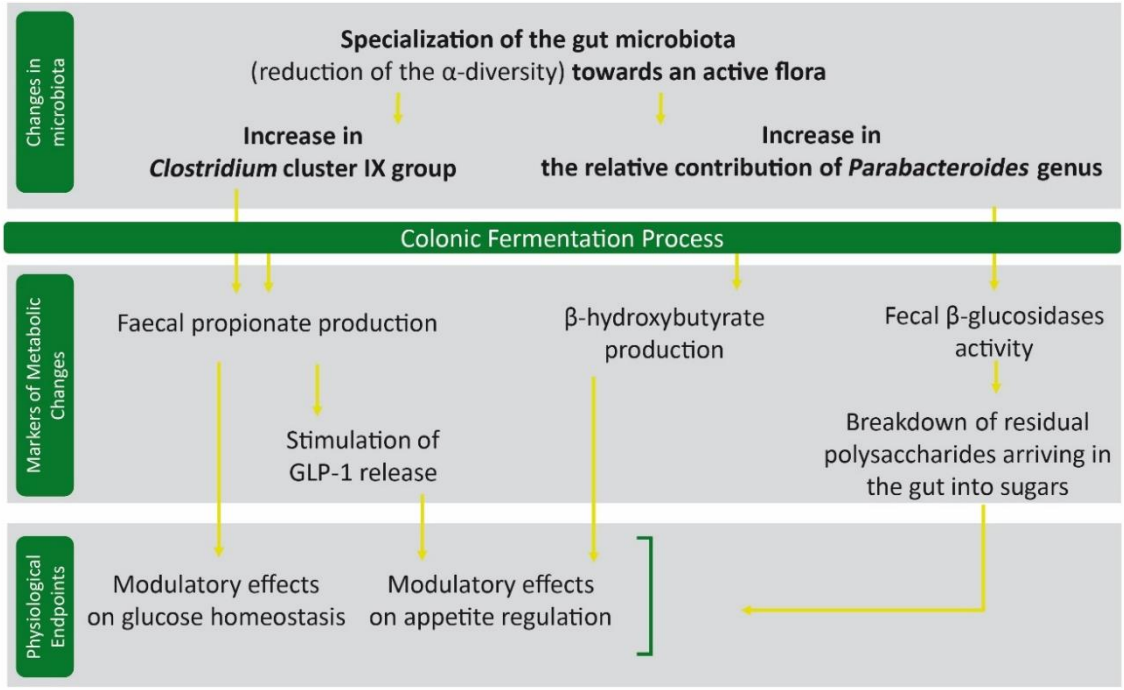
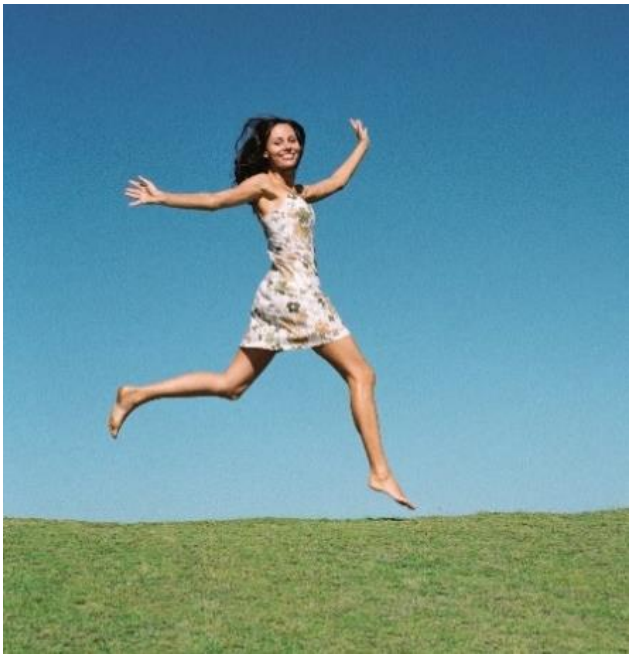


Figure 24: Proposition of mechanism of action to explain the influence of colonic microbiota in the modulation of physiological endpoints

Conclusion: NUTRIOSE® is a **well-tolerated fiber**. This soluble fiber displays beneficial impacts on the overall **colonic environment** showing that NUTRIOSE® acts as a **prebiotic**. The observed effects occurring in the colon may explain the systemic effects of NUTRIOSE® on **physiological endpoints** as **blood glucose management** and **satiety**.

