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Key references related to the physiological benefits of BENEO's chicory root fibres (inulin, oligofructose/FOS)

Inulin is a non-digestible carbohydrate naturally occurring as a storage carbohydrate in many plants that have always been part of the human diet, including many vegetables, fruits and cereals such as leeks, onions, garlic, wheat, chicory, artichokes and bananas. Chicory is presently the preferred crop for large-scale inulin production. Inulin is gained from the chicory root by hot water extraction.

Chicory root fibres are fructans mainly composed of fructose units joined by $\beta(2-1)$ fructosyl-fructose linkages as linear chains. Chicory inulin is an umbrella term that comprises the whole range of shorter chain (oligosaccharide type, degree of polymerization (DP) from 2 to 9) and longer chain (DP of more than 9 up to 60 or even more) inulin. Due to enzyme activity in the root the shorter chain inulin increases the later the harvest is. Oligofructose (the shorter chain inulin, also called fructo-oligosaccharide (FOS)) is produced by the partial enzymatic hydrolysis of chicory inulin.

Chicory root fibres are non-digestible in the small intestine and are fermented in the large intestine. They are the preferred food for some beneficial microbiota species like bifidobacteria and lactic acid bacteria. These bacteria produce enzymes than can break down the $\beta(2-1)$ linkages in fructans and thus have a competitive advantage leading to their selective growth. This has positive impact on the microbiota composition and on the production of break down products and metabolites which have benefits for digestive health and beyond. Chicory root fibre is one of the very few scientifically proven prebiotics. The most recent scientific definition of prebiotics, elaborated by the International Scientific Association for Probiotics and Prebiotics (ISAPP) in 2017, is: "A prebiotic is a substrate that is selectively utilised by host microorganisms conferring a health benefit" (<u>Gibson et al. 2017</u>).

Research related to prebiotic chicory root fibres (inulin, oligofructose/fructo-oligosaccharides/FOS) has been ongoing for more than 20 years with continuous interest in the microbiota influence and beyond. In the last 3 years alone more than 4000 publications related to prebiotics were released. This document provides a selection of the most relevant studies for the main physiological aspects and benefits of chicory root fibres. It by far does not represent a complete list of references.

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1. Selective growth of bifidobacteria

Prebiotics are non-digestible digestible food ingredients that beneficially affect the host (consumer) by selectively stimulating the growth and/or activity of one or more of a limited number of bacteria in the colon and thus improving host health. Chicory root fibres are among the very few ingredients scientifically proven to be prebiotics. More than 70 studies in infants, young children and adults have been carried out to investigate the prebiotic effect of chicory root fibres. Selective changes of the microbiota composition, especially an increase in bifidobacteria that are acknowledged as beneficial bacteria, were convincingly demonstrated after chicory root fibre consumption. The activities of the gut microbiota, and notably the saccharolytic fermentation, further contribute to colonic function by generating short-chain fatty acids (SCFA) and further metabolites, decreasing the production of potentially harmful nitrogen-containing compounds and modulating toxic enzymatic activities in the colon.

Chicory root fibres contribute accordingly to a healthy state of microbiota structure called normobiosis, as opposed to dysbiosis in which one or more potentially harmful bacterial species is dominant. The effect of increased bifidobacteria levels due to intake of chicory root fibres has been confirmed by numerous studies. More than 20 years research has confirmed this benefit independent of intake conditions and target groups including age, sex, ethnicity or health status.

Key references in adults:

• Study showing increase of bifidobacteria with a low dose of inulin

Bouhnik et al. (2007) Prolonged administration of low-dose inulin stimulates the growth of bifidobacteria in humans. Nutr Res 27:187–193. http://www.sciencedirect.com/science/article/pii/S0271531707000358

• Study showing increase of bifidobacteria with a low dose of oligofructose

Rao (2001) The prebiotic properties of oligofructose at low intake levels. Nutr Res 21:843–848. http://www.sciencedirect.com/science/article/pii/S0271531701002846

 Study showing selective effect on microbiota, including increase of bifidobacteria, with nextgeneration sequencing technology

Vandeputte et al. (2017) Prebiotic inulin-type fructans induce specific changes in the human gut microbiota. Gut 66(11):1968–1974. <u>http://gut.bmj.com/content/gutjnl/66/11/1968.full.pdf</u>

