Original Article

Dietary galacto-oligosaccharides improve skin health: a randomized double blind clinical trial

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Background and Objectives: To study the effects of galacto-oligosaccharides (GOS) on the skin, we investigated skin-related parameters in healthy adults who received GOS for 12 weeks. **Methods and Study Design:** This double-blind, randomized, placebo-controlled study included subjects divided into two groups (control and GOS) by stratified block randomization. The GOS group received 1.0 g of GOS twice a day, whereas the control group received only vehicle. **Results:** The results showed that the increase in corneometer values from baseline to week 12 was significantly greater in the GOS group than in the control group (6.91 vs 2.88 arbitrary units, $p<0.05$). The transepidermal water loss (TEWL) in the GOS group was reduced significantly after 12 weeks of GOS treatment (20.1 g/h/m^2 at baseline vs 17.5 g/h/m^2 at week 12, $p<0.05$). The differences in total and percentage of wrinkle areas between the two groups were statistically significant after 12 weeks of GOS treatment ($p<0.05$). **Conclusion:** Our findings support that oral treatment with GOS is beneficial to the skin and present the possibility of new nutritional strategies for skin care.

Key Words: galacto-oligosaccharide, prebiotics, probiotics, skin hydration, wrinkle

INTRODUCTION

Oligosaccharides show interesting properties, and some are already recognized and included in foods as ingredients.[1] They are an important factor that promotes the growth of intestinal flora dominated by bifidobacteria and lactobacilli.[2] On the basis of the analysis of human milk oligosaccharides, a mixture of 90% short-chain galacto-oligosaccharides (GOS) and 10% long-chain fructooligosaccharides (FOS) have been developed.[3] Studies in preterm and term infants have shown that food supplementation with GOS and FOS produces an intestinal flora similar to that found in breastfed infants.[4] FOS are well known for their contribution to digestive health. GOS have also emerged, with strong clinical evidence, as beneficial to both digestive and immune health.[5] As a stable, soluble ingredient, GOS are an ideal choice for formulating foods and beverages for digestive and immune health. Owing to its similarity to the human milk oligosaccharides, GOS have attracted worldwide attention from researchers.[5,6]

Because GOS are hydrolyzed only by a specific group of colonic bacteria, they are classified as prebiotics.[1] Prebiotics are typically nondigestible fibre compounds that pass undigested through the upper part of the gastrointestinal tract and stimulate the growth or activity of advantageous bacteria that colonize the large bowel by acting as a substrate for them.[1,7] Prebiotics can provide benefits not only for the gut but also for the skin. The intestine is the body's main immune organ, and the mucosal immune system of the gut is linked to the immune system of the skin through migration of immune cells. Prebiotics may also influence the bioavailability of nutrients and thereby affect the condition of the skin.[8,9]

The skin and digestive tract are the largest organs of the human body. They are also two of the oldest structures developed in the evolutionary process to provide the organism with essential information about the outside world, largely by delivering nutrients from the outside world. The digestive tract has a similar and parallel role to that of the skin in providing nutrients to the body. Nutrients, whether delivered through the digestive tract or skin, can be seen as a source of information that literally transforms the body.[10] Cosmetics have long been applied to prevent skin aging. However, while the benefits of cosmetics to skin are promising, they are limited to the topical site of application.[11] On the other hand, the con-

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Manuscript received 17 December 2015. Initial review completed 19 January 2016. Revision accepted 04 March 2016.
doi: 10.6133/apjcn.052016.05

sumption of foods that contain prebiotics has been found to improve the condition of the skin.[12] Functional foods targeting "beauty from within" are already on the market, and some have limited scientific evidence suggesting their efficacy.[13]

In this study, we investigated whether intake of GOS had beneficial effects on human skin and may represent a novel approach for skin care. To this end, we investigated skin-related parameters in healthy adults who received GOS for 12 weeks.

