DESCRIPTION

METHODS FOR PROMOTING NEURONAL DEVELOPMENT AND/OR HEALTH

TECHNICAL FIELD

[0001] The present disclosure relates to method(s) for promoting neuronal health and development, as well as neurogenesis, in a subject, comprising providing a nutritional composition suitable for administration to adult and pediatric subjects that include a neurologic component. The neurologic component may include lactoferrin, as well as zinc sulfate, at least one organosulfur compound, and combinations thereof. Suitable non-limiting organosulfur compounds include alpha-lipoic acid ("ALA"), allyl sulfide, allyl disulfide, sulforaphane ("SFN"), and/or L-sulforaphane ("L-SFN").

BACKGROUND ART

[0002] The brain makes up only 2% of total body weight, yet it is a demanding organ that uses up to 30% of the day's calories and nutrients. (Harris, J.J. et al, *The Energetics of CN5 White Matter.* Jour. of. Neuroscience, Jan. 2012: 32(1): 356-371). The human brain and nervous system begin forming very early in prenatal life and both continue to develop until about the age of three. This early development can have lifelong effects on overall brain and nervous system health. Accordingly, brain nutrients can be important additives in the diets of infants, children and pregnant and lactating women because of their ability to promote early brain development. Additionally, brain nutrients are important for adults, as many nutrients promote nervous system repair and provide neuroprotective health benefits.

[0003] Numerous nutrients are believed to be involved with supporting healthy brain development. Recently, however, it has been discovered that certain organosulfur compounds, for example ALA, when combined with lactoferrin promote neurogenesis and/or neuronal differentiation on human adipose-derived stem cells ("hADSCs") and human neuronal stem cells ("hNSCs").

[0004] Lactoferrin, an iron-binding glycoprotein, is one of the major multifunctional agents present in human milk. It has the capacity to bind two molecules of iron in a reversible fashion and can facilitate the uptake of iron within the intestines.

examples of organosulfur compounds include ALA, allyl sulfide, allyl disulfide, sulforaphane ("SFN"), and/or L-sulforaphane ("L-SFN").

[0010] In certain embodiments the nutritional composition may further comprise a long chain polyunsaturated fatty acid ("LCPUFA"), such as docosahexanoic acid ("DHA"), sialic acid, a prebiotic, a probiotic, P-glucan, an iron source, fisetin, Kaempferol, urosolic acid, or mixtures of one or more thereof.

[0011] Due to critical brain development during the first years of life, in one embodiment the method includes providing a nutritional composition which comprises an infant formula or a pediatric nutritional composition that includes the neurologic component described herein. The nutritional compositions of the present disclosure may provide neuroprotective health benefits and promote overall brain and nervous system health.

[0012] It is to be understood that both the foregoing general description and the following detailed description present embodiments of the disclosure and are intended to provide an overview or framework for understanding the nature and character of the disclosure as it is claimed. The description serves to explain the principles and operations of the claimed subject matter. Other and further features and advantages of the present disclosure will be readily apparent to those skilled in the art upon a reading of the following disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **Fig. 1A** is a phase contrast microscopy image of hADSCs under the neuronal differentiation condition without treatment of a neurologic component. The morphology of the hADSCs represents a condition of undifferentiation, with a large and flat morphology, as well as no obvious neurite outgrowth.

[0014] **Fig. 1B** is a phase contrast microscopy image of hADSCs forming morphologies that resembles bi-polar, tri-polar, and multi-polar neural cells.

[0015] **Fig. 2A** is a phase contrast microscopy image of a control well containing hADSCs with no treatment of a neurologic component or DHA.

[0127] In certain embodiments, the nutritional composition is hypoallergenic. In other embodiments, the nutritional composition is kosher and/or halal. In still further embodiments, the nutritional composition contains non-genetically modified ingredients. In an embodiment, the nutritional formulation is sucrose-free. The nutritional composition may also be lactose-free. In other embodiments, the nutritional composition does not contain any medium-chain triglyceride oil. In some embodiments, no carrageenan is present in the composition. In other embodiments, the nutritional composition is free of all gums.

[0128] The nutritional composition of the present disclosure is not limited to compositions comprising nutrients specifically listed herein. Any nutrients may be delivered as part of the composition for the purpose of meeting nutritional needs and/or in order to optimize the nutritional status in a subject.

[0129] Moreover, in some embodiments, the nutritional composition is nutritionally complete, containing suitable types and amounts of lipids, carbohydrates, proteins, vitamins and minerals to be a subject's sole source of nutrition. Indeed, the nutritional composition may optionally include any number of proteins, peptides, amino acids, fatty acids, probiotics and/or their metabolic by-products, prebiotics, carbohydrates and any other nutrient or other compound that may provide many nutritional and physiological benefits to a subject. Further, the nutritional composition of the present disclosure may comprise flavors, flavor enhancers, sweeteners, pigments, vitamins, minerals, functional food ingredients, food ingredients, processing ingredients or combinations thereof.

[0130] The nutritional composition of the present disclosure may be standardized to a specific caloric content, it may be provided as a ready-to-use product, or it may be provided in a concentrated form.

[0131] In some embodiments, the nutritional composition of the present disclosure is a growing-up milk. Growing-up milks are fortified milk-based beverages intended for children over 1 year of age (typically from 1-3 years of age, from 4-6 years of age or from 1-6 years of age). They are not medical foods and are not intended as a meal replacement or a supplement to address a particular nutritional deficiency. Instead, growing-up milks are designed with the intent to serve as a complement to a diverse diet to provide additional insurance that a child achieves

selection of suitable emulsifier(s) will depend, in part, upon the formulation and final product.

