GALACTOOLIGOSACCHARIDES FOR PREVENTING INJURY AND/OR PROMOTING HEALING OF THE GASTROINTESTINAL TRACT

FIELD OF THE DISCLOSURE

[0001] The present disclosure relates to the use of galactooligosaccharides for preventing injury to the gastrointestinal tract and/or enhancing the healing of an injured gastrointestinal tract in an individual. More particularly, the present disclosure relates to human milk fortifiers, preterm and term infant formulas, pediatric formulas, follow on formulas, and adult nutritionals comprising galactooligosaccharides that can enhance the expression of various mucin-associated proteins, thereby improving an individual's gastrointestinal prevention and repair function.

BACKGROUND OF THE DISCLOSURE

[0002] Individuals undergoing various therapies or having various diseases and/or conditions are generally more susceptible to intestinal mucosa (gastrointestinal) injury than are healthy individuals. The expression of mucin-associated proteins, or secretory proteins, is an integral part of an individual's natural ability to prevent and/or repair intestinal injuries. Specifically, the expression of these mucin-associated proteins aids in the healing of intestinal mucosa injuries and in the prevention of further injuries by protecting the mucosa from insults, stabilizing the mucus layer, reducing inflammation of the mucus layer, and promoting the healing of the epithelial tissue.

[0003] Not all individuals, however, have an adequate expression of mucin-associated proteins to affect prevention and needed intestinal repair, which may result in an increased risk of translocation, sepsis, and possibly death. Further, there are currently no commercially available nutritional compositions that contain mucin-associated proteins, such as trefoil factor 3 (TFF3), or known methods of increasing the expression of mucin-associated proteins through the administration of an additional component to aid individuals having inadequate natural intestinal repair functions.

[0004] As such, it would be desirable to provide nutritional compositions that can produce nutritional benefits such as aiding in the prevention and healing of intestinal mucosal injuries by enhancing the expression of mucin-associated proteins. It would

additionally be beneficial if the nutritional compositions could also improve the barrier function and reduce the inflammation of the injured gastrointestinal tract.

SUMMARY OF THE DISCLOSURE

[0005] The present disclosure is directed to the use of nutritional compositions, including human milk fortifiers, preterm and term infant formulas, pediatric formulas, follow on formulas and adult formulas including galactooligosaccharides alone or in combination with other components such as other prebiotic oligosaccharides and/or probiotics, for preventing injury to the gastrointestinal tract and/or enhancing the healing of the gastrointestinal tract of an infant, toddler, child, or adult. More particularly, the nutritional compositions can improve gastrointestinal healing through enhancing the expression of various mucin-associated proteins, which can stabilize the mucus layer, reduce inflammation, and promote healing of epithelial tissue.

[0006] One embodiment is directed to a method of enhancing healing of the gastrointestinal tract of an individual. The method comprises identifying an individual having an injured gastrointestinal tract and administering to the individual a nutritional composition comprising a galactooligosaccharide.

[0007] Another embodiment is directed to a method of reducing the incidence of intestinal mucosa injury. The method comprises identifying an individual susceptible to an intestinal mucosa injury and administering to the individual a nutritional composition comprising a galactooligosaccharide.

[0008] Another embodiment is directed to a method of improving the barrier function in the gastrointestinal tract of an individual. The method comprises identifying an individual in need of an increased barrier function of the gastrointestinal tract and administering to the individual a nutritional composition comprising a galactooligosaccharide.

[0009] Another embodiment is directed to a method of reducing the incidence of inflammation of the gastrointestinal tract of an individual. The method comprises identifying an individual susceptible to inflammation of the gastrointestinal tract and

administering to the individual a nutritional composition comprising a galactooligosaccharide.

[0010] It has now been discovered that galactooligosaccharides can enhance the expression of various mucin-associated proteins, such as TFF3, MUC-2, and RELMb, which are an integral part of the intestinal repair system. Specifically, it has been found that enhancing the expression of these mucin-associated proteins through the administration of a composition containing galactooligosaccharides, aids in cell healing, resolution of inflammation, and promotion of barrier function.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIGS. 1A-1C are charts depicting the effect of galactooligosaccharides on the expression of several genes involved in the healing response of the gastrointestinal tract as measured in Example 20.

[0012] FIGS. 2A-2E are charts depicting the dose dependency of galactooligosaccharides on the expression of several genes involved in the healing response of the gastrointestinal tract as measured in Example 21.

[0013] FIGS. 3A and 3B are charts depicting the effect of the combination of galactooligosaccharides and *Bifidobacterium lactis* on the expression of several genes involved in the healing response of the gastrointestinal tract as measured in Example 22.

[0014] FIGS. 4A-4E are charts depicting the effect of the combinations of galactooligosaccharides and *Bifidobacterium lactis* and galactooligosaccharides and *Lactobacillus acidophilus* on the expression of several genes involved in the healing response of the gastrointestinal tract as measured in Example 23.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0015] The nutritional compositions and methods described herein utilize galactooligosaccharides (GOS) alone or in combination with one or more additional components for preventing injury to the gastrointestinal tract and/or enhancing the healing of the gastrointestinal tract. These and other essential features of the nutritional

compositions and methods, as well as some of the many optional variations and additions, are described in detail hereafter.

[0016] The term "retort packaging" and "retort sterilizing" are used interchangeably herein, and unless otherwise specified, refer to the common practice of filling a container, most typically a metal can or other similar package, with a nutritional liquid and then subjecting the liquid-filled package to the necessary heat sterilization step, to form a sterilized, retort packaged, nutritional liquid product.

[0017] The term "aseptic packaging" as used herein, unless otherwise specified, refers to the manufacture of a packaged product without reliance upon the above-described retort packaging step, wherein the nutritional liquid and package are sterilized separately prior to filling, and then are combined under sterilized or aseptic processing conditions to form a sterilized, aseptically packaged, nutritional liquid product.

[0018] The terms “fat” and “oil” as used herein, unless otherwise specified, are used interchangeably to refer to lipid materials derived or processed from plants or animals. These terms also include synthetic lipid materials so long as such synthetic materials are suitable for oral administration to humans.

[0019] The term "human milk oligosaccharide” or “HMO", unless otherwise specified, refers generally to a number of complex carbohydrates found in human breast milk that can be in acidic or neutral form, and to precursors thereof. Exemplary non-limiting human milk oligosaccharides include 3’-sialyllactose, 6’-sialyllactose, 3’-fucosyllactose, 2’-fucosyllactose, and lacto-N-neo-tetraose. An exemplary human milk oligosaccharide precursor includes sialic acid.

[0020] The term “shelf stable” as used herein, unless otherwise specified, refers to a nutritional product that remains commercially stable after being packaged and then stored at 18-24^{o}C for at least 3 months, including from about 6 months to about 24 months, and also including from about 12 months to about 18 months.

[0021] The terms “nutritional formulation” or “nutritional composition” as used herein, are used interchangeably and, unless otherwise specified, refer to synthetic formulas including nutritional liquids, nutritional powders, nutritional supplements, and any other

nutritional food product as known in the art. The nutritional powders may be reconstituted to form a nutritional liquid, all of which comprise one or more of fat, protein and carbohydrate and are suitable for oral consumption by a human.

[0022] The term "nutritional liquid" as used herein, unless otherwise specified, refers to nutritional compositions in ready-to-drink liquid form, concentrated form, and nutritional liquids made by reconstituting the nutritional powders described herein prior to use.

[0023] The term "nutritional powder" as used herein, unless otherwise specified, refers to nutritional compositions in flowable or scoopable form that can be reconstituted with water or another aqueous liquid prior to consumption and includes both spraydried and drymixed/dryblended powders.

[0024] The term "infant" as used herein, unless otherwise specified, refers to a person 12 months or younger. The term "preterm infant" as used herein, refers to a person born prior to 36 weeks of gestation.

[0025] The term "toddler" as used herein, unless otherwise specified, refers to a person greater than one year of age up to three years of age.

[0026] The term "child" as used herein, unless otherwise specified, refers to a person greater than three years of age up to twelve years of age.

[0027] The term "newborn" as used herein, unless otherwise specified, refers to a person from birth up to four weeks of age.

[0028] The terms "infant formula" or "synthetic infant formula" as used herein, unless otherwise specified, are used interchangeably and refer to liquid and solid human milk replacements or substitutes that are suitable for consumption by an infant. The synthetic formulas include components that are of semi-purified or purified origin. As used herein, unless otherwise specified, the terms "semi-purified" or "purified" refer to a material that has been prepared by purification of a natural material or by synthesis. The terms "infant formula" or "synthetic infant formula" do not include human breast milk.

[0029] The term "preterm infant formula" as used herein, unless otherwise specified, refers to liquid and solid nutritional products suitable for consumption by a preterm infant.

[0030] The term "human milk fortifier" as used herein, unless otherwise specified, refers to liquid and solid nutritional products suitable for mixing with breast milk or preterm infant formula or infant formula for consumption by a preterm or term infant.

[0031] The terms "susceptible" and "at risk" as used herein, unless otherwise specified, mean having little resistance to a certain condition or disease, including being genetically predisposed, having a family history of, and/or having symptoms of the condition or disease.

[0032] All percentages, parts and ratios as used herein, are by weight of the total composition, unless otherwise specified. All such weights, as they pertain to listed ingredients, are based on the active level and, therefore, do not include solvents or by-products that may be included in commercially available materials, unless otherwise specified.

[0033] Numerical ranges as used herein are intended to include every number and subset of numbers within that range, whether specifically disclosed or not. Further, these numerical ranges should be construed as providing support for a claim directed to any number or subset of numbers in that range. For example, a disclosure of from 1 to 10 should be construed as supporting a range of from 2 to 8, from 3 to 7, from 5 to 6, from 1 to 9, from 3.6 to 4.6, from 3.5 to 9.9, and so forth.