MATERIALS AND METHODS

Preparation of GOS

The GOS used in this study were provided by Neo Cremar Co. (Seoul, South Korea). Briefly, batch reactions were performed by incubating β-galactosidase with a 40°Bx to 45°Bx lactose solution in a 100-L incubator shaker at 150 rpm. Lactose (25 kg) was dissolved in distilled water (60 L), and 0.08% β-galactosidase from *Bacillus circulans* was added to synthesize GOS at 55°C and pH 6.0 for 24 h. All reactions were terminated by incubation at 100°C for 10 min. Then, 100 mL of 20% GOS syrup produced by the β-galactosidase was fermented by using 9% weight fresh yeast (*Saccharomyces cerevisiae* L1) in an incubator shaker at 100 rpm and 30°C for 24 h. The resulting solution was then filtered and treated with active carbon for decolorization. Ion exchange chromatography (Amberlite CG-120-II1 × 8, Fluka, Buchs, Switzerland) was applied for further purification. The pooled fractions were evaporated to 45°Bx and dried with a spray dryer.

Subjects

Subjects were recruited through advertisements in a local newspaper. Individuals who responded to the advertisements were interviewed in order to ensure they met the experiment criteria. Eighty-four healthy Korean volunteers, aged 30–69 years, with fine wrinkles at the outer corner of the eyes, called lateral canthal lines, were chosen for this study. Before enrolling in the study, all the participants were informed of the risks, benefits, and possible complications of the treatment, and each participant provided investigators with a written informed consent. The exclusion criteria were Fitzpatrick skin types I or IV, allergies, photosensitivity, tanning sunburns, infections, pregnancy, and breastfeeding. Also excluded were subjects who had undergone wrinkle removal or peeling procedures within the previous 6 months.

Study protocol

The study was conducted in accordance with Good Clinical Practice guidelines, the Declaration of Helsinki, and local laws and regulations. The protocol was approved by Korea University and patients gave written informed consent (KU-IRB-14-119-A-2-[R-P-1]). The double-blind, randomized, placebo-controlled study included subjects who were divided into two (control and GOS) groups by stratified block randomization. For 12 weeks, the subjects in the GOS group were asked to take GOS (1 g in a capsule) twice a day. The total daily GOS dose was 2 g. This dosage was selected based on preliminary studies.[14,15] The control group received only the vehicle (100% dextrin), which was the same size and color as the GOS capsule. The subjects were asked not to change their diet or lifestyle during the study.

Skin assessments

The corneometer value was measured by using Corneometer CM 825 (Courage and Khazaka Electronic GmbH, Cologne, Germany). Corneometer CM 825 uses the high dielectric constant of water for analyzing the water-related changes in the electrical capacitance of the skin. It displays hydration measurements in system-specific arbitrary units (AU).[16] Transepidermal water loss (TEWL) was measured by using TEWAmeter TM 300 (Courage and Khazaka Electronic GmbH). The TEWAmeter TM 300 measurements were based on diffusion in an open chamber and measured as $g/m^2/h$.[17] Extent of wrinkling was measured by using a replica method. Briefly, after an adhesive paper (diameter, 11 mm) was attached, translucent silicon was mixed in a small plastic cup containing two components, a basic substance and a catalyst (Courage and Khazaka Electronic GmbH). A layer of the silicone mixture was spread over the restricted area of the adhesive paper and left to dry for 5 min. When the silicone mixture had dried sufficiently, the specimen was stored in a tracing paper envelope until analysis. The skin replica was analyzed by using Skin-Visiometer SV 600 (Courage and Khazaka Electronic GmbH). The total wrinkle area (mm^2), percentage of wrinkle area (%), average wrinkle depth (μm), and number of wrinkles were measured.

No skin-care products were applied to the measured sites for at least 2 h before the measurements. A small area of each location was wiped with ethanol 1 h before the parameters were measured in a room at a temperature of 20-25°C and relative humidity of 30-40%. The crow's foot area was measured three times, and the mean value was recorded and analyzed. The Corneometer and TEWL measurements were repeated for each subject every fourth week (four times), and wrinkling was measured for each subject twice, at baseline and week 12. After week 12, adverse effects, including erythema, edema, bruising, and altered pigmentation, were assessed by questioning subjects and observing skin responses.

