Key references related to the physiological benefits of Palatinose™

Palatinose™ – a carbohydrate with unique physiological properties

Palatinose™ (generic name: isomaltulose) is a disaccharide carbohydrate that occurs naturally in honey and sugar cane juice. It is derived from sucrose by enzymatic conversion. And it is a "slow release carbohydrate" with a unique combination of physiological properties: As result of its slow yet complete digestion and absorption, Palatinose™ has a low effect on blood glucose levels (GI: 32) and insulin release. It provides carbohydrate energy in a more balanced way over a longer period of time. And thus it contributes to modern energy management with characteristics like steadier energy supply and a higher contribution of fat oxidation. Apart from that, Palatinose™ is kind to teeth. The slow release properties, the higher fat oxidation and tooth-friendliness are all unique to Palatinose™ and make it different from sugars like fructose or sucrose and HFCS or from malto-oligosaccharides.
BENEO has undertaken comprehensive research to study the unique nutritional and physiological properties of this functional carbohydrate. This document provides a list of the most relevant publications per physiological aspect, while it – by far – does not represent a complete list of references. More detailed information can be provided upon request.

Table of Content:

1. Palatinose™ - a fully available carbohydrate for slow and sustained energy release

a) Palatinose™ is a fully available carbohydrate

The essentially complete digestion and absorption of Palatinose™ within the small intestine has been confirmed in human and animal studies. Palatinose™ is a fully digestible carbohydrate and as such provides the full carbohydrate energy (4 kcal/g), respectively.

Key reference:

Holub I, Gostner A, Theis S, Nosek L, Kudlich T, Melcher R, Scheppach W (2010) Novel findings on the metabolic effects of the low glycaemic carbohydrate isomaltulose (Palatinose™). Br J Nutr 103(12):1730–1737. (see trial 1 for ileostomy study) http://www.ncbi.nlm.nih.gov/pubmed/20211041

b) Palatinose™ is a slow and sustained release carbohydrate

The "slow release" aspect is evidenced by enzyme kinetic studies (animal and human enzymes) which show that the enzymatic hydrolysis of Palatinose™ in the small intestine occurs much slower than that of e.g. sucrose (i.e. difference in V_{max} by a factor of 4 to 5). Observations on incretin hormones illustrate that the digestion of Palatinose™ and subsequent absorption is a slow process that is extended to more distal parts of the small intestine. Relevant for the enzymatic hydrolysis in the small intestine is the 2-center-enzyme complex "ucrase-Isomaltase", responsible for the breakdown of starch-type (respective their break down product isomaltose with an α-1-6 linkage) and disaccharide-type carbohydrates with α-1,2 linkages. Isomaltulose is hydrolysed as the starch-center of the enzyme complex with a slower rate of hydrolysis.

Enzyme kinetic references:

Dahlqvist A (1961) Hydrolysis of palatinose (Isomaltulose) by pig intestinal glycosidases. Acta Chem Scand 15(4):808–816. http://actachemscand.org/pdf/acta_vol_15_p0808-0816.pdf

Grupp U, Siebert G (1978) Metabolism of hydrogenated palatinose, an equimolar mixture of alpha-D-glucopyranosido-1,6-sorbitol and alpha-D-glucopyranosido-1,6-mannitol. Res Exp Med (Berlin) 173(3):261–278. http://www.ncbi.nlm.nih.gov/pubmed/364572

Heinz F (1987) The enzymatic splitting of sugar substitutes by isolated enzymes and enzyme complexes from the small intestinal mucosa. Hanover University Medical School, Biochemistry Centre, Research Project No. 6539. See also: Heymann, H., Heinz, F. (1987) Kinetic studies on glucoamylase/maltase and sucrase/isomaltase complex of human, pig and rat intestinal mucosa. 4th European Carbohydrate Symposium, Darmstadt, (12.-17.07.87).