[0034] All references to singular characteristics or limitations of the present disclosure shall include the corresponding plural characteristic or limitation, and vice versa, unless otherwise specified or clearly implied to the contrary by the context in which the reference is made.

[0035] All combinations of method or process steps as used herein can be performed in any order, unless otherwise specified or clearly implied to the contrary by the context in which the referenced combination is made.

[0036] The nutritional compositions and methods may comprise, consist of, or consist essentially of the essential elements of the compositions and methods as described herein, as well as any additional or optional element described herein or otherwise useful in nutritional composition applications.

Product Form

[0037] The nutritional compositions of the present disclosure including the GOS may be formulated and administered in any known or otherwise suitable oral product form. Any solid, liquid, or powder product form, including combinations or variations thereof, are suitable for use herein, provided that such forms allow for safe and effective oral delivery to the individual of the essential ingredients and any optional ingredients, as also defined herein.

[0038] The nutritional compositions of the present disclosure are preferably formulated as dietary product forms, which are defined herein as those embodiments comprising the essential ingredients of the present disclosure in a product form that then contains at least one of fat, protein, and carbohydrate, and preferably also contains vitamins, minerals, or combinations thereof. The nutritional compositions will comprise GOS, desirably in combination with at least one of protein, fat, vitamins, and minerals, to produce a nutritional combination.

[0039] The nutritional composition may be formulated with sufficient kinds and amounts of nutrients to provide a sole, primary, or supplemental source of nutrition, or to provide a specialized nutritional composition for use in individuals afflicted with specific diseases, disorders, or conditions or with a targeted nutritional benefit as described below.

[0040] Specific non-limiting examples of product forms suitable for use with the GOS-containing compositions as disclosed herein include, for example, liquid and powdered dietary supplements, liquid and powdered human milk fortifiers, liquid and powdered preterm infant formulas, liquid and powdered infant formulas, liquid and powdered elemental and semi-elemental formulas, liquid and powdered pediatric formulas, liquid and powdered toddler formulas, liquid and powdered follow-on formulas, liquid, powdered and solid adult nutritional formulas suitable for use with individuals suffering from enteric infection, inflammatory bowel disease, colitis, bowel obstruction, chronic

stress, and other gastrointestinal diseases, conditions, and/or disorders or undergoing antibiotic therapy, radiation therapy, other chemotherapy, surgery, or other treatments or therapies.

Nutritional Liquids

[0041] Nutritional liquids include both concentrated and ready-to-feed nutritional liquids. These nutritional liquids are most typically formulated as suspensions or emulsions, although other liquid forms are within the scope of the present disclosure.

[0042] Nutritional emulsions suitable for use may be aqueous emulsions comprising proteins, fats, and carbohydrates. These emulsions are generally flowable or drinkable liquids at from about 1°C to about 25°C and are typically in the form of oil-in-water, water-in-oil, or complex aqueous emulsions, although such emulsions are most typically in the form of oil-in-water emulsions having a continuous aqueous phase and a discontinuous oil phase.

[0043] The nutritional emulsions may be and typically are shelf stable. The nutritional emulsions typically contain up to about 95% by weight of water, including from about 50% to about 95%, also including from about 60% to about 90%, and also including from about 70% to about 85%, by weight of water. The nutritional emulsions may have a variety of product densities, but most typically have a density greater than about 1.03 g/mL, including greater than about 1.04 g/mL, including greater than about 1.055 g/mL, including from about 1.06 g/ml to about 1.12 g/mL, and also including from about 1.085 g/mL to about 1.10 g/mL.

[0044] The nutritional emulsions may have a caloric density tailored to the nutritional needs of the ultimate user, although in most instances the emulsions comprise generally at least 19 kcal/fl oz (660 kcal/liter), more typically from about 20 kcal/fl oz (675-680 kcal/liter) to about 25 kcal/fl oz (820 kcal/liter), even more typically from about 20 kcal/fl oz (675-680 kcal/liter) to about 24 kcal/fl oz (800-810 kcal/liter). Generally, the 22-24 kcal/fl oz formulas are more commonly used in preterm or low birth weight infants, and the 20-21 kcal/fl oz (675-680 to 700 kcal/liter) formulas are more often used in term infants. In some embodiments, the emulsion may have a caloric density of from about 50-100 kcal/liter to about 2000 kcal/liter, including from about 150 kcal/liter to about 500

kcal/liter. In some specific embodiments, the emulsion may have a caloric density of 25, or 50, or 75, or 100 kcal/liter.

[0045] The nutritional emulsion may have a pH ranging from about 3.5 to about 8, but are most advantageously in a range of from about 4.5 to about 7.5, including from about 5.5 to about 7.3, including from about 6.2 to about 7.2.

[0046] Although the serving size for the nutritional emulsion can vary depending upon a number of variables, a typical serving size is generally at least about 1 mL, or even at least about 2 mL, or even at least about 5 mL, or even at least about 10 mL, or even at least about 25 mL, including ranges from about 2 mL to about 500 mL, including from about 4 mL to about 340 mL, and including from about 10 mL to about 240 mL.

Nutritional Solids

[0047] The nutritional solids may be in any solid form, but are typically in the form of flowable or substantially flowable particulate compositions, or at least particulate compositions. Particularly suitable nutritional solid product forms include spray dried, agglomerated and/or dryblended powder compositions. The compositions can easily be scooped and measured with a spoon or similar other device, and can easily be reconstituted by the intended user with a suitable aqueous liquid, typically water, to form a nutritional composition for immediate oral or enteral use. In this context, "immediate" use generally means within about 48 hours, most typically within about 24 hours, preferably right after reconstitution.

[0048] The nutritional powders may be reconstituted with water prior to use to a caloric density tailored to the nutritional needs of the ultimate user, although in most instances the powders are reconstituted with water to form compositions comprising at least 19 kcal/fl oz (660 kcal/liter), more typically from about 20 kcal/fl oz (675-680 kcal/liter) to about 25 kcal/fl oz (820 kcal/liter), even more typically from about 20 kcal/fl oz (675-680 kcal/liter) to about 24 kcal/fl oz (800-810 kcal/liter). Generally, the 22-24 kcal/fl oz formulas are more commonly used in preterm or low birth weight infants, and the 20-21 kcal/fl oz (675-680 to 700 kcal/liter) formulas are more often used in term infants. In some embodiments, the reconstituted powder may have a caloric density of from about 50-100 kcal/liter to about 2000 kcal/liter, including from about 150 kcal/liter to about 500

kcal/liter. In some specific embodiments, the emulsion may have a caloric density of 25, or 50, or 75, or 100 kcal/liter.

Galactooligosacchrides

[0049] The nutritional compositions of the present disclosure include galactose-containing oligosaccharides, commonly referred to as galactooligosaccharides (GOS). GOS are indigestible oligosaccharides containing one or more galactose molecule and one molecule of glucose connected through β(1,4) and/or β(1,6) glycosidic bonds. The GOS used in the compositions of the present disclosure may be selected from β-galactooligosaccharides, α-galactooligosaccharides, and combinations thereof. In some embodiments, the GOS may be trans-galactooligosaccharides (T-GOS), which are a mixture of oligosaccharides consisting of D-glucose and D-galactose alone, or in combination with one or more other forms of GOS. T-GOS are produced from D-lactose via the action of the enzyme beta-galactosidase obtained from Aspergillus oryzae. T-GOS are resistant to digestion in the upper gastrointestinal tract and stimulate the growth of bifidobacteria in the large intestine.

[0050] The GOS may be generally represented by the formula: [galactose]n-glucose, wherein n is an integer between 1 and 20, and preferably is selected from 2, 3, 4, 5, 6, 7, 8, 9, or 10. The term "galactooligosaccharide" or "GOS" may also refer to a mixture of galactooligosaccharides having different chain lengths; that is, long chain lengths and/or short chain lengths. Galactooligosaccharides are commercially available as, for example, Vivinal® GOS (75% total solids, 60% of total solids GOS; Friesland) and GOS (Clasado).

[0051] The GOS is present in the nutritional compositions in a total amount of from about 5 kg to about 160 kg per 1000 kg of nutritional composition, including from about 8 kg to about 160 kg per 1000 kg of nutritional composition, including from about 8 kg to about 80 kg per 1000 kg, including from about 8 kg to about 64 kg per 1000 kg, and including from about 164 kg to about 818 kg per 18,000 pounds of nutritional composition. In one embodiment, the nutritional composition is a human milk fortifier that provides GOS to a 1 kg preterm infant in an amount of from about 0.11 g to about 0.55 g of GOS per day.

Additional Prebiotic Oligosaccharides

[0052] The nutritional compositions of the present disclosure may, in addition to the GOS described above, comprise an additional source or sources of prebiotic oligosaccharides. Suitable additional sources of prebiotic oligosaccharides for use in the nutritional compositions include any prebiotic oligosaccharide that is suitable for use in a nutritional composition and is compatible with the essential elements and features of such compositions. In some embodiments, the nutritional composition includes a combination of GOS and one or more additional prebiotic oligosaccharide such that the composition provides a synergistic benefit to the end user, such as a synergistic benefit in improving the barrier function of the gastrointestinal tract.

[0053] Non-limiting examples of suitable additional prebiotic oligosaccharides for use in the nutritional compositions described herein include prebiotic oligosaccharides that have a degree of polymerization (DP) of at least 2 monose units, which are not or only partially digested in the intestine by the action of acids or digestive enzymes present in the human upper digestive tract (small intestine and stomach), but which are fermentable by the human intestinal flora. The term "monose units" refers to units having a closed ring structure, preferably hexose, e.g., the pyranose or furanose forms. Particularly preferred oligosaccharides for use in combination with the GOS in the nutritional compositions of the present disclosure include fructooligosaccharides (FOS), short chain fructooligosaccharides, inulin, polydextrose (PDX), pectin hydrolysate, and gum fiber.