Statistical analysis

All statistical analyses were performed by using the Statistical Package for Social Sciences version 12.0 (SPSS Inc., Chicago, IL, USA). The differences between the two groups (control vs GOS group) were statistically evaluated by performing a *t* test. A repeated-measures analysis of variance followed by Bonferroni-adjusted pairwise comparisons was used to assess the differences in the change from baseline to each week within groups. All data were two-sided at the 5% significance level and were reported as means ± standard error of the mean (SEM).

RESULTS

The baseline characteristics are listed in Table 1. Eighty-four individuals were selected for participation in this study. Of these individuals, five were withdrawn from the trial as follows: four (two from the control group and two from the GOS group) failed to complete the study, and

Table 1. Baseline skin characteristics of healthy adults

Variable	GOS group (n=39)	Control group (n=40)
Gender, n (%)		
Women	36 (92.3)	37 (92.5)
Men	3 (7.7)	3 (7.5)
Age (years)		
Mean	51.1±1.31	50.4±1.33
Range (min-max)	34-68	32-66
Menopausal status, n (%)	14 (35.9)	15 (37.5)
Blood pressure (mmHg)		
Systolic blood pressure	125±9.46	129±5.67
Diastolic blood pressure	91.1±6.25	87.3±5.51
Pulse (beats/min)	70.2±6.78	71.2±6.68
Blood glucose (mg/dL)	138±20.7	130±12.2
Body mass index (kg/m^2)	22.9±3.02	23.5±2.13
Energy intake (kcal/day)	2011±416	1879±358
Carbohydrate (%)	69.1±4.02	68.7±2.33
Protein (%)	17.8±2.15	17.2±1.72
Fat (%)	13.1±2.28	14.1±2.12
Metabolic disease, n (%)	0 (0)	0 (0)
Skin diseases, n (%)	0 (0)	0 (0)
Drug use, n (%)	0 (0)	0 (0)
Corneometer value (AU)	70.5±1.76	73.0±1.45
TEWL (g/h/m^2)	20.1±1.09	17.8±1.12
Total wrinkle area (mm^2)	14.1±1.08	15.0±0.99
Percentage of wrinkle area (%)	53.0±4.06	56.3±3.70
Wrinkle depth (cm)	5.54±0.57	5.09±0.77
Number of wrinkles	304±32.4	244±35.6

AU: arbitrary units; GOS: galacto-oligosaccharide; TEWL: transepidermal water loss.
All data were reported as means±standard error of the mean.

one (from GOS group) was noncompliant. As a result, 79 participants met the study requirements (male: 6 female: 73, age 30–39 years: 3, 40–49 years: 37, 50–59 years: 25, 60–69 years: 14). None of the participants withdrew from the study because of GOS treatment-related adverse effects. No adverse effects were experienced by the subjects, and none of the withdrawals were considered to be due to the study products. The control (age: 50.4 years) and GOS groups (age: 51.1 years) ultimately consisted of 40 and 39 participants, respectively. The control and GOS groups had mean Corneometer values of 73.0 and 70.5 AU and TEWL of 17.8 and 20.1 g/h/m^2, respectively. Furthermore, the control and GOS groups had similar results regarding the following wrinkle parameters: total wrinkle area, percentage of wrinkle area, wrinkle depth, and number of wrinkles. The initial values of all the variables did not significantly differ between the two groups. The subjects were healthy adults who did not have metabolic diseases, use any pharmaceutical drugs, or consume alcohol.

Figure 1 and 2 shows the changes in Corneometer values and TEWL, respectively. The increase in Corneometer value from the baseline to week 12 was significantly greater in the GOS group than in the control group (6.91 vs 2.88 AU, respectively; $p<0.05$). The Corneometer values in the control group were not significantly different between baseline and week 12, whereas GOS treatment significantly influenced the Corneometer values at 4 weeks (70.5 AU at baseline vs 73.0 AU at week 4, $p<0.05$).

The initial values of TEWL did not significantly differ between the two groups (Table 1). At week 4, the reduction in TEWL from the baseline in the GOS group was significantly greater than that in the control group (−1.93 vs. −0.52 g/h/m^2, respectively; $p<0.05$). TEWL did not significantly differ between the baseline and week 12 in the control group but was significantly reduced in the GOS group after 12 weeks of GOS treatment (20.1 g/h/m^2 at baseline vs 17.4 g/h/m^2 at week 12, $p<0.05$).