Citizen science study showing increase of bifidobacteria under free-life conditions

Kordowski et al. (2022) Palatinose[™] (Isomaltulose) and Prebiotic Inulin-Type Fructans Have Beneficial Effects on Glycemic Response and Gut Microbiota Composition in Healthy Volunteers—A Real-Life, Retrospective Study of a Cohort That Participated in a Digital Nutrition Program. Front Nutr 9. <u>https://www.frontiersin.org/articles/10.3389/fnut.2022.829933/full</u>

Review articles:

• Systematic review and meta-analysis showing increase of bifidobacteria and lactic acid bacteria (following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and the Cochrane Handbook for Systematic Reviews and Interventions)

So et al. (2018) Dietary fiber intervention on gut microbiota composition in healthy adults: A systematic review and meta-analysis. Am J Clin Nutr 107(6):965–983. https://www.ncbi.nlm.nih.gov/pubmed/29757343





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• Systematic review showing increase of bifidobacteria, lactic acid bacteria and *Faecalibacterium prausnitzii* (following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)

Hughes et al. (2021) The Prebiotic Potential of Inulin-type Fructans: A Systematic Review. Adv Nutr. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8970830/pdf/</u>

2. Normal bowel function by increased stool frequency per week

The fermentation of chicory root fibres by the colonic microbiota results in an increased bacterial cell mass which stimulates mechanically, while the production of SCFA stimulates bowel movements chemically. Due to the high water content of intestinal bacteria, the moisture content of faeces is increased after chicory root fibres supplementation which softens stools for easier excretion. As such the consumption of inulin and oligofructose supports normal bowel function. This is especially shown by increased stool frequency per week which is proven in more than 10 studies.

Key references in adults:

• Study proving benefits of 12 g/d inulin for bowel regularity by increased stool frequency

Micka et al. (2017) Effect of consumption of chicory inulin on bowel function in healthy subjects with constipation: A randomized, double-blind, placebo-controlled trial. Int J Food Sci Nutr Feb 68 (1):82–89. <u>http://www.tandfonline.com/doi/pdf/10.1080/09637486.2016.1212819</u>

· Study proving benefits of oligofructose for bowel regularity

Buddington et al. (2017) Oligofructose Provides Laxation for Irregularity Associated with Low Fiber Intake. Nutrients 9(12):1372. <u>http://www.mdpi.com/2072-6643/9/12/1372/pdf</u>

Review articles:

 Positive scientific opinion by European Food Safety Authority (EFSA) as basis for approved health claim on normal bowel function by increasing stool frequency per week with 12 g/d chicory inulin

EFSA Panel on Dietetic Products, Nutrition and Allergies (2015) Scientific Opinion on the substantiation of a health claim related to "native chicory inulin" and maintenance of normal defecation by increasing stool frequency pursuant to Article 13.5 of Regulation (EC) No 1924/20061. EFSA Journal 13 (1) 3951. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3951.pdf

- http://www.elsa.europa.eu/sites/deladi/mes/scientine_outpu/mes/main_documents/3951.pdi
- Systematic review and meta-analysis showing that inulin improves bowel function

Collado Yurrita et al. (2014) Effectiveness of inulin intake on indicators of chronic constipation; a meta-analysis of controlled randomized clinical trials. Nutr Hosp 30 (2)(1699-5198):244–252. http://www.aulamedica.es/nh/pdf/7565.pdf

3. Increased calcium absorption for supporting bone health

Seven studies have shown that chicory root fibre intake, especially Orafti[®]Synergy1, results in a significant increase in calcium absorption in adolescence and adulthood. Especially bone





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mineralisation is the gold standard marker for the support of bone health on a long term. Colonic fermentation of Orafti[®]Synergy1 is thought to be the main mechanism contributing to its effect on the stimulation of calcium absorption over the whole length of the large intestine.