Probiotics

[0054] The nutritional compositions of the present disclosure may further comprise one or more probiotics in addition to the GOS.

[0055] Non-limiting examples of suitable probiotic strains for use in the nutritional compositions including GOS herein include the genus Lactobacillus including *L. acidophilus*, *L. amylovorus*, *L. brevis*, *L. bulgaricus*, *L. casei spp. casei*, *L. casei spp. rhamnosus*, *L. crispatus*, *L. delbrueckii ssp. lactis*, *L. fermentum*, *L. helveticus*, *L. johnsonii*, *L. paracasei*, *L. pentosus*, *L. plantarum*, *L. reuteri*, and *L. sake*; the genus Bifidobacterium including: *B. animalis*, *B. bifidum*, *B. breve*, *B. infantis*, *B. lactis* and *B. longum*; the genus Pediococcus including: *P. acidilactici*; the genus Propionibacterium

including: *P. acidipropionici*, *P. freudenreichii*, *P. jensenii*, and *P. theonii*; and the genus Streptococcus including: *S. cremoris*, *S. lactis*, and *S. thermophilus*. Particularly preferred probiotics include *B. lactis and L. acidophilus*.

[0056] The probiotics may be present in the nutritional compositions in a total amount of at least about 10^4 CFU/g composition, including from about 10^4 CFU/g composition to about 10^{11} CFU/g composition, and including from about 10^5 CFU/g composition to about 10^{10} CFU/g composition.

Macronutrients

[0057] The nutritional compositions including the GOS may be formulated to include at least one of protein, fat, and carbohydrate. In many embodiments, the nutritional compositions will include the GOS in combination with protein, carbohydrate and fat.

[0058] Although total concentrations or amounts of the fat, protein, and carbohydrates may vary depending upon the product type (i.e., human milk fortifier, preterm infant formula, infant formula, toddler formula, pediatric formula, follow-on formula, adult nutritional, etc.), product form (i.e., nutritional solid, powder, ready-to-feed liquid, or concentrated liquid), and targeted dietary needs of the intended user, such concentrations or amounts most typically fall within one of the following embodied ranges, inclusive of any other essential fat, protein, and/or carbohydrate ingredients as described herein.

[0059] For the liquid preterm and term infant formulas, carbohydrate concentrations (including both GOS and any other carbohydrate/oligosaccharide sources) most typically range from about 5% to about 40%, including from about 7% to about 30%, including from about 10% to about 25%, by weight of the preterm or term infant formula; fat concentrations most typically range from about 1% to about 30%, including from about 2% to about 15%, and also including from about 3% to about 10%, by weight of the preterm or term infant formula; and protein concentrations most typically range from about 0.5% to about 30%, including from about 1% to about 15%, and also including from about 2% to about 10%, by weight of the preterm or term infant formula.

[0060] For the liquid human milk fortifiers, carbohydrate concentrations (including both GOS and any other carbohydrate/oligosaccharide sources) most typically range from about 10% to about 75%, including from about 10% to about 50%, including from about 20% to about 40%, by weight of the human milk fortifier; fat concentrations most typically range from about 10% to about 40%, including from about 15% to about 37%, and also including from about 18% to about 30%, by weight of the human milk fortifier; and protein concentrations most typically range from about 5% to about 40%, including from about 10% to about 30%, and also including from about 15% to about 25%, by weight of the human milk fortifier.

[0061] For the adult nutritional liquids, carbohydrate concentrations (including both GOS and any other carbohydrate/oligosaccharide sources) most typically range from about 5% to about 40%, including from about 7% to about 30%, including from about 10% to about 25%, by weight of the adult nutritional; fat concentrations most typically range from about 2% to about 30%, including from about 3% to about 15%, and also including from about 5% to about 10%, by weight of the adult nutritional; and protein concentrations most typically range from about 0.5% to about 30%, including from about 1% to about 15%, and also including from about 2% to about 10%, by weight of the adult nutritional.

[0062] The amount of carbohydrates, fats, and/or proteins in any of the liquid nutritional compositions described herein may also be characterized in addition to, or in the alternative, as a percentage of total calories in the liquid nutritional composition as set forth in the following table. These macronutrients for liquid nutritional compositions of the present disclosure are most typically formulated within any of the caloric ranges (embodiments A-F) described in the following table (each numerical value is preceded by the term "about").

Nutrient % Total Cal.	**Embodiment A**	**Embodiment B**	**Embodiment C**
Carbohydrate	0-98	2-96	10-75
Protein	0-98	2-96	5-70
Fat	0-98	2-96	20-85
	Embodiment D	**Embodiment E**	**Embodiment F**

Nutrient % Total Cal.	Embodiment A	Embodiment B	Embodiment C
Carbohydrate	30-50	25-50	25-50
Protein	15-35	10-30	5-30
Fat	35-55	1-20	2-20

[0063] In one specific example, liquid infant formulas (both ready-to-feed and concentrated liquids) include those embodiments in which the protein component may comprise from about 7.5% to about 25% of the caloric content of the formula; the carbohydrate component (including both GOS and any other carbohydrate/oligosaccharide sources) may comprise from about 35% to about 50% of the total caloric content of the infant formula; and the fat component may comprise from about 30% to about 60% of the total caloric content of the infant formula. These ranges are provided as examples only, and are not intended to be limiting. Additional suitable ranges are noted in the following table (each numerical value is preceded by the term "about").

Nutrient % Total Cal.	Embodiment G	Embodiment H	Embodiment I
Carbohydrates:	20-85	30-60	35-55
Fat:	5-70	20-60	25-50
Protein:	2-75	5-50	7-40

[0064] When the nutritional composition is a powdered preterm or term infant formula, the protein component is present in an amount of from about 5% to about 35%, including from about 8% to about 12%, and including from about 10% to about 12% by weight of the preterm or term infant formula; the fat component is present in an amount of from about 10% to about 35%, including from about 25% to about 30%, and including from about 26% to about 28% by weight of the preterm or term infant formula; and the carbohydrate component (including both GOS and any other carbohydrate/oligosaccharide sources) is present in an amount of from about 30% to about 85%, including from about 45% to about 60%, including from about 50% to about 55% by weight of the preterm or term infant formula.

[0065] For powdered human milk fortifiers, the protein component is present in an amount of from about 1% to about 55%, including from about 10% to about 50%, and including from about 10% to about 30% by weight of the human milk fortifier; the fat component is present in an amount of from about 1% to about 30%, including from about 1% to about 25%, and including from about 1% to about 20% by weight of the human milk fortifier; and the carbohydrate component (including both GOS and any other carbohydrate/oligosaccharide sources) is present in an amount of from about 15% to about 75%, including from about 15% to about 60%, including from about 20% to about 50% by weight of the human milk fortifier.

[0066] For powdered adult nutritionals, the protein component is present in an amount of from about 10% to about 90%, including from about 30% to about 80%, and including from about 40% to about 75% by weight of the adult nutritional; the fat component is present in an amount of from about 0.5% to about 20%, including from about 1% to about 10%, and including from about 2% to about 5% by weight of the adult nutritional; and the carbohydrate component (including both GOS and any other carbohydrate/oligosaccharide sources) is present in an amount of from about 5% to about 40%, including from about 7% to about 30%, including from about 10% to about 25% by weight of the adult nutritional.

[0067] The total amount or concentration of fat, carbohydrate, and protein, in the powdered nutritional compositions of the present disclosure can vary considerably depending upon the selected composition and dietary or medical needs of the intended user. Additional suitable examples of macronutrient concentrations are set forth below. In this context, the total amount or concentration refers to all fat, carbohydrate, and protein sources in the powdered composition. For powdered nutritional compositions, such total amounts or concentrations are most typically and preferably formulated within any of the embodied ranges described in the following table (each numerical value is preceded by the term "about').

Nutrient % Total Cal.	Embodiment J	Embodiment K	Embodiment L
Carbohydrate	1-85	30-60	35-55
Fat	5-70	20-60	25-50
Protein	2-75	5-50	7-40

Fat

[0068] The nutritional compositions of the present disclosure may optionally comprise any source or sources of fat. Suitable sources of fat for use herein include any fat or fat source that is suitable for use in an oral nutritional composition and is compatible with the essential elements and features of such composition. For example, in one specific embodiment, the fat is derived from long chain polyunsaturated fatty acids (LCPUFAs).

[0069] Exemplary LCPUFAs for use in the nutritional compositions include, for example, ω-3 LCPUFAs and ω-6 LCPUFAs. Specific LCPUFAs include docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), arachidonic acid (ARA), linoleic acid, linolenic acid (alpha linolenic acid) and gamma-linolenic acid derived from oil sources such as plant oils, marine plankton, fungal oils, and fish oils. In one particular embodiment, the LCPUFAs are derived from fish oils such as menhaden, salmon, anchovy, cod, halibut, tuna, or herring oil. Particularly preferred LCPUFAs for use in the nutritional compositions with the HMOs include DHA, ARA, EPA, and combinations thereof.

[0070] In order to reduce potential side effects of high dosages of LCPUFAs in the nutritional compositions, the content of LCPUFAs preferably does not exceed 3% by weight of the total fat content, including below 2% by weight of the total fat content, and including below 1% by weight of the total fat content in the nutritional composition.

[0071] The LCPUFA may be provided as free fatty acids, in triglyceride form, in diglyceride form, in monoglyceride form, in phospholipid form, or as a mixture of one or more of the above, preferably in triglyceride form. In another specific embodiment, the fat is derived from short chain fatty acids.

[0072] Additional non-limiting examples of suitable fats or sources thereof for use in the nutritional compositions described herein include coconut oil, fractionated coconut oil, soybean oil, corn oil, olive oil, safflower oil, high oleic safflower oil, oleic acids (EMERSOL 6313 OLEIC ACID, Cognis Oleochemicals, Malaysia), MCT oil (medium chain triglycerides), sunflower oil, high oleic sunflower oil, palm and palm kernel oils, palm olein, canola oil, marine oils, fish oils, fungal oils, algae oils, cottonseed oils, and combinations thereof.