Figure 3 presents the changes in wrinkle formation after 12 weeks of GOS treatment. The differences in total and percentage of wrinkle area between the control and

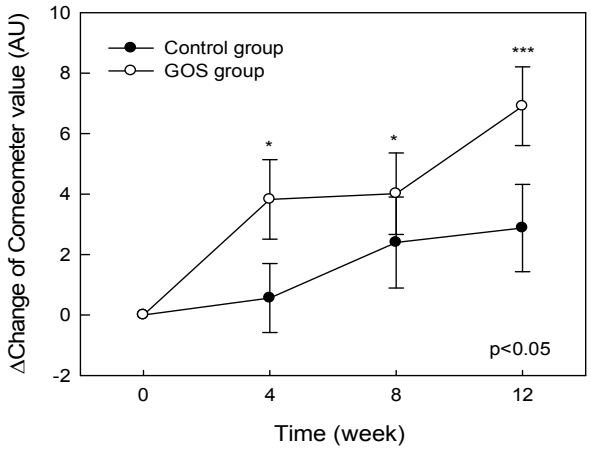

Figure 1. Effects of galacto-oligosaccharides (GOS) on the Corneometer value in the healthy adults. The asterisks indicate significant differences ($^*p<0.05$, $^{***}p<0.001$) between the baseline and the indicated week by a repeated-measures analysis of variance followed by Bonferroni-adjusted pairwise comparisons within groups. The *p*-value shown on the graph indicates a significant difference between changes in the two groups at the indicated week by *t* test. All data were two-sided at the 5% significance level and are reported as means±standard error of the mean.

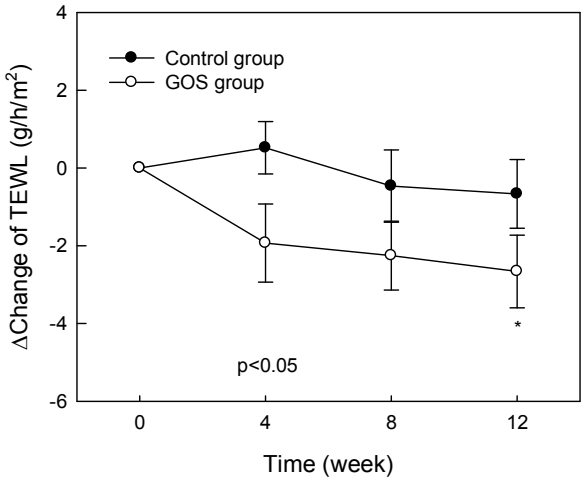

Figure 2. Effects of galacto-oligosaccharides (GOS) on transepidermal water loss (TEWL) in healthy adults. Asterisks indicate a significant difference ($^{*}p<0.05$) between the baseline and the indicated week by a repeated-measures analysis of variance followed by Bonferroni-adjusted pairwise comparisons within groups. The p value shown on the graph indicates a significant difference between changes in the two groups at the indicated week by t test. All data were two-sided at the 5% significance level and are reported as means±standard error of the mean.

GOS groups were significant after 12 weeks of GOS treatment ($p<0.05$). The GOS group showed a reduction in total wrinkle area and percentage of wrinkle area after 12 weeks of GOS treatment (total wrinkle area: −3.25 mm^2; percentage of wrinkle area: −12.2%), whereas the control group showed a slight increase in these parameters (total wrinkle area: 1.07 mm^2, percentage of wrinkle area: 4.02%). Furthermore, the wrinkle depths and number of wrinkles in the GOS group were also lower than those in the control group, although these differences were not significant. As shown in Figure 4, the replica photographs of a subject who received GOS for 12 weeks showed that wrinkles in the crow's feet region were markedly improved compared with the baseline.

DISCUSSION

Purba et al investigated the association between actinic skin damage and dietary intake.[18] This study addressed whether food and nutrient intakes were correlated with skin wrinkling in a sun-exposed site. The results suggested that subjects with a lower intake of milk/milk-products, butter, margarine and sugar products had less skin wrinkling in a sun-exposed site. This study illustrated that skin wrinkling in a sun-exposed site in older people of various ethnic backgrounds may be influenced by the types of foods consumed.