Tsuji Y (1986) Digestion and absorption of sugars and sugar substitutes in rat small intestine. J Nutr Sci Vitaminol 32:93–100. http://www.ncbi.nlm.nih.gov/pubmed/3712112

Yamada K, Shinohara H, Hosoya N (1985) Hydrolysis of 1-O-α-D-glucopyranosyl-D-fructofuranose (trehalulose) by rat intestinal sucrase-isomaltase complex. Nutr Rep Int 32(5):1221-1220.

Ziesenitz SC (1986a) Zur Verwertung des Zuckeraustauschstoffes Palatinit im Stoffwechsel. [Utilization of the sugar substitute Palatinit® in metabolism]. In: Bässler K, Grünert A, Kleinberger G, Reissigl H (eds) Beiträge zu Infusionstherapie und klinische Ernährung 16. Karger, Basel, pp 120–132.

Ziesenitz SC (1986b) Stufenweises Prüfschema für Zuckeraustauschstoffe - Vorprüfung mittels Enzymen. 3. Carbohydrasen aus Jejunalmucosa des Menschen. [A stepwise method of evaluating sugar substitutes - a preliminary study using enzymes. 3. Carbohydrases from the human jejunal mucosa]. Z Ernahrungswiss 25:253–258. http://link.springer.com/article/10.1007/BF02019577

Incretin response references:

Ang M, Linn T (2014) Comparison of the effects of slowly and rapidly absorbed carbohydrates on postprandial glucose metabolism in type 2 diabetes mellitus patients: a randomized trial. Am J Clin Nutr 100(4):1059–1068.
http://ajcn.nutrition.org/content/early/2014/07/16/ajcn.113.076638.full.pdf+html

Keyhani-Nejad F, Kemper M, Schueler R, Pivovarova O, Rudovich N, Pfeiffer AF (2016) Effects of Palatinose and Sucrose Intake on Glucose Metabolism and Incretin Secretion in Subjects With Type 2 Diabetes. Dia Care 39(3):e38-e39. http://www.ncbi.nlm.nih.gov/pubmed/26721819

Maeda A, Miyagawa J, Miuchi M, Nagai E, Konishi K, Matsuo T, Tokuda M, Kusunoki Y, Ochi H, Murai K, Katsuno T, Hamaguchi T, Harano Y, Namba M (2013) Effects of the naturally-occurring disaccharides, palatinose and sucrose, on incretin secretion in healthy non-obese subjects. J Diabetes Investig. 4(3):281–286. http://www.ncbi.nlm.nih.gov/pubmed/24843667

Pfeiffer AFH, Keyhani-Nejad F (2018) High glycemic index metabolic damage - a pivotal role of GIP and GLP-1. Trends Endocrinol Metab 29(5):289-299. https://www.cell.com/trends/endocrinology-metabolism/fulltext/S1043-2760(18)30046-8