NUTRIOSE® AND SUSTAINED ENERGY RELEASE



The sustained energy release properties were demonstrated in two clinical trials (van den Heuvel *et al.*, 2004, Nazare *et al.*, 2011, Guérin-Deremaux *et al*. 2018a, Guérin-Deremaux *et al*. 2018b, Guérin-Deremaux *et al*. 2018d).

- In a first intermediate-term cross-over study, 10 healthy volunteers consumed 10g or 15g/day of either NUTRIOSE® or maltodextrin as a control. Each dose was consumed for 7 days. The colonic fermentation pattern was assessed by measuring the breath H_2 excretion over the day as a marker of the colonic fermentations. The breath H_2 excretion increased in the 15g/day NUTRIOSE® group as compared to the control group; *Figure 25*.

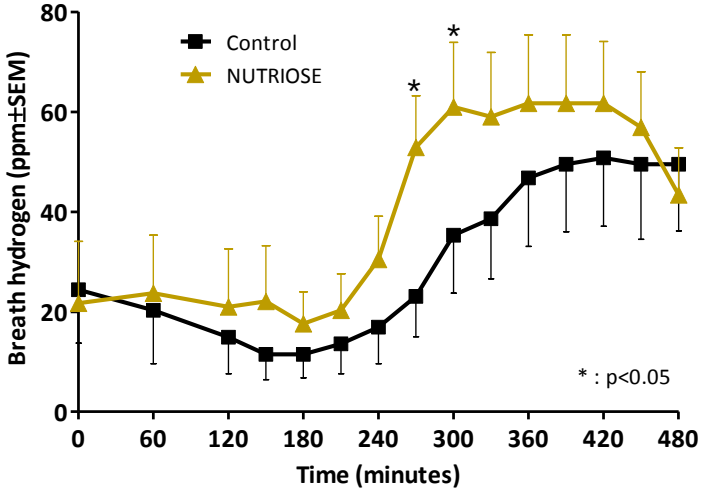
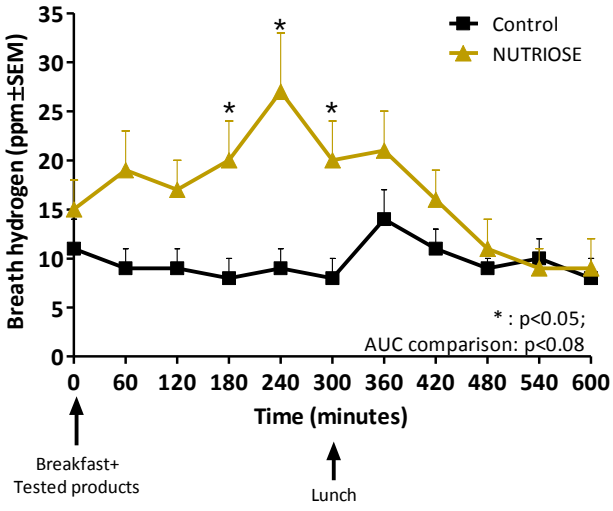
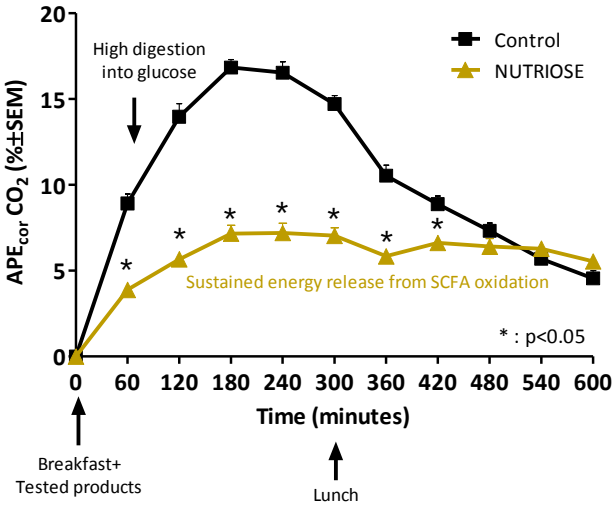