Currently, the use of prebiotics as functional food ingredients to manipulate the composition of gut microbiota in order to improve health has sparked great interest.[19] For the live microbiota (probiotics), which are intended to colonize the large intestine and confer physiological health benefits to the host, specific substrates (prebiotics), which confer a health benefit to the host associated with modulating the microbiota, may be used.[20] Prebiotics can improve the survival of a probiotic organism because its specific substrate is readily available for its fermentation and results in advantages to the host that the live microorganisms and prebiotic offer.[20,21]

Probiotics are known for their potential to modify host immune responses, providing an additional possible mechanism aimed at skin health. The mechanistic basis of skin effects induced by probiotics is thought to be represented by changes in systemic immune responses. In particular, the modulation of specific T-cell subsets such as stimulation of T-helper type 1 cells in the gut mucosa,

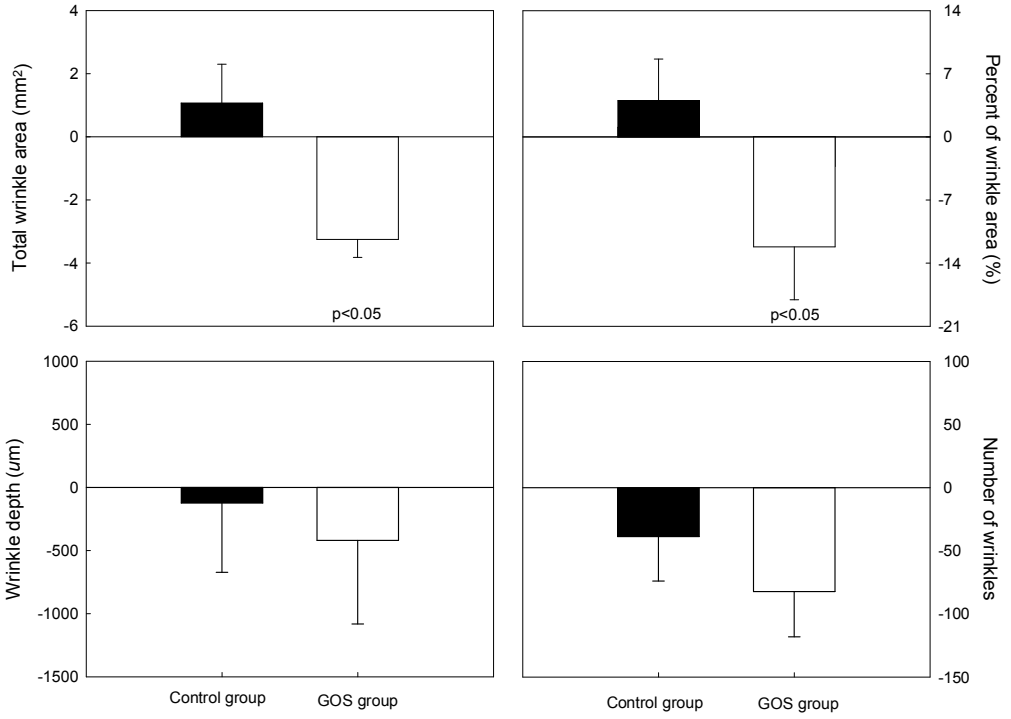

Figure 3. Effects of galacto-oligosaccharides (GOS) on wrinkle formation in healthy adults. The p values indicate a significant difference between changes in the two groups at each week by t test. All data were two-sided at the 5% significance level and are reported as means±standard error of the mean.