[0140] The nutritional compositions may optionally include one or more preservatives that may also be added to extend product shelf life. Suitable preservatives include, but are not limited to, potassium sorbate, sodium sorbate, potassium benzoate, sodium benzoate, calcium disodium EDTA, and mixtures thereof.

[0141] The nutritional compositions may optionally include one or more stabilizers. Suitable stabilizers for use in practicing the nutritional composition of the present disclosure include, but are not limited to, gum arabic, gum ghatti, gum karaya, gum tragacanth, agar, furcellaran, guar gum, gellan gum, locust bean gum, pectin, low methoxyl pectin, gelatin, microcrystalline cellulose, CMC (sodium carboxymethylcellulose), methylcellulose hydroxypropyl methyl cellulose, hydroxypropyl cellulose, DATEM (diacetyl tartaric acid esters of mono- and diglycerides), dextran, carrageenans, CITREM (citric acid esters of mono- and diglycerides of fatty acids), and mixtures thereof.

[0142] The present disclosure further provides method(s) for promoting brain and nervous system health by providing a nutritional composition comprising a neurologic component described herein to a target subject. Without being bound by any particular theory, it is believed that providing a nutritional composition comprising the neurologic component will support neurogenesis, and/or neuronal health and development.

[0143] In some embodiments the target subject may be a pediatric subject. Further, in one embodiment, the nutritional composition provided to the pediatric subject may be an infant formula. The neurologic component added to the infant formula may be selected from a specific source and concentrations thereof may be adjusted to maximize health benefits. In another embodiment of this method, the nutritional composition comprising a neurologic component that is provided to a pediatric subject is a growing up milk.

[0144] In yet another embodiment, the nutritional composition comprising a neurologic component may be provided to

any target subject to promote neuroprotection. In still other embodiments, the method is directed toward promoting neurogenesis by providing a nutritional composition comprising a neurologic component to a pregnant or lactating mother. Additionally, the nutritional compositions comprising a neurologic component described herein may provide a supplemental source of neurological nutrition to target subjects.

[0145] The present disclosure further provides a method for promoting neuronal health and/or development, as well as other benefits enumerated herein, and includes administering to a subject an effective amount of the nutritional composition of the present disclosure. In some embodiments, the nutritional composition may be expelled directly into a subject's intestinal tract and/or directly into the gut. In some embodiments, the composition may be formulated to be consumed or administered enterally.

[0146] The methods of the present disclosure directed toward providing the nutritional compositions described herein deliver enhanced neurological nutritional and health benefits to their target subjects. The disclosure of the methods for providing the nutritional composition described herein to a particular target subject are not to be limiting, instead they further serve as examples where administration of the nutritional composition described herein may be appropriate.

EXAMPLES

[0147] Examples are provided to illustrate the neurogenesis of the nutrients included in the neurologic component of the nutritional composition(s) described herein. Briefly, the neurogenesis capabilities of ALA were tested on human adipose derived stem cells ("hADSCs") by the procedure described herein. These examples should not be interpreted as any limitation on the nutritional compositions disclosed herein, but serve as illustrations of neurogenesis of the neurologic component. It is intended that the specification, together with the example, be considered to be exemplary only, with the scope and spirit of the disclosure being indicated by the claims which follow the examples. The procedures of U.S. Patent Application Serial No. 13/408,485 filed by Kuang, et al. and U.S. Patent Application Serial No. 13/408,490 filed by Kuang, et al., each of which filed on February 29, 2012, may be

CLAIMS

What is claimed is:

1. A method for promoting neuronal health and/or development, comprising providing a nutritional composition which comprises a carbohydrate source, a fat source, a protein source, and a neurologic component, wherein the neurologic component comprises lactoferrin, zinc sulfate, and at least one organosulfur compound, wherein the organosulfur compound comprises alpha-lipoic acid present in an amount from about 0.1 mg/100 kcal to about 35 mg/100 kcal of the nutritional composition.
2. The method of claim 1, wherein zinc sulfate is present in an amount of from about 0.1 mg/100 kcals to about 2 mg/100 kcals of nutritional composition.
3. The method of claim 1, wherein the at least one organosulfur compound further comprises at least one compound selected from the group consisting of allyl sulfide, allyl disulfide, and sulforaphane.
4. The method of claim 1, wherein the nutritional composition further comprises sialic acid.
5. The method of claim 1, wherein the nutritional composition further comprises a prebiotic.
6. The method of claim 1, wherein the nutritional composition further comprises docosahexaenoic acid.
7. The method of claim 1, wherein the nutritional composition is an infant formula.
8. The method of claim 1, wherein the nutritional composition further comprises a probiotic.
9. A method for promoting neuronal health and/or development, comprising providing a nutritional composition which comprises per 100 kcal:
    (i) between about 6 g and about 22 g of a carbohydrate source;
    (ii) between about 1 g and about 7 g of a protein source;
    (iii) between about 1.3 g and about 7.2 g of a fat source; and
    (iv) a neurologic component comprising lactoferrin, zinc sulfate, and at least one organosulfur compound,
    wherein the at least one organosulfur compound comprises alpha-lipoic acid in an amount of between about 0.1 mg to about 37 mg per 100 kcals of the nutritional composition.