Key reference:

 One 1-year study with 8 g/d Orafti[®]Synergy1 showing increase in calcium absorption and bone mineralization in adolescents

Abrams et al. (2005) A combination of prebiotic short- and long-chain inulin-type fructans enhances calcium absorption and bone mineralization in young adolescents. Am J Clin Nutr 82(2):471–476. <u>https://academic.oup.com/ajcn/article-pdf/82/2/471/23960080/znu00805000471.pdf</u>

Review article:

• Narrative review on effects on nutrient absorption

Costa et al. (2020) Changes in nutrient absorption in children and adolescents caused by fructans, especially fructooligosaccharides and inulin. Archives de Pédiatrie 27(3):166–169. https://pubmed.ncbi.nlm.nih.gov/32127241/

4. Blood sugar management

Since inulin and oligofructose are non-digestible carbohydrates, they do not contribute to post-prandial glycaemia. Replacing digestible and glycaemic carbohydrates partially or completely with inulin or oligofructose on a weight-by-weight basis in a food product reduces the amount of available carbohydrates and consequently the postprandial blood glucose response of the food. Human studies show significant reductions in the postprandial glycaemic response for different foods in which sugars have been replaced by oligofructose at levels of 20% or more. A linear relationship between the extent of sugar replacement and a reduction in the resulting blood glucose response shows that higher fructan levels will result in greater effects, respectively. Also, the corresponding insulin levels were measured and confirmed to be lower as well.

Key reference related to postprandial blood glucose response:

• Study showing lower blood glucose and insulin after replacement of sucrose by inulin or oligofructose and summary of further studies showing a linear relationship between sugars replacement by chicory root fibre and reduction of postprandial blood glucose response

Lightowler et al. (2017) Replacement of glycaemic carbohydrates by inulin-type fructans from chicory (oligofructose, inulin) reduces the postprandial blood glucose and insulin response to foods: Report of two double-blind, randomized, controlled trials. Eur J Nutr 57(3):1259–1268. https://rd.springer.com/article/10.1007%2Fs00394-017-1409-z

 Citizen science study showing a significantly more balanced blood glucose profile over the day under free-life conditions

Kordowski et al. (2022) Palatinose™ (Isomaltulose) and Prebiotic Inulin-Type Fructans Have Beneficial Effects on Glycemic Response and Gut Microbiota Composition in Healthy Volunteers—A Real-Life, Retrospective Study of a Cohort That Participated in a Digital Nutrition Program. Front Nutr 9. <u>https://www.frontiersin.org/articles/10.3389/fnut.2022.829933/full</u>





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Key reference related to long-term blood glucose control:

• Study showing reduced fasting glucose, HbA1c and HOMA-IR

Russo et al. (2010) Metabolic effects of a diet with inulin-enriched pasta in healthy young volunteers. Curr Pharm Des 16(7):825–831. <u>http://www.ncbi.nlm.nih.gov/pubmed/20388093</u>

Review articles:

• Approved health claim on lower blood glucose response with 30% sugars replacement by chicory root fibre based on positive scientific opinion by European Food Safety Authority (EFSA)

EFSA Panel on Dietetic Products, Nutrition and Allergies (2014) Scientific Opinion on the substantiation of health claims related to non-digestible carbohydrates and a reduction of postprandial glycaemic responses pursuant to Article 13 (5) of Regulation (EC) No. 1924/2006. EFSA Journal 12(1):3513. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3513.pdf

Systematic review and meta-analysis showing lower postprandial blood glucose and insulin

Kellow et al. (2014) Metabolic benefits of dietary prebiotics in human subjects: a systematic review of randomised controlled trials. Br J Nutr 111(7):1147–1161. http://journals.cambridge.org/article_S0007114513003607

5. Body weight management by lower energy intake

Chicory root fibres help you to eat less, naturally. This is important for losing weight and for keeping a healthy weight especially after weight loss – in other words, it is relevant for everyone. Research with chicory root fibres is available related to the parameters of appetite/satiety, hormonal influences (GLP-1, PYY) and energy intake, in particular for mid-term and long-term durations and for weight loss. The most reliable data are related to energy intake as these type of study designs take next meal or next day compensation in caloric intake into account and thus provide reliable information. In the case of chicory root fibres more than 20 human intervention studies are available, in healthy, overweight and obese adults and children, that investigated the effects on energy intake for improved body weight management.