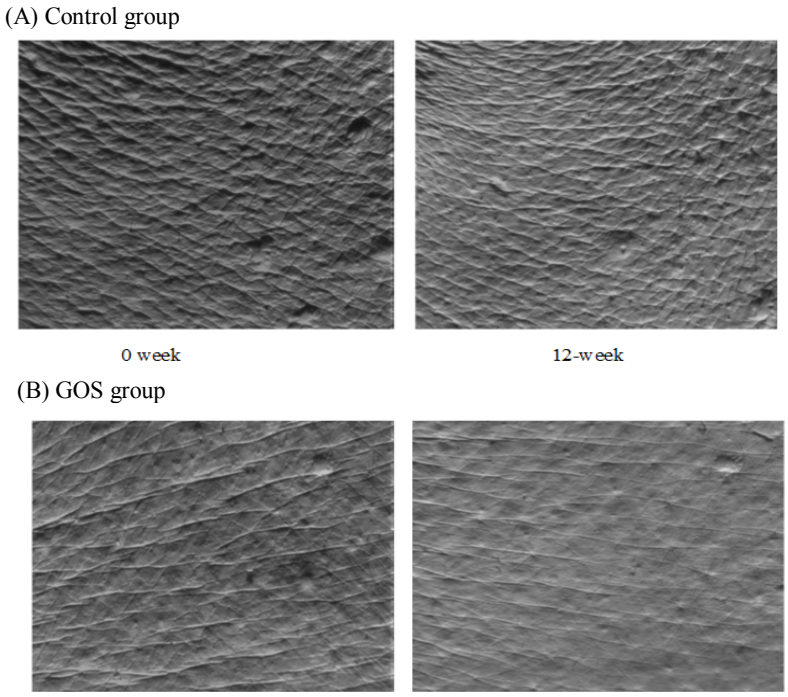

Figure 4. Replica photography of crow's feet in healthy adults who received galacto-oligosaccharides (GOS) for 12 weeks.

which may subsequently influence immune responses in other tissues, may play a role.[22,23] Probiotics protect the skin immune system against ultraviolet B radiation-induced immunosuppressive effects in hairless mice.[22] Similar effects have been described in humans, and it has been proposed that the consumption of probiotics may represent a novel approach to protect the skin immune system.[24,25] The significant improvement on the course of atopic dermatitis has been reported in infants given probiotic-supplemented elimination diets.[26,27] Another target for probiotics may be skin barrier function. A double-blind, randomized clinical study has shown that a 24-week skin intervention with a fermented dairy product in female volunteers significantly reduced TEWL and improved stratum corneum barrier function compared with a placebo product.[28]

GOS as a prebiotic also effectively blocked atopic dermatitis-like skin lesions in a human-like model of atopic dermatitis, NC/Ng a mice, by at least partly inducing production of interleukin 10 and suppressing the production of cytokines such as interleukin 17, which are involved in skin inflammation.[29] In our preliminary tests,[12] we found that GOS administration in hairless mice suppressed the increase in TEWL and concomitant decrease in skin hydration, which reflects barrier function perturbation after ultraviolet B irradiation. Furthermore, GOS administration also resulted in increased *CD44* gene expression, which was associated with maintenance of hyaluronic acid homeostasis, compared with no treatment. The effects of GOS plus a mixture of four probiotics in preventing allergic diseases were reported in pregnant women and their infants.[30] It has been speculated that not only diseased but also healthy skin may benefit from oral treatment with prebiotics.

In this study, oral treatment with GOS in healthy adults improved skin hydration (Corneometer value and TEWL), which is critical for maintaining healthy skin and an important component of basic skin care (Figure 1 and 2). Our results also indicated that GOS improved total and percentage of wrinkle area in healthy adults compared with non-treated subjects after 12 weeks of treatment (Figure 3 and 4).

In our preliminary tests,[31] several probiotics (*Lactobacillus acidophilus*, *Lactobacillus casei*, *Bifidobacterium longum*, and *Bifidobacterium bifidum*) in GOS showed higher cell growth than the other GOS after 12 h of culture except *B. longum* culture at 36 h. These results suggest that GOS was a good substrate and carbon source for supporting the growth of probiotics. The intestinal flora is part of a complex ecosystem, and many of its constituent bacteria remain unidentified.[32] However, strong evidence suggests that the intestinal flora influences the postnatal development of the immune system. Stimulation of the entire intestinal flora by prebiotics might be a more effective method of altering immune development than by adding bacterial species to the intestinal ecosystem. In contrast to probiotics that introduce exogenous bacteria into the colonic microbiota, prebiotics aim to stimulate the growth of one or a limited number of the potentially health-promoting indigenous microorganisms, thus modulating the composition of the natural ecosystem.[32,33]

Therefore, GOS as a prebiotic might more effectively promote skin health than single or complex probiotics because of the increase of health-promoting indigenous microorganisms. In conclusion, our findings support that oral treatment with GOS was beneficial to the skin, and present the possibility of new nutritional strategies for skin care. However, further research is necessary to fully understand the effects of GOS on skin health and to understand in detail how ingested prebiotics might influence the skin through intestine-mediated changes.