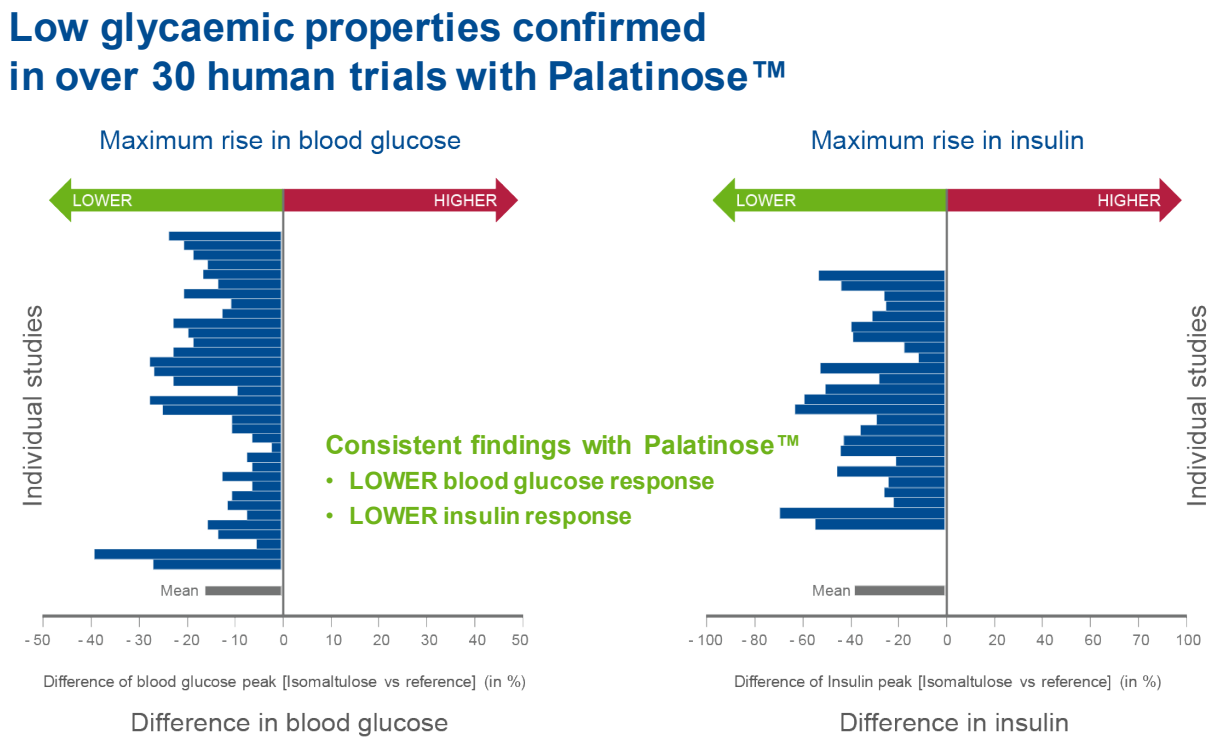
c) Palatinose™ - the carbohydrate for sustained energy supply

The sustained energy supply of Palatinose™ is a result of its slow yet complete digestion and absorption along the small intestine. It is additionally reflected in subsequent metabolic processes: In comparison with readily available carbohydrates, Palatinose™ shows a slower, overall lower and sustained rise in blood glucose levels. Since blood glucose means fuel for the body and its energy metabolism, the sustained glucose supply from Palatinose™ is associated with a more steady and sustained energy gain from carbohydrate oxidation: Palatinose™ provides sustained energy.

Numerous blood glucose response studies have been conducted on behalf of BENEO and specifically analyzed to test whether the characteristics of sustained glucose supply from Palatinose™ can be shown in this methodology with its high variance. The sustained glucose supply of Palatinose™ has been concomitantly shown in all of these studies. Moreover, individual studies confirm the link between sustained glucose supply and sustained carbohydrate oxidation.

2. Palatinose™ - a low glycemic carbohydrate

As result of its slow (yet complete) intestinal release, Palatinose™ has a low effect on blood glucose levels and insulin release. A Glycemic Index (GI) of 32 has been determined for Palatinose™ by Sydney University.
The “low glycemic” properties of Palatinose™ have been experimentally verified in extensive research initiated by BENEO - including more than 30 human trials from the past 10 to 15 years conducted according to internationally recognized standard methodology in leading test centers worldwide (see Figure on the right) - and are well described in literature. A corresponding claim has been laid down in EU legislation following the publication of a positive EFSA opinion.



Confirmation in a study population of in total >250 adults, and also children, covering healthy people with normal body weight or overweight/obese, with normal or impaired glucose tolerance (including type 1 and type 2 diabetes mellitus).