Key references in adults:

• Study showing increased satiety ratings and lower energy intake with 16 g/d oligofructose

Cani et al. (2006) Oligofructose promotes satiety in healthy human: a pilot study. Eur J Clin Nutr 60(5):567–572. <u>http://www.nature.com/ejcn/journal/v60/n5/pdf/1602350a.pdf</u>

• Study showing lower energy intake with 12 g/d Orafti®Synergy1

McCann et al. (2011) Oligofructose-enriched inulin supplementation decreases energy intake in overweight and obese men and women. Obesity reviews 12(S1):63–279. http://onlinelibrary.wiley.com/doi/10.1111/j.1467-789X.2011.00889.x/pdf

• Study showing lower energy intake, body fat and weight

Parnell and Reimer (2009) Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. Am J Clin Nutr 89(6):1751–1759. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827013/pdf/</u>





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Key references in children and young adolescents:

• Study showing lower energy intake, improved appetite ratings, lower body fat and weight with 8 g/d Orafti[®]Synergy1 in overweight or obese children for healthy weight gain

Hume et al. (2017) Prebiotic supplementation improves appetite control in children with overweight and obesity: a randomized controlled trial: A randomized controlled trial. Am J Clin Nutr 105(4):790–799. <u>https://www.ncbi.nlm.nih.gov/pubmed/28228425</u>

Nicolucci et al. (2017) Prebiotic Reduces Body Fat and Alters Intestinal Microbiota in Children With Overweight or Obesity. Gastroenterology 153(3):711–722. http://www.gastrojournal.org/article/S0016-5085(17)35698-6/pdf.

Review article:

• Systematic review and meta-analysis showing reduced blood glucose and insulin responses

Kellow et al. (2014) Metabolic benefits of dietary prebiotics in human subjects: a systematic review of randomised controlled trials. Br J Nutr 111(7):1147–1161. http://journals.cambridge.org/article_S0007114513003607

6. Prebiotics from chicory as bioactive substances in infants and children

The development of the gut microbiota is a critical and essential process early in life as it impacts later health outcomes. Inulin and oligofructose can be used safely in milks for infants from birth onwards, showing beneficial effects on the colonisation of the microbiota towards a breastfed-type composition higher in bifidobacteria. At the same time stools become softer when formula is enriched with prebiotics from chicory, while standard formula feeding is often associated with hard stools. In addition, studies show that prebiotics from chicory influence immunity from early on, e.g., by a fewer number of infectious diseases. These benefits are not only important in infancy, but are also observed in childhood for improved digestive health and immunity.

Key references in infants:

• Safety and efficacy study showing on microbiota and stool consistency

Closa-Monasterolo et al. (2013) Safety and efficacy of inulin and oligofructose supplementation in infant formula: results from a randomized clinical trial. Clin Nutr 32(6):918–927. http://www.ncbi.nlm.nih.gov/pubmed/23498848

 Long-term safety and efficacy study showing benefits for microbiota, stool consistency, wellbeing and immunity support

Neumer et al. (2021) Long-Term Safety and Efficacy of Prebiotic Enriched Infant Formula—A Randomized Controlled Trial. Nutrients 13(4):1276. <u>https://www.mdpi.com/2072-6643/13/4/1276</u>

Key references in children above 3 years of age:

• Study showing immunity support and benefits for microbiota and stool consistency

Lohner et al. (2018) Inulin-type fructan supplementation of 3 to 6 year-old children is associated with higher fecal bifidobacterium concentrations and fewer Febrile Episodes Requiring Medical Attention. J Nutr 102(Suppl 2):261. <u>https://academic.oup.com/jn/advance-article/doi/10.1093/jn/nxy120/5048772</u>





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• Study showing stable bifidobacteria also under antibiotic treatment

Soldi et al. (2019) Prebiotic supplementation over a cold season and during antibiotic treatment specifically modulates the gut microbiota composition of 3-6 year-old children. Benef Microbes 19; 10 (3):253–263. <u>https://www.wageningenacademic.com/doi/pdf/10.3920/BM2018.0116</u>

Review articles:

• Systematic review and meta-analysis showing immunity support

Lohner et al. (2014) Prebiotics in healthy infants and children for prevention of acute infectious diseases: a systematic review and meta-analysis. Nutr Rev 72(8):523–531. http://www.ncbi.nlm.nih.gov/pubmed/24903007

• Systematic review showing benefits for microbiota and stool consistency

Skórka et al. (2018) Infant formulae supplemented with prebiotics: Are they better than unsupplemented formulae? An updated systematic review. Br J Nutr:1–16. https://www.ncbi.nlm.nih.gov/pubmed/29457570





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