Protein

[0073] The nutritional compositions of the present disclosure may optionally further comprise protein. Any protein source that is suitable for use in oral nutritional compositions and is compatible with the essential elements and features of such compositions is suitable for use in the nutritional compositions.

[0074] Non-limiting examples of suitable proteins or sources thereof for use in the nutritional compositions include hydrolyzed, partially hydrolyzed or non-hydrolyzed proteins or protein sources, which may be derived from any known or otherwise suitable source such as milk (e.g., casein, whey), animal (e.g., meat, fish), cereal (e.g., rice, corn), vegetable (e.g., soy) or combinations thereof. Non-limiting examples of such proteins include milk protein isolates, milk protein concentrates as described herein, casein protein isolates, extensively hydrolyzed casein, whey protein, sodium or calcium caseinates, whole cow milk, partially or completely defatted milk, soy protein isolates, soy protein concentrates, and so forth. In one specific embodiment, the nutritional compositions include a protein source derived from milk proteins of human and/or bovine origin.

[0075] In one embodiment, the protein source is a hydrolyzed protein hydrolysate. In this context, the terms "hydrolyzed protein" or "protein hydrolysates" are used interchangeably herein and include extensively hydrolyzed proteins, wherein the degree of hydrolysis is most often at least about 20%, including from about 20% to about 80%, and also including from about 30% to about 80%, even more preferably from about 40% to about 60%. The degree of hydrolysis is the extent to which peptide bonds are broken by a hydrolysis method. The degree of protein hydrolysis for purposes of characterizing the extensively hydrolyzed protein component of these embodiments is easily determined by one of ordinary skill in the formulation arts by quantifying the amino nitrogen to total

nitrogen ratio (AN/TN) of the protein component of the selected liquid formulation. The amino nitrogen component is quantified by USP titration methods for determining amino nitrogen content, while the total nitrogen component is determined by the Tecator Kjeldahl method, all of which are well known methods to one of ordinary skill in the analytical chemistry art.

[0076] Suitable hydrolyzed proteins may include soy protein hydrolysate, casein protein hydrolysate, whey protein hydrolysate, rice protein hydrolysate, potato protein hydrolysate, fish protein hydrolysate, egg albumen hydrolysate, gelatin protein hydrolysate, combinations of animal and vegetable protein hydrolysates, and combinations thereof. Particularly preferred protein hydrolysates include whey protein hydrolysate and hydrolyzed sodium caseinate.

[0077] When used in the nutritional compositions, the protein source may include at least about 20% (by weight total protein) protein hydrolysate, including from about 30% to 100% (by weight total protein) protein hydrolysate, and including from about 40% to about 80% (by weight total protein) protein hydrolysate, and including about 50% (by weight total protein) protein hydrolysate. In one particular embodiment, the nutritional composition includes 100% (by weight total protein) protein hydrolysate.

Carbohydrate

[0078] In addition to the GOS, the nutritional compositions of the present disclosure may further optionally comprise any other carbohydrates that are suitable for use in an oral nutritional composition and are compatible with the essential elements and features of such compositions.

[0079] Non-limiting examples of suitable carbohydrates or sources thereof for use in the nutritional compositions described herein may include maltodextrin, hydrolyzed or modified starch or cornstarch, glucose polymers, corn syrup, corn syrup solids, rice-derived carbohydrates, pea-derived carbohydrates, potato-derived carbohydrates, tapioca, sucrose, glucose, fructose, lactose, high fructose corn syrup, honey, sugar alcohols (e.g., maltitol, erythritol, sorbitol), artificial sweeteners (e.g., sucralose, acesulfame potassium, stevia) and combinations thereof. A particularly desirable carbohydrate is a low dextrose equivalent (DE) maltodextrin.

Other Optional Ingredients

[0080] The nutritional compositions of the present disclosure may further comprise other optional components that may modify the physical, chemical, aesthetic or processing characteristics of the compositions or serve as pharmaceutical or additional nutritional components when used in the targeted population. Many such optional ingredients are known or otherwise suitable for use in medical food or other nutritional products or pharmaceutical dosage forms and may also be used in the compositions herein, provided that such optional ingredients are safe for oral administration and are compatible with the essential and other ingredients in the selected product form.

[0081] Non-limiting examples of such optional ingredients include human milk oligosaccharides, preservatives, emulsifying agents, buffers, pharmaceutical actives, anti-inflammatory agents, additional nutrients as described herein, colorants, flavors, thickening agents and stabilizers, emulsifying agents, lubricants, and so forth.

[0082] The nutritional compositions may further comprise a sweetening agent, preferably including at least one sugar alcohol such as maltitol, erythritol, sorbitol, xylitol, mannitol, isolmalt, and lactitol, and also preferably including at least one artificial or high potency sweetener such as acesulfame K, aspartame, sucralose, saccharin, stevia, and tagatose. These sweetening agents, especially as a combination of a sugar alcohol and an artificial sweetener, are especially useful in formulating liquid beverage embodiments of the present disclosure having a desirable favor profile. These sweetener combinations are especially effective in masking undesirable flavors sometimes associated with the addition of vegetable proteins to a liquid beverage. Optional sugar alcohol concentrations in the nutritional composition may range from at least 0.01%, including from 0.1% to about 10%, and also including from about 1% to about 6%, by weight of the nutritional composition. Optional artificial sweetener concentrations may range from about 0.01%, including from about 0.05% to about 5%, also including from about 0.1% to about 1.0%, by weight of the nutritional composition.

[0083] A flowing agent or anti-caking agent may be included in the nutritional compositions as described herein to retard clumping or caking of the powder over time and to make a powder embodiment flow easily from its container. Any known flowing or anti-caking agents that are known or otherwise suitable for use in a nutritional powder or

product form are suitable for use herein, non-limiting examples of which include tricalcium phosphate, silicates, and combinations thereof. The concentration of the flowing agent or anti-caking agent in the nutritional composition varies depending upon the product form, the other selected ingredients, the desired flow properties, and so forth, but most typically range from about 0.1% to about 4%, including from about 0.5% to about 2%, by weight of the nutritional composition.

[0084] A stabilizer may also be included in the nutritional compositions. Any stabilizer that is known or otherwise suitable for use in a nutritional composition is also suitable for use herein, some non-limiting examples of which include gums such as xanthan gum. The stabilizer may represent from about 0.1% to about 5.0%, including from about 0.5% to about 3%, including from about 0.7% to about 1.5%, by weight of the nutritional composition.

[0085] Additionally, the nutritional compositions may comprise one or more antioxidants to provide nutritional support, as well as to reduce oxidative stress. Any antioxidants suitable for oral administration may be included for use in the nutritional compositions of the present disclosure, including, for example, vitamin A, vitamin E, vitamin C, retinol, tocopherol, and carotenoids.

[0086] In one specific embodiment, the antioxidants for use in the nutritional compositions include carotenoids such as lutein, zeaxanthin, lycopene, beta-carotene, and combinations thereof, and particularly, combinations of the carotenoids lutein, lycopene, and beta-carotene. Nutritional compositions containing these combinations, as selected and defined herein, can be used to modulate inflammation and/or levels of C-reactive protein in preterm and term infants

[0087] The nutritional compositions may further comprise any of a variety of other vitamins or related nutrients, non-limiting examples of which include vitamin D, vitamin K, thiamine, riboflavin, pyridoxine, vitamin B_{12}, niacin, folic acid, pantothenic acid, biotin, choline, inositol, salts and derivatives thereof, and combinations thereof.

[0088] The nutritional compositions may further comprise any of a variety of other additional minerals, non-limiting examples of which include calcium, phosphorus, magnesium, iron, zinc, manganese, copper, sodium, potassium, molybdenum, chromium, chloride, and combinations thereof.

[0089] The nutritional compositions of the present disclosure may additionally comprise nucleotides and/or nucleotide precursors selected from the group consisting of nucleoside, purine base, pyrimidine base, ribose and deoxyribose to further improve intestinal barrier integrity and/or maturation. The nucleotide may be in monophosphate, diphosphate, or triphosphate form. The nucleotide may be a ribonucleotide or a deoxyribonucleotide. The nucleotides may be monomeric, dimeric, or polymeric (including RNA and DNA). The nucleotide may be present in the nutritional composition as a free acid or in the form of a salt, preferably a monosodium salt.

[0090] Suitable nucleotides and/or nucleosides for use in the nutritional compositions include one or more of cytidine 5'-monophosphate, uridine 5'-monophosphate, adenosine 5'-monophosphate, guanosine 5'-1-monophosphate, and/or inosine 5'-monophosphate, more preferably cytidine 5'-monophosphate, uridine 5'-monophosphate, adenosine 5'-monophosphate, guanosine 5'-monophosphate, and inosine 5'-monophosphate.

Methods of Manufacture

[0091] The nutritional compositions of the present disclosure may be prepared by any known or otherwise effective manufacturing technique for preparing the selected product solid or liquid form. Many such techniques are known for any given product form such as nutritional liquids or powders and can easily be applied by one of ordinary skill in the art to the nutritional compositions described herein.

[0092] The nutritional compositions of the present disclosure can therefore be prepared by any of a variety of known or otherwise effective formulation or manufacturing methods. In one suitable manufacturing process, for example, at least three separate slurries are prepared, including a protein-in-fat (PIF) slurry, a carbohydrate-mineral (CHO-MIN) slurry, a protein-in-water (PIW) slurry. The PIF slurry is formed by heating and mixing the oil (e.g., canola oil, corn oil, etc.) and then adding an emulsifier (e.g., lecithin),

fat soluble vitamins, and a portion of the total protein (e.g., milk protein concentrate, etc.) with continued heat and agitation. The CHO-MIN slurry is formed by adding with heated agitation to water: minerals (e.g., potassium citrate, dipotassium phosphate, sodium citrate, etc.), trace and ultra trace minerals (TM/UTM premix), thickening or suspending agents (e.g. avicel, gellan, carrageenan). The resulting CHO-MIN slurry is held for 10 minutes with continued heat and agitation before adding additional minerals (e.g., potassium chloride, magnesium carbonate, potassium iodide, etc.), and/or carbohydrates (e.g., GOS, HMOs, fructooligosaccharide, sucrose, corn syrup, etc.). The PIW slurry is then formed by mixing with heat and agitation the remaining protein, if any.