References of published blood glucose response studies:

Sydney University's Glycaemic Research Service (SUGiRS) (2002): See GI Database at www.glycemicindex.com

Ang M, Linn T (2014) Comparison of the effects of slowly and rapidly absorbed carbohydrates on postprandial glucose metabolism in type 2 diabetes mellitus patients: a randomized trial. Am J Clin Nutr 100(4):1059–1068. http://ajcn.nutrition.org/content/early/2014/07/16/ajcn.113.076638.full.pdf+html

Henry CJ, Kaur B, Quek RYC, Camps SG (2017) A Low Glycaemic Index Diet Incorporating Isomaltulose Is Associated with Lower Glycaemic Response and Variability, and Promotes Fat Oxidation in Asians. Nutrients 9(5). http://www.mdpi.com/2072-6643/9/5/473/htm

Holub I, Gostner A, Theis S, Nosek L, Kudlich T, Melcher R, Scheppach W (2010) Novel findings on the metabolic effects of the low glycaemic carbohydrate isomaltulose (Palatinose™). Br J Nutr 103(12):1730–1737. (see trial 1 for ileostomy study) http://www.ncbi.nlm.nih.gov/pubmed/20211041

Kahlhöfer J, Karschin J, Silberhorn-Bühler H, Breusing N, Bosy-Westphal A, Kahlhofer J, Silberhorn-Buhler H (2016) Effect of low glycemic-sugar-sweetened beverages on glucose metabolism and macronutrient oxidation in healthy men. Int J Obes (Lond) 40(6):990–997. http://www.nature.com/ijo/journal/v40/n6/full/ijo201625a.html

Kawai K, Okuda Y, Yamashita K (1985) Changes in blood glucose and insulin after an oral palatinose administration in normal subjects. Endocrinol Jpn 32:933–936. http://www.ncbi.nlm.nih.gov/pubmed/3914416

Kawai K, Yoshikawa H, Murayama Y, Okuda Y, Yamashita K (1989) Usefulness of palatinose as a caloric sweetener for diabetic patients. Horm Metab Res 21(6):338–340. http://www.ncbi.nlm.nih.gov/pubmed/2673967

Keyhani-Nejad F, Kemper M, Schueler R, Pivovarova O, Rudovich N, Pfeiffer AF (2016) Effects of Palatinose and Sucrose Intake on Glucose Metabolism and Incretin Secretion in Subjects With Type 2 Diabetes. Dia Care 39(3):e38-e39. http://www.ncbi.nlm.nih.gov/pubmed/26721819

König D, Theis S, Kozianowski G, Berg A (2012) Postprandial substrate use in overweight subjects with the metabolic syndrome after isomaltulose (Palatinose™) ingestion. Nutrition 28(6):651–656. http://www.ncbi.nlm.nih.gov/pubmed/22264450

Maeda A, Miyagawa J, Miuchi M, Nagai E, Konishi K, Matsuo T, Tokuda M, Kusunoki Y, Ochi H, Murai K, Katsuno T, Hamaguchi T, Harano Y, Namba M (2013) Effects of the naturally-occurring disaccharides, palatinose and sucrose, on incretin secretion in healthy non-obese subjects. J Diabetes Investig. 4(3):281–286. http://www.ncbi.nlm.nih.gov/pubmed/24843667

Pfeiffer AFH, Keyhani-Nejad F (2018) High glycemic index metabolic damage - a pivotal role of GIP and GLP-1. Trends Endocrinol Metab 29(5):289-299. https://www.cell.com/trends/endocrinology-metabolism/fulltext/S1043-2760(18)30046-8

Reviews:

Maresch CC, Petry SF, Theis S, Bosy-Westphal A, Linn T (2017) Low Glycemic Index Prototype Isomaltulose-Update of Clinical Trials. Nutrients 9(4). http://www.mdpi.com/2072-6643/9/4/381

EFSA Panel on Dietetic Products, Nutrition and Allergies (2011) Scientific Opinion on the substantiation of health claims related to the sugar replacers xylitol, sorbitol, mannitol, lactitol, isomalt, erythritol, D-tagatose, isomaltulose, sucralose and polydextrose and maintenance of tooth mineralization by decreasing tooth demineralization (…), and reduction of post-prandial glycemic responses (…) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 9(4):2076. http://www.efsa.europa.eu/de/efsajournal/doc/2076.pdf

3. Palatinose™ and long-term blood glucose control and insulin sensitivity

Longer-term studies investigated the effects of Palatinose™ on blood glucose control and insulin sensitivity. Some examples are listed here.