ACKNOWLEDGMENTS

This work was financially supported by the Ministry of Trade,

Industry and Energy (MOTIE); the Korea Institute for Advancement of Technology (KIAT); and the Honam Institute for Regional Program Evaluation through the Leading Industry Development for Economic Region.

AUTHOR DISCLOSURES

None of the authors have any conflicts of interest associated with this study. None of the authors had a financial interest or personal affiliation that compromised the scientific integrity of this work.

REFERENCES

1. Roberfroid M. Health benefits of non-digestible oligosaccharides. In: David Kritchevsky CB, editor. Dietary Fiber in Health and Disease. New York, USA: Springer; 1997. pp. 211-9.
2. Boehm G, Stahl B. Oligosaccharides. In: Mattila-Sandholm T, Saarela M, editors. Functional Dairy Products. Amsterdam, Netherlands: Elsevier B.V.; 2003. pp. 203-43.
3. Boehm G, Jelinek J, Stahl B, van Laere K, Knol J, Fanaro S, Moro G, Vigi V. Prebiotics in infant formulas. J Clin Gastroenterol. 2004;38:S76-9.
4. Knol J, Scholtens P, Kafka C, Steenbakkers J, Gro S, Helm K et al. Colon microflora in infants fed formula with galacto-and fructo-oligosaccharides: more like breast-fed infants. J Pediatr Gastr Nutr. 2005;40:36-42.
5. Sangwan V, Tomar S, Singh R, Singh A, Ali B. Galactooligosaccharides: novel components of designer foods. J Food Sci. 2011;76:R103-R11.
6. Depeint F, Tzortzis G, Vulevic J, I'Anson K, Gibson GR. Prebiotic evaluation of a novel galactooligosaccharide mixture produced by the enzymatic activity of Bifidobacterium bifidum NCIMB 41171, in healthy humans: a randomized, double-blind, crossover, placebo-controlled intervention study. Am J Clin Nutr. 2008;87:785-91.
7. Sousa V, Santos E, Sgarbieri V. The Importance of prebiotics in functional foods and clinical practice. Food Nutr Sci. 2011;2:133-44.
8. Krutmann J. Pre-and probiotics for human skin. J Dermatol Sci. 2009;54:1-5.
9. Bockmühl D, Jassoy C, Nieveler S, Scholtyssek R, Wadle A, Waldmann-Laue M. Prebiotic cosmetics: an alternative to antibacterial products. Int J Cosmetic Sci. 2007;29:63-4.
10. Badmaev V, Majeed M. Advantage of combined nutraceuticals and cosmeceuticals: Nourishment through the skin and the digestive tract. Nutra Cos. 2005;4:18-21.
11. Kawada A, Konishi N, Momma T, Oiso N, Kawara S. Evaluation of anti-wrinkle effects of a novel cosmetic containing retinol using the guideline of the Japan Cosmetic Industry Association. J Dermatol. 2009;36:583-6.
12. Hong K-B, Jeong MG, Kim JH, Park Y, Suh HJ. Photoprotective effects of reinforced galactooligosaccharides supplementation against skin damage in hairless mice (LB357). FASEB J. 2014; 28:LB357.
13. Piccardi N, Manissier P. Nutrition and nutritional supplementation: impact on skin health and beauty. Dermatoendocrinol. 2009;1:271-4.
14. Tamai S, Ohtsuka K, Ozawa O, Uchida T. Effect of a small amount of galactooligosaccharide on fecal Bifidobacterium. J Jpn Soc Nutr Food Sci. 1992;45:456-60.
15. Ito M, Deguchi Y, Matsumoto K, Kimura M, Onodera N, Yajima T. Influence of galactooligosaccharides on the human fecal microflora. J Nutr Sci Vitaminol. 1993;39:635-40.
16. Gerhardt L-C, Strässle V, Lenz A, Spencer N, Derler S. Influence of epidermal hydration on the friction of human skin against textiles. J Roy Soc Interface. 2008;5:1317-28.