[0093] The resulting slurries are then blended together with heated agitation and the pH adjusted to 6.6-7.0, after which the composition is subjected to high-temperature short-time (HTST) processing during which the composition is heat treated, emulsified and homogenized, and then allowed to cool. Water soluble vitamins and ascorbic acid are added, the pH is adjusted to the desired range if necessary, flavors are added, and water is added to achieve the desired total solid level. The composition is then aseptically packaged to form an aseptically packaged nutritional emulsion. This emulsion can then be further diluted, heat-treated, and packaged to form a ready-to-feed or concentrated liquid, or it can be heat-treated and subsequently processed and packaged as a reconstitutable powder, e.g., spray dried, drymixed, agglomerated.

[0094] The nutritional solid, such as a spray dried nutritional powder or drymixed nutritional powder, may be prepared by any collection of known or otherwise effective techniques, suitable for making and formulating a nutritional powder.

[0095] For example, when the nutritional powder is a spray dried nutritional powder, the spray drying step may likewise include any spray drying technique that is known for or otherwise suitable for use in the production of nutritional powders. Many different spray drying methods and techniques are known for use in the nutrition field, all of which are suitable for use in the manufacture of the spray dried nutritional powders herein.

[0096] One method of preparing the spray dried nutritional powder comprises forming and homogenizing an aqueous slurry or liquid comprising predigested fat, and optionally protein, carbohydrate, and other sources of fat, and then spray drying the slurry

or liquid to produce a spray dried nutritional powder. The method may further comprise the step of spray drying, drymixing, or otherwise adding additional nutritional ingredients, including any one or more of the ingredients described herein, to the spray dried nutritional powder.

[0097] Other suitable methods for making nutritional compositions are described, for example, in U.S. Pat. No. 6,365,218 (Borschel, et al.), U.S. Patent No. 6,589,576 (Borschel, et al.), U.S. Pat. No. 6,306,908 (Carlson, et al.), U.S. Patent Application No. 20030118703 A1 (Nguyen, et al.), which descriptions are incorporated herein by reference to the extent that they are consistent herewith.

Methods of Use

[0098] The nutritional compositions as described herein and containing GOS can be used to prevent injury to the gastrointestinal tract and/or to enhance the healing of an injured gastrointestinal tract of preterm infants, infants, toddlers, children, and adults. Any of this group may actually have an injured gastrointestinal tract and thus benefit from the healing action of the GOS-containing nutritional composition, or may be at risk of or susceptible to sustaining injuries to the gastrointestinal tract and thus benefit from the preventative action of the GOS-containing nutritional composition.

[0099] The nutritional compositions as described herein comprise GOS, alone or in combination with one or more additional components, such as a probiotic as noted above, to provide a nutritional source for improving at least the intestinal repair/healing function of an individual. Specifically, the nutritional compositions can enhance the expression of mucin-associated proteins, such as trefoil factor 3 (TFF3), mucin 2 (MUC-2), and relm-beta (RELMb) to stabilize the mucus layer; promote healing of epithelial cells; improve barrier function; and reduce inflammation, each of which enhance the overall healing of the epithelial tissue and mucus layer of the stomach, small intestine, and large intestine.

[0100] More particularly, in some embodiments, the nutritional compositions may be administered to an individual who has sustained injury to the gastrointestinal tract or who is more susceptible to or at risk of injury to the gastrointestinal tract by having undergone various therapies, which may include, for example, antibiotic therapy, radiation

therapy, chemotherapy, or surgery or by having various diseases or disorders, which may include, for example, enteric infection, inflammatory bowel diseases, colitis, bowel obstruction, and chronic stress.

[0101] The individual desirably consumes at least one serving of the GOS-containing nutritional composition daily, and in some embodiments, may consume two, three, or even more servings per day. Each serving is desirably administered as a single undivided dose, although the serving may also be divided into two or more partial or divided servings to be taken at two or more times during the day. The methods of the present disclosure include continuous day after day administration, as well as periodic or limited administration, although continuous day after day administration is generally desirable.

[0102] The nutritional composition may be administered to the individual orally or via tube feeding. The nutritional compositions of the present disclosure could also be given to preterm or term infants prior to the initiation of enteral feeding and/or concurrently with feeding. Furthermore, the nutritional composition may be given to infants, children, or adults prior to or concurrently with re-feeding after partial or total parenteral nutrition.

EXAMPLES

[0103] The following examples illustrate specific embodiments and/or features of the nutritional compositions and methods of the present disclosure. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present disclosure, as many variations thereof are possible without departing from the spirit and scope of the disclosure. All exemplified amounts are weight percentages based upon the total weight of the composition, unless otherwise specified.

[0104] The exemplified compositions are shelf stable nutritional compositions prepared in accordance with the manufacturing methods described herein, such that each exemplified composition, unless otherwise specified, includes an aseptically processed embodiment and a retort packaged embodiment.

[0105] The nutritional liquid embodiments are aqueous oil-in-water emulsions that are packaged in 240 mL plastic containers and remain physically stable for 12-18 months after composition/packaging at storage temperatures ranging from 1-25°C.

EXAMPLES 1-5

[0106] Examples 1-5 illustrate spray dried nutritional powders of the present disclosure, the ingredients of which are listed in the table below. All ingredient amounts are listed as kilogram per 1000 kilogram batch of product, unless otherwise specified.

Ingredient	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5
Corn syrup	256.86 kg	256.86 kg	256.86 kg	256.86 kg	256.86 kg
Corn Maltodextrin	216.25 kg	216.25 kg	216.25 kg	216.25 kg	216.25 kg
Sucrose	177.95 kg	177.95 kg	177.95 kg	177.95 kg	177.95 kg
Corn oil	155.40 kg	155.40 kg	155.40 kg	155.40 kg	155.40 kg
Casein	132.97 kg	132.97 kg	132.97 kg	132.97 kg	132.97 kg
Soy protein isolate	29.84 kg	29.84 kg	29.84 kg	29.84 kg	29.84 kg
Calcium caseinate	19.46 kg	19.46 kg	19.46 kg	19.46 kg	19.46 kg
20% potassium citrate	16.09 kg	16.09 kg	16.09 kg	16.09 kg	16.09 kg
Vanilla	14.55 kg	14.55 kg	14.55 kg	14.55 kg	14.55 kg
20% sodium hydroxide	13.77 kg	13.77 kg	13.77 kg	13.77 kg	13.77 kg
Galactooligosaccharides	8 kg	40 kg	80 kg	120 kg	160 kg
Potassium citrate	7.54 kg	7.54 kg	7.54 kg	7.54 kg	7.54 kg
Magnesium chloride	7.53 kg	7.53 kg	7.53 kg	7.53 kg	7.53 kg
Tricalcium phosphate	6.23 kg	6.23 kg	6.23 kg	6.23 kg	6.23 kg
Sodium citrate	5.66 kg	5.66 kg	5.66 kg	5.66 kg	5.66 kg
Potassium chloride	3.79 kg	3.79 kg	3.79 kg	3.79 kg	3.79 kg
Soy lecithin	3.44 kg	3.44 kg	3.44 kg	3.44 kg	3.44 kg
Ascorbic acid	1.91 kg	1.91 kg	1.91 kg	1.91 kg	1.91 kg
Choline chloride	1.64 kg	1.64 kg	1.64 kg	1.64 kg	1.64 kg
45% KOH	1.26 kg	1.26 kg	1.26 kg	1.26 kg	1.26 kg
Zinc sulfate	0.1558 kg	0.1558 kg	0.1558 kg	0.1558 kg	0.1558 kg
Ferrous sulfate	0.121700 kg	0.121700 kg	0.121700 kg	0.121700 kg	0.121700 kg
Manganese sulfate	0.036900 kg	0.036900 kg	0.036900 kg	0.036900 kg	0.036900 kg
Cupric sulfate	0.021100 kg	0.021100 kg	0.021100 kg	0.021100 kg	0.021100 kg
Chromium chloride	0.001280 kg	0.001280 kg	0.001280 kg	0.001280 kg	0.001280 kg
Sodium molybdate	0.001012 kg	0.001012 kg	0.001012 kg	0.001012 kg	0.001012 kg
Sodium selenate	0.000434 kg	0.000434 kg	0.000434 kg	0.000434 kg	0.000434 kg
Niacinamide	0.124200 kg	0.124200 kg	0.124200 kg	0.124200 kg	0.124200 kg
D-calcium pantothenate	0.083000 kg	0.083000 kg	0.083000 kg	0.083000 kg	0.083000 kg
Thiamine chloride hydrochloride	0.020510 kg	0.020510 kg	0.020510 kg	0.020510 kg	0.020510 kg

Pyridoxine hydrochloride	0.019750 kg	0.019750 kg	0.019750 kg	0.019750 kg	0.019750 kg
Riboflavin	0.016000 kg	0.016000 kg	0.016000 kg	0.016000 kg	0.016000 kg
Folic acid	0.002783 kg	0.002783 kg	0.002783 kg	0.002783 kg	0.002783 kg
Biotin	0.002419 kg	0.002419 kg	0.002419 kg	0.002419 kg	0.002419 kg
Cyanocobalamin	0.000055 kg	0.000055 kg	0.000055 kg	0.000055 kg	0.000055 kg
dl-alpha-tocopheryl acetate	0.129600 kg	0.129600 kg	0.129600 kg	0.129600 kg	0.129600 kg
Phylloquinone	0.002162 kg	0.002162 kg	0.002162 kg	0.002162 kg	0.002162 kg
Vitamin D3	0.000028 kg	0.000028 kg	0.000028 kg	0.000028 kg	0.000028 kg
Vitamin A palmitate	0.010373 kg	0.010373 kg	0.010373 kg	0.010373 kg	0.010373 kg
Potassium iodide	0.000440 kg	0.000440 kg	0.000440 kg	0.000440 kg	0.000440 kg

AN = as needed

EXAMPLES 6-10

[0107] Examples 6-10 illustrate spray dried nutritional powders of the present disclosure, the ingredients of which are listed in the table below. All ingredient amounts are listed as kilogram per 1000 kilogram batch of product, unless otherwise specified.