References:

Holub I, Gostner A, Theis S, Nosek L, Kudlich T, Melcher R, Scheppach W (2010) Novel findings on the metabolic effects of the low glycaemic carbohydrate isomaltulose (Palatinose™). Br J Nutr 103(12):1730–1737. http://www.ncbi.nlm.nih.gov/pubmed/20211041

Keller J, Kahlhöfer J, Peter A, Bosy-Westphal A (2016) Effects of Low versus High Glycemic Index Sugar-Sweetened Beverages on Postprandial Vasodilatation and Inactivity-Induced Impairment of Glucose Metabolism in Healthy Men. Nutrients 8(12):802. www.mdpi.com/2072-6643/8/12/802/pdf

Okuno M, Kim MK, Mizu M, Mori M, Mori H, Yamori Y (2010) Palatinose-blended sugar compared with sucrose: different effects on insulin sensitivity after 12 weeks supplementation in sedentary adults. Int J Food Sci Nutr 61(6):643–651. http://www.ncbi.nlm.nih.gov/pubmed/20367218

4. Palatinose™ and its role in weight management

As result of its slow release properties and resulting lower and sustained blood glucose response, Palatinose™ triggers less insulin release and therefore enables higher fat oxidation in energy metabolism. Higher levels of fat burning with Palatinose™ in comparison with conventional carbohydrates such as e.g. sucrose or maltodextrin (but also in comparison with fructose) have been observed in human intervention studies with healthy and overweight individuals at mostly sedentary conditions (see below) as well as with physically active trained persons (see 5.).
Related long-term benefits of Palatinose™ refer to body weight and body composition: Longer-term feeding studies in animals reported beneficial effects of Palatinose™ on body fat accumulation and body weight. Some publications provide first human data on the effect of Palatinose™ on body composition, i.e. visceral fat accumulation.

a) Palatinose™ and its influence on fat oxidation in energy metabolism

König D, Theis S, Kozianowski G, Berg A (2012) Postprandial substrate use in overweight subjects with the metabolic syndrome after isomaltulose (Palatinose™) ingestion. Nutrition 28(6):651–656. http://www.ncbi.nlm.nih.gov/pubmed/22264450

Arai H, Mizuno A, Sakuma M, Fukaya M, Matsuo K, Muto K, Sasaki H, Matsuura M, Okumura H, Yamamoto H, Taketani Y, Doi T, Takeda E (2007) Effects of a palatinose-based liquid diet (Inslow) on glycemic control and the second-meal effect in healthy men. Metabolism 56(1):115–121. (*Note: this study also shows a second meal effect*). http://www.ncbi.nlm.nih.gov/pubmed/17161233

Henry CJ, Kaur B, Quek RYC, Camps SG (2017) A Low Glycaemic Index Diet Incorporating Isomaltulose Is Associated with Lower Glycaemic Response and Variability, and Promotes Fat Oxidation in Asians. Nutrients 9(5). http://www.mdpi.com/2072-6643/9/5/473/htm

Review:
Maresch CC, Petry SF, Theis S, Bosy-Westphal A, Linn T (2017) Low Glycemic Index Prototype Isomaltulose-Update of Clinical Trials. Nutrients 9(4). http://www.mdpi.com/2072-6643/9/4/381

b) Long-term benefits of Palatinose™ on body weight and body composition

Okuno M, Kim MK, Mizu M, Mori M, Mori H, Yamori Y (2010) Palatinose-blended sugar compared with sucrose: different effects on insulin sensitivity after 12 weeks supplementation in sedentary adults. Int J Food Sci Nutr 61(6):643–651. http://www.ncbi.nlm.nih.gov/pubmed/20367218