Figure 25: Breath hydrogen response at day 7

- In a second short-term cross-over study, 12 healthy volunteers ingested a standardized breakfast with either 50g of NUTRIOSE® or 50g of maltodextrin, both enriched in ^{13}C to follow their metabolic fate. Oxidation ($^{13}CO_2$) and fermentation (H_2) patterns were assessed using breath testing over the day. H_2 excretion was significantly enhanced in the NUTRIOSE® group as compared to control; *Figure 26*. The appearance of $^{13}CO_2$ increased dramatically in the maltodextrin group shortly after breakfast ingestion, reflecting intestinal digestion into glucose and further glucose oxidation. The $^{13}CO_2$ appearance from breakfast related to NUTRIOSE® was significantly lower in the early postprandial phase, reflecting a slight digestion of the fiber in the small intestine. Then, the $^{13}CO_2$ appearance with NUTRIOSE® remained steady and prolonged over 10 hours. Maintenance of $^{13}CO_2$ excretion from NUTRIOSE® was parallel to the H_2 increase because of the colonic fermentation process of the fiber; *Figure 27*. It is consistent with minor intestinal absorption of glucose contrasted with major and prolonged colonic fermentations and NUTRIOSE®-metabolites's oxidation. Possible explanations for these results include: a) Short Chain fatty Acids (SCFAs) produced by the fermentation of NUTRIOSE® in the colon could be used as neoglucogenic substrates before being oxidized and b) the ^{13}C-labeled SCFA produced could be oxidized in colonocytes or other tissues. Regardless of the mechanism, it is evident that the colonic fermentation of NUTRIOSE® provided a more sustained overall energy supply for oxidation.





Figures 26 and 27: Breath hydrogen response and metabolites oxidation levels occurring during intestinal digestion and colonic fermentation through $^{13}CO_2$ expired

Conclusion: NUTRIOSE® displays a **predominantly colonic fermentation** and **oxidation pattern** as a **metabolic fuel**. **Sustained colonic fermentations** from NUTRIOSE® combined with minor glucose absorption from its partial digestion in the small intestine may contribute to a **prolonged daily energy supply for whole-body metabolism**. Thus, NUTRIOSE® may be considered as a **long-lasting, or sustained, source of energy**.

OTHER HEALTH BENEFITS

▸ NUTRIOSE® and metabolic syndrome, satiety, weight management

- In a clinical trial conducted in China, supplementation with 34 g per day of NUTRIOSE® during 12 weeks induced a significant decrease in hunger associated with significant reductions in caloric intakes and body weight of overweight subjects, as compared to placebo (Guérin-Deremaux *et al*., 2011a). Interestingly, several biomarkers of the metabolic syndrome were improved by NUTRIOSE® ingestion in this study: blood lipid profile (reduction in total cholesterol and low-density lipoprotein cholesterol, increase in high-density lipoprotein cholesterol), markers of insulin sensitivity (increase in plasma concentration of adiponectin and decrease in homeostasis model assessment of insulin resistance), and long-term blood glucose control (decrease in glycosylated hemoglobin) (Li *et al*., 2010).

- These results were confirmed in another trial performed in Chinese overweight volunteers. It showed that a 9-week consumption of NUTRIOSE® displayed significant time- and dose-related effects on short-term satiety, hunger and caloric intakes, for dosages from 8 to 24 g per day (Guérin-Deremaux *et al*., 2011b; Guérin-Deremaux *et al*., 2013; Hobden *et al*. 2015). These observations were correlated with a significant reduction in body weight starting with the 14 g per day dosage; *Figure 28*.