Ingredient	Ex. 6	Ex. 7	Ex. 8	Ex. 9	Ex. 10
Skim milk	695.30 kg	695.30 kg	695.30 kg	695.30 kg	695.30 kg
Lactose	380.80 kg	380.80 kg	380.80 kg	380.80 kg	380.80 kg
High oleic safflower oil	118.20 kg	118.20 kg	118.20 kg	118.20 kg	118.20 kg
Soy oil	83.62 kg	83.62 kg	83.62 kg	83.62 kg	83.62 kg
Coconut oil	82.52 kg	82.52 kg	82.52 kg	82.52 kg	82.52 kg
Galactooligosaccharides	8 kg	40 kg	80 kg	120 kg	160 kg
Whey protein concentrate	50.89 kg	50.89 kg	50.89 kg	50.89 kg	50.89 kg
Potassium citrate	8.93 kg	8.93 kg	8.93 kg	8.93 kg	8.93 kg
Calcium carbonate	4.38 kg	4.38 kg	4.38 kg	4.38 kg	4.38 kg
ARA oil	2.86 kg	2.86 kg	2.86 kg	2.86 kg	2.86 kg
Nucleotide-choline premix	2.40 kg	2.40 kg	2.40 kg	2.40 kg	2.40 kg
Ascorbic acid	1.28 kg	1.28 kg	1.28 kg	1.28 kg	1.28 kg
Potassium chloride	1.24 kg	1.24 kg	1.24 kg	1.24 kg	1.24 kg
Soy lecithin	1.12 kg	1.12 kg	1.12 kg	1.12 kg	1.12 kg
Vitamin/mineral/taurine premix	1.12 kg	1.12 kg	1.12 kg	1.12 kg	1.12 kg
DHA oil	1.07 kg	1.07 kg	1.07 kg	1.07 kg	1.07 kg
Magnesium chloride	948.50 g	948.50 g	948.50 g	948.50 g	948.50 g
Vitamin A, D, E, K1	518.40 g	518.40 g	518.40 g	518.40 g	518.40 g
Ferrous sulfate	472.40 g	472.40 g	472.40 g	472.40 g	472.40 g
Choline chloride	432.10 g	432.10 g	432.10 g	432.10 g	432.10 g
Ascorbyl palmitate	364.90 g	364.90 g	364.90 g	364.90 g	364.90 g
Sodium chloride	347.50 g	347.50 g	347.50 g	347.50 g	347.50 g
Carotenoid premix	187.4 g	187.4 g	187.4 g	187.4 g	187.4 g
Mixed tocopherols	161.20 g	161.20 g	161.20 g	161.20 g	161.20 g
L-carnitine	26.30 g	26.30 g	26.30 g	26.30 g	26.30 g

Riboflavin	3.18 g	3.18 g	3.18 g	3.18 g	3.18 g
Tricalcium phosphate	AN	AN	AN	AN	AN
Potassium phosphate monobasic	AN	AN	AN	AN	AN
Potassium hydroxide	AN	AN	AN	AN	AN

AN = as needed

EXAMPLES 11-15

[0108] Examples 11-15 illustrate liquid emulsions of the present disclosure, the ingredients of which are listed in the table below. All ingredient amounts are listed as kilogram per 1000 kilogram batch of product, unless otherwise specified.

Ingredient	Ex. 11	Ex. 12	Ex. 13	Ex. 14	Ex. 15
Water	793.7 kg	793.7 kg	793.7 kg	793.7 kg	793.7 kg
Nonfat milk	97.50 kg	97.50 kg	97.50 kg	97.50 kg	97.50 kg
Corn syrup solids	31.90 kg	31.90 kg	31.90 kg	31.90 kg	31.90 kg
Medium chain triglycerides	17.20 kg	17.20 kg	17.20 kg	17.20 kg	17.20 kg
Lactose	16.45 kg	16.45 kg	16.45 kg	16.45 kg	16.45 kg
Whey protein concentrate	12.69 kg	12.69 kg	12.69 kg	12.69 kg	12.69 kg
Galactooligosaccharides	8 kg	40 kg	80 kg	120 kg	160 kg
Soy oil	10.30 kg	10.30 kg	10.30 kg	10.30 kg	10.30 kg
Coconut oil	6.30 kg	6.30 kg	6.30 kg	6.30 kg	6.30 kg
5% KOH	4.86 kg	4.86 kg	4.86 kg	4.86 kg	4.86 kg
Tricalcium phosphate	2.56 kg	2.56 kg	2.56 kg	2.56 kg	2.56 kg
Vitamin/mineral/taurine premix	1.12 kg	1.12 kg	1.12 kg	1.12 kg	1.12 kg
Magnesium chloride	405.00 g	405.00 g	405.00 g	405.00 g	405.00 g
Soy lecithin	364.00 g	364.00 g	364.00 g	364.00 g	364.00 g
Monoglycerides	364.00 g	364.00 g	364.00 g	364.00 g	364.00 g
AA fungal oil	364.00 g	364.00 g	364.00 g	364.00 g	364.00 g
Potassium citrate	340.00 g	340.00 g	340.00 g	340.00 g	340.00 g
Carrageenan	300.00 g	300.00 g	300.00 g	300.00 g	300.00 g
Nucleotide-choline premix	293.00 g	293.00 g	293.00 g	293.00 g	293.00 g
Sodium citrate	250.00 g	250.00 g	250.00 g	250.00 g	250.00 g
DHA oil	230.00 g	230.00 g	230.00 g	230.00 g	230.00 g
Potassium chloride	138.00 g	138.00 g	138.00 g	138.00 g	138.00 g
Calcium carbonate	101.00 g	101.00 g	101.00 g	101.00 g	101.00 g
Magnesium chloride	948.50 g	948.50 g	948.50 g	948.50 g	948.50 g
Mixed Carotenoid Suspension	110.23 g	110.23 g	110.23 g	110.23 g	110.23 g
Vitamin A, D3, E, K1	82.60 g	82.60 g	82.60 g	82.60 g	82.60 g
Choline chloride	35.48 g	35.48 g	35.48 g	35.48 g	35.48 g
L-carnitine	30.7 g	30.7 g	30.7 g	30.7 g	30.7 g
Vitamin A palmitate	313.00 mg	313.00 mg	313.00 mg	313.00 mg	313.00 mg
Sodium chloride	AN	AN	AN	AN	AN
Potassium phosphate	AN	AN	AN	AN	AN

AN = as needed

EXAMPLES 16-19

[0109] Examples 16-19 illustrate concentrated liquid human milk fortifiers of the present disclosure, the ingredients of which are listed in the table below. All ingredient amounts are listed as kilogram or pound per 18,000 pounds batch of product, unless otherwise specified.

Ingredient (Per 18,000 pounds)	Ex. 16	Ex. 17	Ex. 18	Ex. 19
Nonfat milk solids	7220.00 lbs	7220.00 lbs	7220.00 lbs	7220.00 lbs
Corn syrup solids	2870.00 lbs	2870.00 lbs	2870.00 lbs	2870.00 lbs
Medium chain triglycerides	1760.00 lbs	1760.00 lbs	1760.00 lbs	1760.00 lbs
Whey protein concentrate	3410.00 lbs	3410.00 lbs	3410.00 lbs	3410.00 lbs
Tricalcium phosphate	701.00 kg	701.00 kg	701.00 kg	701.00 kg
Galactooligosaccharides	164 kg	350 kg	650 kg	818 kg
Potassium citrate tribasic	224.00 kg	224.00 kg	224.00 kg	224.00 kg
Ascorbic acid	136.00 kg	136.00 kg	136.00 kg	136.00 kg
Magnesium chloride	117.00 kg	117.00 kg	117.00 kg	117.00 kg
Sodium chloride	4.71 kg	4.71 kg	4.71 kg	4.71 kg
m-Inositol	11.00 kg	11.00 kg	11.00 kg	11.00 kg
Sodium citrate tribasic	23.90 kg	23.90 kg	23.90 kg	23.90 kg
Ferrous sulfate	4.00 kg	4.00 kg	4.00 kg	4.00 kg
Soy lecithin	16.80 kg	16.80 kg	16.80 kg	16.80 kg
Zinc sulfate	11.1 kg	11.1 kg	11.1 kg	11.1 kg
Vitamin E acetate	7.60 kg	7.60 kg	7.60 kg	7.60 kg
Vitamin A palmitate	2.40 kg	2.40 kg	2.40 kg	2.40 kg
Niacinamide	9.80 kg	9.80 kg	9.80 kg	9.80 kg
Riboflavin	1.1 kg	1.1 kg	1.1 kg	1.1 kg
Calcium pantothenate	4.40 kg	4.40 kg	4.40 kg	4.40 kg
Cupric sulfate	1.800 kg	1.800 kg	1.800 kg	1.800 kg
Thiamine hydrochloride	776.00 g	776.00 g	776.00 g	776.00 g
Pyridoxine hydrochloride	665.00 g	665.00 g	665.00 g	665.00 g
Vitamin D3	359.00 g	359.00 g	359.00 g	359.00 g
Biotin	82.00 g	82.00 g	82.00 g	82.00 g
Folic acid	77.00 g	77.00 g	77.00 g	77.00 g
Cyanocobalamin	2.00 g	2.00 g	2.00 g	2.00 g
Phylloquinone	27.00 g	27.00 g	27.00 g	27.00 g
Manganese sulfate	51.00 g	51.00 g	51.00 g	51.00 g
Sodium selenate	1.10 g	1.10 g	1.10 g	1.10 g
Calcium carbonate	0-4 kg	0-4 kg	0-4 kg	0-4 kg
Potassium phosphate monobasic	0-32 kg	0-32 kg	0-32 kg	0-32 kg
Potassium hydroxide	24.00 kg	24.00 kg	24.00 kg	24.00 kg

EXAMPLE 20

[0110] In this Example, the effect of GOS on increasing the expression of TFF3 and other goblet cells that promote gastrointestinal healing is analyzed.