Oizumi T, Daimon M, Jimbu Y, Kameda W, Arawaka N, Yamaguchi H, Ohnuma H, Sasaki H, Kato T (2007) A palatinose-based balanced formula improves glucose tolerance, serum free fatty acid levels

and body fat composition. Tohoku J Exp Med 212(2):91–99.
http://www.ncbi.nlm.nih.gov/pubmed/17548953

Yamori Y, Mori H, Mori M, Kashimura J, Sakamua T, Ishikawa PM, Moriguchi E, Moriguchi Y (2007) Japanese perspective on reduction in lifestyle disease risk in immigrant japanese brazilians: a double-blind, placebo-controlled intervention study on palatinose. Clin Exp Pharmacol Physiol 34(S5-S7). http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1681.2007.04759.x/abstract

5. Palatinose™ in sports nutrition

Palatinose™ provides the desired carbohydrate energy for physical activity in a more steady way and at the same time promotes a higher contribution of fat oxidation in energy metabolism than commonly used readily available carbohydrates. A higher level of fat burning is of particular interest in endurance activity where it may spare carbohydrate sources (glycogen) for enhanced endurance. The effect of Palatinose™ on substrate utilization and fat oxidation has been shown in a series of intervention studies.

References:

König D, Zdzieblik D, Holz A, Theis S, Gollhofer A (2016) Substrate Utilization and Cycling Performance Following Palatinose™ Ingestion: A Randomized, Double-Blind, Controlled Trial. Nutrients 8(7):390. http://www.mdpi.com/2072-6643/8/7/390

König D, Luther W, Poland V, Theis S, Kozianowski G, Berg A (2007) Metabolic effects of low-glycemic Palatinose™ during long lasting endurance exercise. Ann Nutr Metab 51(S1):69.

König D, Luther W, Polland V, Berg A (2007) Carbohydrates in sports nutrition impact of the glycemic index. AgroFood Anno 18(No. 5):9–10. http://www.teknoscienze.com/agro/pdf/SPORT-KONIG.pdf

Achten J, Jentjens RL, Brouns F, Jeukendrup AE (2007) Exogenous oxidation of isomaltulose is lower than that of sucrose during exercise in men. J Nutr 137(5):1143–1148.
http://www.ncbi.nlm.nih.gov/pubmed/17449572

Review:
Maresch CC, Petry SF, Theis S, Bosy-Westphal A, Linn T (2017) Low Glycemic Index Prototype Isomaltulose-Update of Clinical Trials. Nutrients 9(4). http://www.mdpi.com/2072-6643/9/4/381.

Research at Swansea University investigated the benefits of Palatinose™ on fat oxidation, metabolic control and incidences of hypoglycemia during physical activity in men with type 1 diabetes mellitus, which has been published in a series of studies including the following ones:

West DJ, Morton RD, Stephens JW, Bain SC, Kilduff LP, Luzio S, Still R, Bracken RM (2011) Isomaltulose improves postexercise glycemia by reducing CHO oxidation in T1DM. Med Sci Sports Exerc 43(2):204–210.http://journals.lww.com/acsm-msse/Fulltext/2011/02000/Isomaltulose_Improves_Postexercise_Glycemia_by.2.aspx

West DJ, Stephens JW, Bain SC, Kilduff LP, Luzio S, Still R, Bracken RM (2011b) A combined insulin reduction and carbohydrate feeding strategy 30 min before running best preserves blood glucose concentration after exercise through improved fuel oxidation in type 1 diabetes mellitus. J Sports Sci 29(3):279–289. http://www.ncbi.nlm.nih.gov/pubmed/21154013

Bracken RM, Page R, Gray B, Kilduff LP, West DJ, Stephens JW, Bain SC (2012) Isomaltulose improves glycemia and maintains run performance in type 1 diabetes. Med Sci Sports Exerc 44(5):800–808. http://www.ncbi.nlm.nih.gov/pubmed/22051571