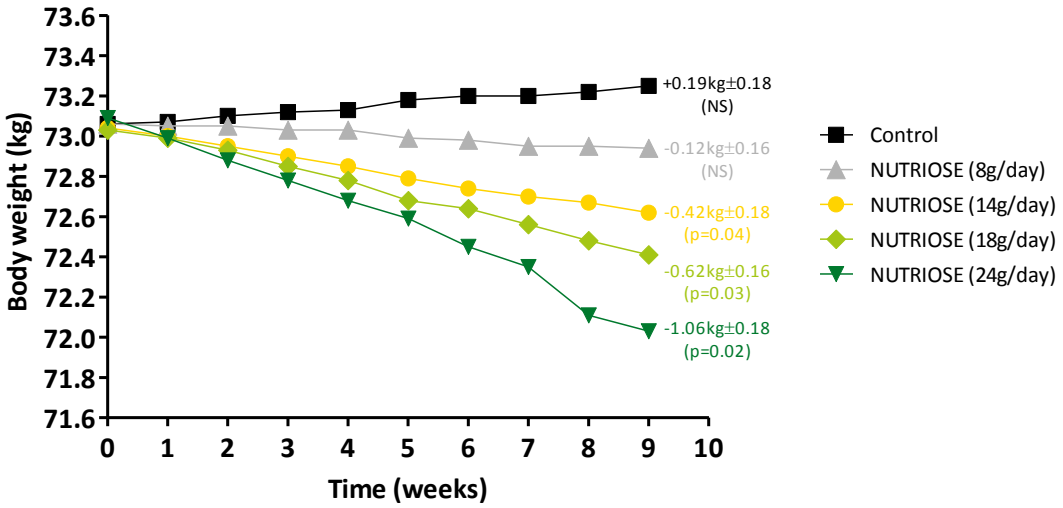
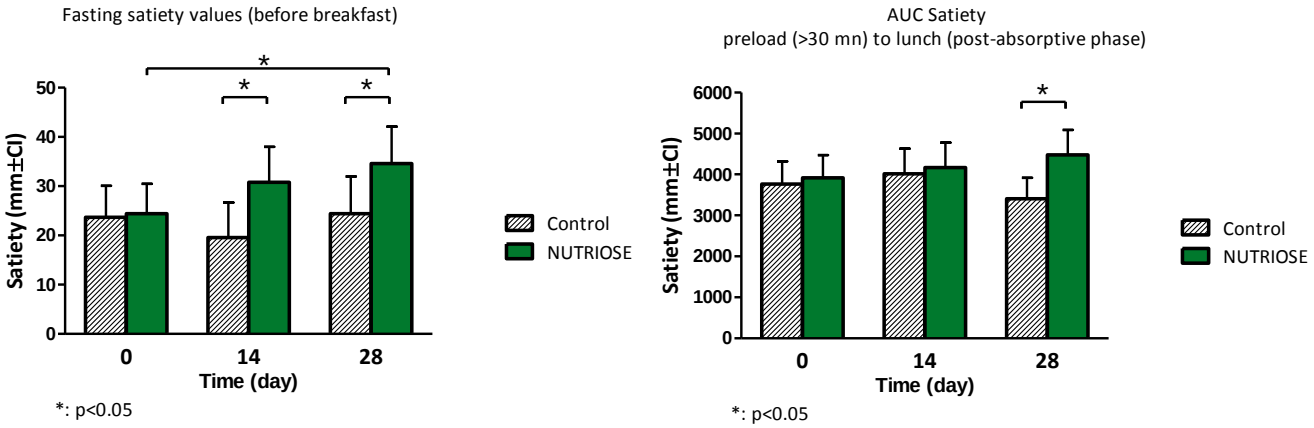


Figure 28: Bodyweight evolution over the 9-week supplementation period

- In a UK-based study, 20 normal weight and 16 overweight volunteers consumed 14g/day of either NUTRIOSE®, or an energy-matched placebo as mid-morning and mid-afternoon drinks for 28 days. Consuming soluble fiber for 28 days increased fasting satiety and postprandial satiety and fullness responses from 30 minutes after the morning drink in the latter postprandial phase, compared to day 0 and placebo drink; *Figures 29* and *30*. Neither treatment altered *ad libitum* test meal energy intake (Hobden *et al*., 2017; Hobden *et al*., 2018, publication pending; Guérin-Deremaux *et al*., 2018e).



Figures 29 and 30: Fasting satiety ratings and Area Under Curve in the latter postprandial phase

- The cholesterol-lowering effect of NUTRIOSE® was evaluated in moderately hypercholesterolemic hamsters during a 3-week study. The NUTRIOSE® diet significantly lowered plasma and LDL cholesterol, prevented hepatic cholesterol accumulation, decreased bile cholesterol and phospholipids concentrations. Reduced cholesterol absorption and bile salt absorptions as well as reduced lowered cholesterol synthesis are likely mechanisms underlying the cholesterol lowering effect of NUTRIOSE® (Juhel *et al*., 2011); *Figure 31*.

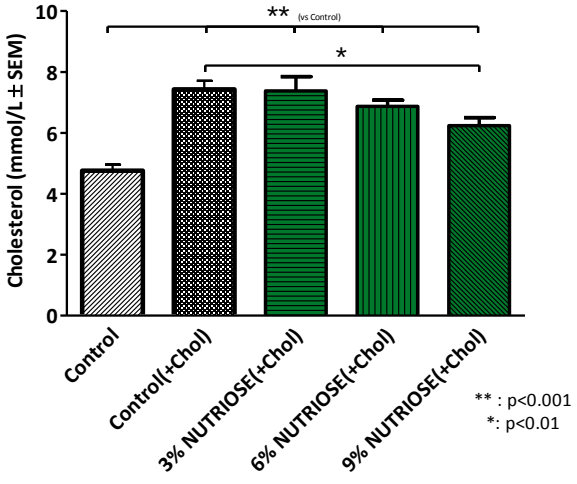


Figure 31: Plasma total cholesterol concentrations

Conclusion: NUTRIOSE® elicits beneficial impact on several determinants of **metabolic syndrome** and on **weight management** in Asian populations.