[0111] GOS is tested with respect to its ability to induce MUC-2, TFF3, RELMb, CHST5, and GAL3ST2 expression in the human LS174T cell culture model of goblet cells. The human LS174T colorectal cancer cell line is obtained from the American Type Culture Collection (ATCC). LS174T cells are maintained in minimum essential medium (MEM) supplemented with 10% Fetalplex (Gemini Biosciences), 1.5 g/L of Na_2CO_3, 10 ml/L penicillin G-streptomycin solution (Gemini Bio-products) at 37°C in 5% CO_2. GOS (Purimine GO-P90) is obtained from GTC Nutrition (Westchester, IL) and dissolved in cell culture grade water to required concentration. The solution is subsequently filter sterilized and used for cell culture studies. The endotoxin level of GOS solution is measured by LAL assay kit (Gen Script) and found to be less than 0.5 EU/ml (Endotoxin Units/ml). LS174T cells are treated with the media described above but with or without 8 g GOS/L for 72 hours.

[0112] LS174T cells are collected and suspended in Trizol reagent and total RNA is isolated using the RNeasy Plus Kit (Qiagen) according to the manufacturer's instructions. The quality and quantity of RNA isolates are determined by Nanodrop (Thermo Fisher Scientific). RNA isolates are reverse transcribed using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems) to create cDNA, which is to assess gene expression via quantitative PCR.

[0113] For quantitative RT-PCR, specific TaqMAN gene expression assays are obtained from Applied Biosystems, which include expression assays for MUC-2 (Hs00159374_m1), TFF3 (Hs00173625_m1), RELMB (Hs00395669_m1), CHST5 (Hs00375495_m1), GAL3ST2 (Hs00223271_m1) and GUSB (Hs99999908_m1). Quantitative real-time PCR is performed using TaqMAN PCR Master Mix (Applied Biosystems). Reactions are run in duplicates in a 384-well plate using an Applied Biosystems 7900HT Fast Real-Time PCR System. The results are analyzed using SDS 2.3 software and calculated by delta delta Ct method. All samples are normalized to Gus-β expression and fold induction is calculated over untreated controls. Gene expression is expressed as fold increase compared to GOS-free control cells. The experiment is repeated

three times. Data represent means+ SEM (n=3 plates per experiment). Statistical differences are indicated by different letters ($P < 0.05$).

[0114] Figures 1A-1C represent the results of three replicate experiments. In each experiment, the treatment with GOS at a level of 8 g/L consistently and significantly increases the expression of the TFF3 gene 6-7 fold compared to control cultures. Additionally, expression of the genes encoding MUC-2, RELMb, and CHST5 are consistently and significantly increased by 2-3, 5-9, and 2-3 fold, respectively. Increased expression of goblet cell genes is specific and not universal, as evidenced by the lack of induction of GAL3ST2 by treatment with GOS at 8g/L.

[0115] These results indicate that GOS promotes the expression of several genes involved in the healing response of the GI tract. First, expression of TFF3, which GOS is shown to enhance, has been positively associated with prevention and restitution of gastrointestinal damage to the epithelial cells in the intestine of mammals. Oral treatment with TFF3 reduces the damage associated with different forms of colitis in animal models. Additionally, GOS induced the expression of MUC-2, which provides a barrier that protects the gastrointestinal tract from infection and other sources of injury. Further, GOS induced the expression of RELMb, which is a protein associated with resolution of inflammation. Because tissue damage is difficult to heal when inflammation is abundant, the inflammation resolving effects of RELMb induced by GOS also supports healing. The combined impact of GOS on expression of TFF3, MUC-2 and RELMb enables a product to support wound healing through its synergistic effects on cell healing, resolution of inflammation, and promotion of barrier function.

EXAMPLE 21

[0116] In this Example, the dose-dependency of the induction of expression of TFF3 and other goblet cells that promote gastrointestinal healing by GOS is analyzed.

[0117] GOS is tested with respect to its ability to dose-dependently induce MUC-2, TFF3, RELMb, CHST5, and GAL3ST2 expression in the human LS174T cell culture model of goblet cells. The human LS174T colorectal cancer cell line is obtained from the American Type Culture Collection (ATCC). LS174T cells are maintained in minimum essential medium (MEM) supplemented with 10% Fetalplex (Gemini Biosciences), 1.5 g/L

of Na_2CO_3, 10 ml/L penicillin G-streptomycin solution (Gemini Bio-products) at 37°C in 5% CO_2. GOS (Purimine GO-P90) is obtained from GTC Nutrition (Westchester, IL) and dissolved in cell culture grade water to required concentration. The solution is subsequently filter sterilized and used for cell culture studies. The endotoxin level of GOS solution is measured by LAL assay kit (Gen Script) and found to be less than 0.5 EU/ml (Endotoxin Units/ml). LS174T cells are treated with the media described above containing 0, 1, 5, 8, 12, 15, or 20 g GOS/L.

[0118] LS174T cells are collected and suspended in Trizol reagent and total RNA is isolated using the RNeasy Plus Kit (Qiagen) according to the manufacturer's instructions. The quality and quantity of RNA isolates are determined by Nanodrop (Thermo Fisher Scientific). RNA isolates are reverse transcribed using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems) to create cDNA, which is to assess gene expression via quantitative PCR.

[0119] For quantitative RT-PCR, specific TaqMAN gene expression assays are obtained from Applied Biosystems, which includes expression assays for MUC-2 (Hs00159374_m1), TFF3 (Hs00173625_m1), RELMB (Hs00395669_m1), CHST5 (Hs00375495_m1), GAL3ST2 (Hs00223271_m1) and GUSB (Hs99999908_m1). Quantitative real-time PCR is performed using TaqMAN PCR Master Mix (Applied Biosystems). Reactions are run in duplicates in a 384-well plate using an Applied Biosystems 7900HT Fast Real-Time PCR System. The results are analyzed using SDS 2.3 software and calculated by delta delta Ct method. All samples are normalized to Gus-β expression and fold induction is calculated over untreated controls. Gene expression is expressed as fold increase compared to GOS-free control cells. The experiment is repeated three times. Data represent means+ SEM (n=3 plates per experiment). Statistical differences are indicated by different letters ($P < 0.05$).

[0120] Figures 2A-2E represent the combined results of three replicate experiments. Specifically, Figure 2B indicates a dose dependent increase in expression of TFF3, with a modest induction (~3 fold) noted at the 1 mg/mL and 5 mg/mL treatment levels and more pronounced increases (10-12 fold) at 8 mg/mL and higher. Similarly the expression levels of MUC-2 (Figure 2A), RELMb (Figure 2C), and CHST5 (Figure 2D) are only modestly or not affected at GOS levels of 1-5 mg/mL but are markedly elevated

(5-6 fold for MUC-2, 3-4 fold for RELMb, and 8-14 fold for CHST5) in response to treatment with GOS at levels of 8 mg/mL or higher. In contrast, gene expression of GAL3ST2 (Figure 2E) is not significantly impacted at any dose. As such, it can be concluded that the impact of GOS on expression of several genes involved in the healing response of the gastrointestinal tract is dose-dependent.

EXAMPLE 22

[0121] In this Example, the ability of GOS to promote the ability of probiotics to induce expression of TFF3 and other goblet cells that promote gastrointestinal healing is analyzed.

[0122] GOS is tested with respect to its impact on the ability of probiotics to induce MUC-2, TFF3, RELMb, CHST5, and GAL3ST2 expression in the human LS174T cell culture model of goblet cells. The human LS174T colorectal cancer cell line is obtained from the American Type Culture Collection (ATCC). LS174T cells are maintained in minimum essential medium (MEM) supplemented with 10% Fetalplex (Gemini Biosciences), 1.5 g/L of Na_2CO_3, 10 ml/L penicillin G-streptomycin solution (Gemini Bio-products) at 37°C in 5% CO_2. GOS (Purimine GO-P90) is obtained from GTC Nutrition (Westchester, IL) and dissolved in cell culture grade water to required concentration. The solution is subsequently filter sterilized and used for cell culture studies. The endotoxin level of GOS solution is measured by LAL assay kit (Gen Script) and found to be less than 0.5EU/ml (Endotoxin Units/ml).

[0123] Probiotic *Bifidobacterium lactis* cultures are grown in sMRS supplemented with 0.5 g/L cysteine in the presence of 1% glucose or 1% GOS. Culture O.D. is measured at 600 nm and, at stationary phase, the culture supernatant is collected after centrifugation at 4000 rpm for 5 min. The culture supernatant is subsequently filter sterilized and lyophilized. The lyophilized product is herein named the "postbiotic" fraction. Bacterial culture media containing 1% GOS or 1% glucose but not inoculated with *Bifidobactrium lactis* is filtered, lyophilized, and used as the controls for the postbiotic fractions. Postbiotic fractions and control fractions are then added to MEM to represent "postbiotic" and control media, respectively. LS174T cells are treated with postbiotic and control media for 72 hours.