Campbell MD, Walker M, Trenell MI, Stevenson EJ, Turner D, Bracken RM, Shaw JA, West DJ (2014) A low-glycemic index meal and bedtime snack prevents postprandial hyperglycemia and associated rises in inflammatory markers, providing protection from early but not late nocturnal hypoglycemia following evening exercise in type 1 diabetes. Diabetes Care 37:371–379. http://www.ncbi.nlm.nih.gov/pubmed/24784832

Campbell MD, Walker M, Bracken RM, Turner D, Stevenson EJ, Gonzalez JT, Shaw JA, West DJ (2015) Insulin therapy and dietary adjustments to normalize glycemia and prevent nocturnal hypoglycemia after evening exercise in type 1 diabetes: a randomized controlled trial. BMJ Open Diabetes Res Care 3(1):e000085. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4442134/pdf/bmjdrc-2015-000085.pdf

6. Palatinose™ and its potential in cognitive performance and mood

Carbohydrates and their supply of glucose to the brain play a central role in cognitive performance and mood. Palatinose™ with its steady and sustained glucose supply is of particular interest with respect to beneficial effects in the later phase after a meal. The potential of Palatinose™ in cognitive performance and mood has been addressed in the following key studies:

Young H, Benton D (2015) The effect of using isomaltulose (Palatinose™) to modulate the glycaemic properties of breakfast on the cognitive performance of children. Eur J Nutr 54(6):1013–1020. http://www.ncbi.nlm.nih.gov/pubmed/25311061

Young H, Benton D (2014) The glycemic load of meals, cognition and mood in middle and older aged adults with differences in glucose tolerance: A randomized trial. e-SPEN.Journal 9(4):e147-e154. http://www.clinicalnutritionespen.com/article/S2212-8263(14)00020-7/pdf

7. Palatinose™ is kind to teeth

Palatinose™ is no substrate for oral bacteria and therefore the first sugar that is kind to teeth. Its tooth-friendliness has been confirmed in pH telemetry studies. A corresponding claim has been accepted a) in the USA by FDA and implemented in the Code of Federal Regulations as well as b) in the EU following the publication of a positive EFSA opinion.

References:

Department of Health and Human Services - Food and Drug Administration (2007) 21 CFR Part 101 [Docket No 2006P-0487] Food labeling, health claims, dietary non-cariogenic carbohydrate sweeteners and dental caries. Federal Register Vol 72 No 179, September 17:p. 52783. http://www.fda.gov/OHRMS/DOCKETS/98fr/cf086.pdf

EFSA Panel on Dietetic Products, Nutrition and Allergies (2011) Scientific Opinion on the substantiation of health claims related to the sugar replacers xylitol, sorbitol, mannitol, lactitol, isomalt, erythritol, D-tagatose, isomaltulose, sucralose and polydextrose and maintenance of tooth mineralization by decreasing tooth demineralization (…), and reduction of post-prandial glycemic responses (…) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 9(4):2076. http://www.efsa.europa.eu/de/efsajournal/doc/2076.pdf

8. Palatinose™ in infant and small children nutrition

Palatinose™ is suitable for infants from the age of about 4-6 months, when complementary feeding starts. It provides benefits to milk formula applications when used in place of maltodextrin, glucose or other high glycemic carbohydrates, as it is slowly and fully available and therefore delivers the necessary energy for the infants and small children in a more balanced way. Hence, Palatinose™ brings the metabolic profile closer to that of mother milk. The suitability and good tolerance of Palatinose™ have both been confirmed in a study with infants.

Reference:

Fleddermann M, Rauh-Pfeiffer A, Demmelmair H, Holdt L, Teupser D, Koletzko B (2016) Effects of a Follow-On Formula Containing Isomaltulose (Palatinose™) on Metabolic Response, Acceptance, Tolerance and Safety in Infants: A Randomized-Controlled Trial. PloS ONE 11(3):e0151614. http://www.ncbi.nlm.nih.gov/pubmed/26987056

In case of question or further enquiries, please, do not hesitate to contact BENEO's Nutrition Communication team.

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