17. Shoaf K, Mulvey GL, Armstrong GD, Hutkins RW. Prebiotic galactooligosaccharides reduce adherence of enteropathogenic Escherichia coli to tissue culture cells. Infect Immun. 2006;74:6920-8.
18. Purba Mb, Kouris-Blazos A, Wattanapenpaiboon N, Lukito W, Rothenberg EM, Steen BC, Wahlqvist ML. Skin wrinkling: can food make a difference? J Am Coll Nutr. 2001;20:71-80.
19. Laparra JM, Sanz Y. Interactions of gut microbiota with functional food components and nutraceuticals. Pharmacol Res. 2010;61:219-25. doi: 10.1016/j. phrs.2009.11.001.
20. Collins MD, Gibson GR. Probiotics, prebiotics, and synbiotics: approaches for modulating the microbial ecology of the gut. Am J Clin Nutr. 1999;69:1052s-7s.
21. Chauhan SV, Chorawala MR. Probiotics, prebiotics and synbiotics. Int J Pharmaceut Sci Res. 2012;3:711-26.
22. Lammers KM, Brigidi P, Vitali B, Gionchetti P, Rizzello F, Caramelli E, Matteuzzi D, Campieri M. Immunomodulatory effects of probiotic bacteria DNA: IL-1 and IL-10 response in human peripheral blood mononuclear cells. FEMS Immunol Med Mic. 2003;38:165-72.
23. Pohjavuori E, Viljanen M, Korpela R, Kuitunen M, Tiittanen M, Vaarala O, Savilahti E. Lactobacillus GG effect in increasing IFN-γ production in infants with cow's milk allergy. J Allergy Clin Immun. 2004;114:131-6.
24. Bouilly D, Jeannes C, Duteil L, Pierard G, Picardi N, Manisier P. Probiotic and carotenoids: an innovative nutritional approach to help skin against sun damage. Paper presented at: 21st Word Congress, Buenos Aires, Argentine, 2007.
25. Guéniche A, Benyacoub J, Buetler TM, Smola H, Blum S. Supplementation with oral probiotic bacteria maintains cutaneous immune homeostasis after UV exposure. Eur J Dermatol. 2006;16:511-7.
26. Isolauri E, Arvola T, Sütas Y, Moilanen E, Salminen S. Probiotics in the management of atopic eczema. Clin Exp Allergy. 2000;30:1605-10.
27. Rosenfeldt V, Benfeldt E, Nielsen SD, Michaelsen KF, Jeppesen DL, Valerius NH, Paerregaard A. Effect of probiotic Lactobacillus strains in children with atopic dermatitis. J Allergy Clin Immun. 2003;111:389-95.
28. Puch F, Samson-Villeger S, Guyonnet D, Blachon JL, Rawlings AV, Lassel T. Consumption of functional fermented milk containing borage oil, green tea and vitamin E enhances skin barrier function. Exp Dermatol. 2008;17: 668-74.
29. Tanabe S, Hochi S. Oral administration of a galactooligosaccharide preparation inhibits development of atopic dermatitis-like skin lesions in NC/Nga mice. Int J Mol Med. 2010;25:331-6.
30. Kukkonen K, Savilahti E, Haahtela T, Juntunen-Backman K, Korpela R, Poussa T, Tuure T, Kuitunen M. Probiotics and prebiotic galacto-oligosaccharides in the prevention of allergic diseases: a randomized, double-blind, placebo-controlled trial. J Allergy Clin Immun. 2007;119:192-8.
31. Hong K-B, Kim K-M, Park Y, Suh HJ. Supplementation of reinforced galactooligosaccharides modulates intestinal l microbiota. FASEB J. 2013;27:LB263.
32. Köhler H, McCormick BA, Walker WA. Bacterial-enterocyte crosstalk: cellular mechanisms in health and disease. J Pediatr Gastr Nutr. 2003;36:175-85.
33. Kalliomäki M, Salminen S, Arvilommi H, Kero P, Koskinen P, Isolauri E. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. Lancet. 2001;357:1076-9.