[0124] At the end of the incubation period, the LS174T cells are collected and suspended in Trizol reagent. Total RNA is isolated using the RNeasy Plus Kit (Qiagen) according to the manufacturer's instructions. The quality and quantity of RNA isolates are determined by Nanodrop (Thermo Fisher Scientific). RNA isolates are reverse transcribed using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems) to create cDNA, which is to assess gene expression via quantitative Real-time PCR. Specific TaqMAN gene expression assays are obtained from Applied Biosystems, which includes expression assays for MUC-2 (Hs00159374_m1), TFF3 (Hs00173625_m1), RELMB (Hs00395669_m1), CHST5 (Hs00375495_m1), GAL3ST2 (Hs00223271_m1) and GUSB (Hs99999908_m1). Quantitative real-time PCR is performed using TaqMAN PCR Master Mix (Applied Biosystems). Reactions are run in duplicates in a 384-well plate using an Applied Biosystems 7900HT Fast Real-Time PCR System. The results are analyzed using SDS 2.3 software and calculated by delta delta Ct method. All samples are normalized to Gus-β expression and fold induction is calculated over untreated controls. Gene expression is expressed as fold increase compared to GOS-free control cells. The experiment is repeated three times. Data represent means + SEM (n=2-3 plates per experiment). Statistical differences are indicated by different letters ($P < 0.05$).

[0125] Figure 3A illustrates the impact of treatment with the *Bifidobacterium lactis* + glucose postbiotic fraction vs. control fraction on the expression of goblet cell products that promote gastrointestinal healing in LS174T cell cultures. The *Bifodobacterium lactis* + glucose postbiotic fraction does not affect the expression levels of MUC-2, RELMb or CHST5. TFF3 expression, however, is reduced by 2/3 by this postbiotic fraction. Figure 3B illustrates the impact of treatment with the *Bifodobacterium lactis* + GOS postbiotic fraction on the expression of goblet cell products that promote gastrointestinal healing in LS174T cell cultures. This postbiotic fraction significantly increases the expression of MUC-2 (2 fold), RELMb (3 fold), CHST5 (1.5 fold) and does not decrease the expression of TFF3.

[0126] These results indicate that incubation of probiotic *Bifidobacterium lactis* with GOS results in production of a supernatant "postbiotic" that induces the expression of genes that can promote gastrointestinal healing. This postbiotic fraction is a model of the products that a probiotic such as *Bifdobacterium lactis* would produce when exposed to GOS in the lumen of an infant's gastrointestinal tract. Therefore these data indicate that

infants fed infant formulas including GOS in combination with a *Bifidobacterium lactis* are provided with greater gastrointestinal protection than those given formulas with GOS or *Bifdobacterium lactis* alone.

EXAMPLE 23

[0127] In this Example, the ability of GOS to promote the ability of probiotics to induce expression of TFF3 and other goblet cells is analyzed.

[0128] GOS is tested with respect to its impact on the ability of probiotics to induce MUC-2, TFF3, RELMb, CHST5, and GAL3ST2 expression in the human LS174T cell culture model of goblet cells. The human LS174T colorectal cancer cell line is obtained from the American Type Culture Collection (ATCC). LS174T cells are maintained in minimum essential medium (MEM) supplemented with 10% Fetalplex (Gemini Biosciences), 1.5 g/L of Na_2CO_3, 10 ml/L penicillin G-streptomycin solution (Gemini Bio-products) at 37°C in 5% CO_2. GOS (Purimine GO-P90) is obtained from GTC Nutrition (Westchester, IL) and dissolved in cell culture grade water to required concentration. The solution is subsequently filter sterilized and used for cell culture studies. The endotoxin level of GOS solution is measured by LAL assay kit (Gen Script) and found to be less than 0.5 EU/ml (Endotoxin Units/ml).

[0129] Probiotic *Bifidobacterium lactis* cultures are grown in sMRS supplemented with 0.5 g/L cysteine in the presence of 1% glucose or 1% GOS while probiotic *Lactobacillus acidophilus* cultures are grown in sMRS in the presence of 1% glucose or 1% GOS. Culture O.D. is measured at 600 nm and at stationary phase the culture supernatant is collected after centrifugation at 4000 rpm for 5 min. The culture supernatants are subsequently filter sterilized and lyophilized. The lyophilized products are herein named the "postbiotic" fraction. Bacterial culture media containing 1% GOS or 1% glucose but not inoculated with probiotic is filtered, lyophilized, and used as the controls for the postbiotic fractions. Postbiotic fractions and control fractions are then added to MEM to represent "postbiotic" and control media, respectively. LS174T cells are treated with postbiotic and control media for 72 hours.

[0130] At the end of the incubation period, the LS174T cells are collected and suspended in Trizol reagent. Total RNA is isolated using the RNeasy Plus Kit (Qiagen) according to the manufacturer's instructions. The quality and quantity of RNA isolates are determined by Nanodrop (Thermo Fisher Scientific). RNA isolates are reverse transcribed using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems) to create cDNA, which is to assess gene expression via quantitative Real-time PCR. Specific TaqMAN gene expression assays are obtained from Applied Biosystems, which include expression assays for MUC-2 (Hs00159374_m1), TFF3 (Hs00173625_m1), RELMB (Hs00395669_m1), CHST5 (Hs00375495_m1), GAL3ST2 (Hs00223271_m1) and GUSB (Hs99999908_m1). Quantitative real-time PCR is performed using TaqMAN PCR Master Mix (Applied Biosystems). Reactions are run in duplicates in a 384-well plate using an Applied Biosystems 7900HT Fast Real-Time PCR System. The results are analyzed using SDS 2.3 software and calculated by delta delta Ct method. All samples are normalized to Gus-β expression and fold induction is calculated over untreated controls. Gene expression is expressed as fold increase compared to GOS-free control cells. Data represent means+ SEM (n=3). Statistical differences are indicated by different letters ($P < 0.05$).

[0131] Figures 4A-4E report the impact of treatment with the *B. lactis* postbiotic fraction or *L. acidophilus* postbiotic fraction vs. control fractions on the expression of goblet cell products that promote gastrointestinal healing in LS174T cell cultures. Treatment of those cells with *L. acidophilus* postbiotic fraction significantly increases the expression of MUC-2 and RELMb but only at the high dose. The *L. acidophilus* postbiotic does not impact the expression of TFF3, CHST5 or GAL3ST2. Treatment of LS174T cells with *B. lactis* postbiotic fraction significantly increases TFF3, RELMb and CHST5 expression but only at the highest dose. MUC-2 and GAL3ST2 expression are not significantly increased by treatment with that postbiotic fraction.

[0132] These results indicate that incubation of probiotic *B. lactis* or *L. acidophilus* with GOS results in production of a supernatant "postbiotic" that induces the expression of genes that can promote gastrointestinal healing. This postbiotic fraction is a model of the products that a probiotic, such as *B. lactis* or *L. acidophilus*, would produce when exposed to GOS in the lumen of an infant's gastrointestinal tract. Therefore, these data indicate that infants fed formulas including GOS and *B. lactis* or GOS and *L. acidophilus* are provided with greater gastrointestinal protection than those given formulas with *B. lactis*, *L. acidophilus* or GOS alone.

WHAT IS CLAIMED IS:

1. A method of enhancing healing of the gastrointestinal tract of an individual, the method comprising:

identifying an individual having an injured gastrointestinal tract; and

administering to the individual a nutritional composition comprising a galacto-oligosaccharide.

2. The method of claim 1 wherein the gastrointestinal tract is injured as the result of at least one of antibiotic therapy, radiation therapy, chemotherapy, surgery, enteric infection, inflammatory bowel disease, colitis, bowel obstruction, and chronic stress.

3. The method of claim 1 wherein the nutritional composition further comprises at least one probiotic.

4. The method of claim 1 wherein the nutritional composition is selected from the group consisting of a human milk fortifier, an infant formula, a pediatric formula, a follow on formula, and an adult nutritional composition.

5. The method of claim 4 wherein the nutritional composition comprises galactooligosaccharide in a concentration of from about 8 kg/1000 kg nutritional composition to about 160 kg/1000 kg nutritional composition.

6. The method of claim 1 wherein the nutritional composition comprises galactooligosaccharide in a concentration of from about 164 kg/18,000 pounds nutritional composition to about 818 kg/18,000 pounds nutritional composition.

7. The method of claim 1 wherein the nutritional composition further comprises at least one human milk oligosaccharide.

8. A method of reducing the incidence of intestinal mucosa injury, the method comprising:

identifying an individual susceptible to an intestinal mucosa injury; and

administering to the individual a nutritional composition comprising a galacto-oligosaccharide.

9. The method of claim 8 wherein the nutritional composition further comprises at least one probiotic.

10. The method of claim 8 wherein the nutritional composition is selected from the group consisting of a human milk fortifier, an infant formula, a pediatric formula, a follow on formula, and an adult nutritional composition.

11. The method of claim 10 wherein the nutritional composition comprises galactooligosaccharide in a concentration of from about 8 kg/1000 kg nutritional composition to about 160 kg/1000 kg nutritional composition.

12. The method of claim 8 wherein the nutritional composition comprises galactooligosaccharide in a concentration of from about 164 kg/18,000 pounds nutritional composition to about 818 kg/18,000 pounds nutritional composition.

13. A method of improving the barrier function in the gastrointestinal tract of an individual; the method comprising:

identifying an individual in need of an increased barrier function of the gastrointestinal tract; and

administering to the individual a nutritional composition comprising a galacto-oligosaccharide.

14. The method of claim 13 wherein the nutritional composition further comprises at least one probiotic.

15. A method of reducing the incidence of inflammation of the gastrointestinal tract of an individual, the method comprising:

identifying an individual susceptible to inflammation of the gastrointestinal tract; and

administering to the individual a nutritional composition comprising a galacto-oligosaccharide.