► NUTRIOSE® and dental health

Three clinical study aimed at evaluating the effect of NUTRIOSE® on dental plaque pH using a telemetric method implemented in a recognized lab in Switzerland. The results demonstrated that NUTRIOSE®06 is "safe for teeth" or "toothfriendly" according to the standard operation procedures of Toothfriendly International Association; *Figure 32*.

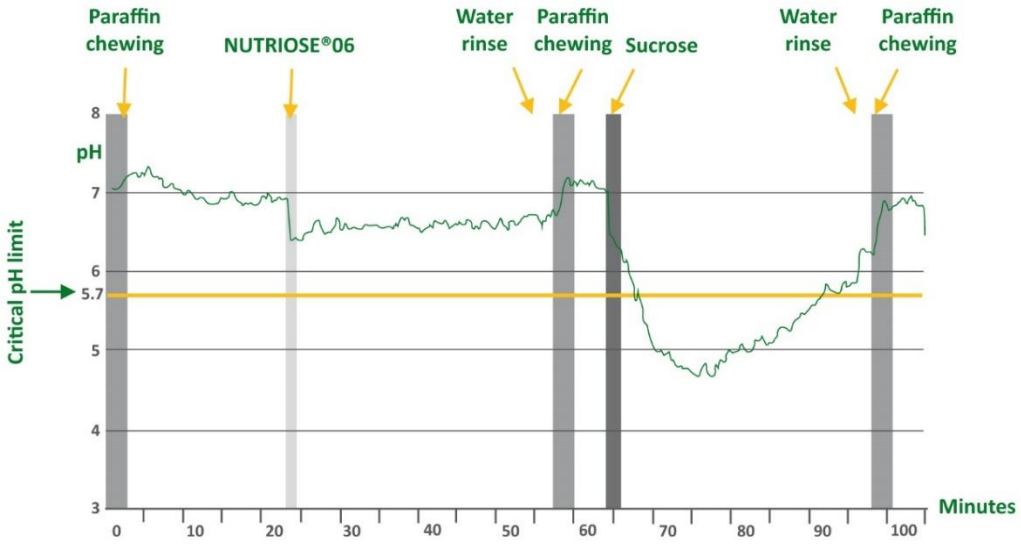


Figure 32: Telemetric recorded pH of interdental plaque after NUTRIOSE®06 intake

Based on these data Roquette submitted a claims application to EFSA related to NUTRIOSE®. The accepted claim has been published in Regulation (EU) no. 2016/854 in 2016. This confirms that NUTRIOSE® contributes to the maintenance of tooth mineralization. It is supported by 3 clinical studies. The claim is: "Consumption of foods/drinks containing NUTRIOSE®* instead of fermentable carbohydrates contributes to the maintenance of tooth mineralisation" (*: recommended wordings are "NUTRIOSE®", "non-digestible carbohydrates", "non-digestible carbohydrates (such as NUTRIOSE®)", "NUTRIOSE®(soluble fiber)", "NUTRIOSE®, soluble fiber").

Conclusion: NUTRIOSE®06 can be used as a sugar substitute without inducing any negative effects on **dental health**.

CONCLUSION

NUTRIOSE® offers a wide range of **benefits for health prevention** in addition to simply fortifying the fiber content of food and drink.

This soluble fiber may be used as part of an integrated solution to **improve blood glucose management** as NUTRIOSE® helps maintaining healthy **blood glucose** levels and **controls fluctuations** after a carbohydrates challenge.

NUTRIOSE® soluble fiber is a **well-tolerated fiber**, acting as a **targeted prebiotic** on general intestinal well-being.

Sustained colonic fermentations from NUTRIOSE® contribute to the daily energy supply for whole-body metabolism, and may be a key factor **in providing long-lasting energy**.

The **health benefits** of NUTRIOSE® may be attributed to the modulation of **specific aspects of the gut ecosystem.**

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