

**USE OF SPECIFIC CARBOHYDRATE SYSTEMS DURING
PREGNANCY FOR EFFECTING THE OFFSPRING**

FIELD OF THE DISCLOSURE

[0001] The present disclosure is directed to the administration of specific carbohydrate systems to a pregnant woman for improving the health of the woman, improving lean body mass development and formation in the offspring, reducing long term adverse health effects, including obesity, in the offspring later in life, and exerting a significant protective effect against detrimental metabolic and body composition changes induced by an obesogenic environment in adult life. More specifically, the present disclosure is directed to the administration of a carbohydrate system comprising a slow rate of digestion simple carbohydrate and a complex carbohydrate in combination with a non-absorbent carbohydrate and/or an indigestible carbohydrate to a pregnant woman, and optionally during lactation, to improve the health of the woman, improve lean body mass formation in the offspring, and reduce long term adverse health effects such as sarcopenia, sarcopenic obesity, obesity and glucose intolerance and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension) later in life in the offspring.

BACKGROUND OF THE DISCLOSURE

[0002] Breastfeeding to provide human milk is generally recommended for all infants as human milk is known to provide multiple benefits to the growing and developing infant. In some cases, however, human milk is not available as the mother chooses not to breast feed, or only breast feeds for a short time. In other cases, the human milk is inadequate or inadvisable for medical reasons. As such, synthetic infant formulas have been developed and utilized for some time.

[0003] The prevalence of obesity, overweight, and glucose intolerance in adolescents and adults has increased rapidly over the past 20 years in the United States and

globally and continues to rise. Overweight and obesity are classically defined based on the percentage of body fat or, more recently, the body mass index or BMI. The BMI is defined as the ratio of weight in kilograms divided by the height in meters, squared. As overweight and obesity become more prevalent in all age groups, it is inevitable that the number of women giving birth who are also overweight and/or diabetic will also increase. It is known that overweight and obese women who become pregnant have a greater risk of developing gestational diabetes. Maternal hyperglycemia may lead to infants with increased body size and fat mass and such infants are themselves prone to develop obesity and diabetes later in life, including during adolescence and adulthood. Additionally, recent research has suggested that obese women who themselves have normal glucose tolerance give birth to infants with a higher fat mass than those born to women who are not obese.

[0004] An increasing body of scientific evidence suggests that infants born to overweight and obese mothers have a greater risk of becoming overweight or obese later in life than infants born to mothers who are not overweight or obese. This predisposition appears to be higher if both parents are affected. Childhood overweight and obesity currently affects millions of children worldwide.

[0005] It would therefore be desirable to provide nutritional compositions and methods that could improve the health of the offspring and prevent or reduce the incidence or risk of multiple diseases or conditions, such as obesity, glucose intolerance, and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension) later in the life of infants. It would be further beneficial if such methods could be utilized early in the life of the child to program the child against such diseases and conditions.

[0006] The present disclosure is directed to methods for blunting the glycemic response and improving glycemia and insulinemia during gestational and lactating periods for preventing or reducing the incidence in the offspring of developing obesity and/or glucose intolerance later in life. The present disclosure is further directed to methods of improving the lean body mass development and formation of an offspring to prevent or reduce sarcopenia and sarcopenic obesity later in life.

SUMMARY OF THE DISCLOSURE

[0007] The present disclosure is directed to the administration of specific carbohydrate systems, generally as part of a nutritional composition, to a pregnant woman

for improving the health of the woman, improving the lean body mass development and formation of the offspring, and reducing long term adverse health effects, including obesity, glucose intolerance, related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension), sarcopenia, and sarcopenic obesity in the offspring later in life. Specifically, the present disclosure is directed to the administration of a carbohydrate system comprising a slow rate of digestion simple carbohydrate, such as isomaltulose, and a complex carbohydrate, such as a maltodextrin, in combination with a non-absorbent carbohydrate, such as an insoluble dietary fiber, and/or an indigestible carbohydrate, such as fructooligosaccharides, to a pregnant woman, and optionally to the woman during lactation, to improve the health of the woman, improve lean body mass development and formation in the offspring, and reduce long term adverse health effects, such as obesity, sarcopenia, sarcopenic obesity, glucose intolerance, and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension) later in life in the offspring. In addition to the substantial long term health benefits that the carbohydrate system can provide the offspring, the system may also provide the pregnant or pregnant and then lactating mother with improved glycemia and insulinemia during gestational and lactation periods, which may not only benefit the mother's health during these periods, but may also benefit the offspring.

[0008] Thus, in one embodiment, the present disclosure is directed to a method of reducing sarcopenia later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0009] In another embodiment, the present disclosure is directed to a method of improving lean body mass development and formation in an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0010] Thus, in one embodiment, the present disclosure is directed to a method of reducing obesity later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system. The

carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0011] In another embodiment, the present disclosure is directed to a method of reducing glucose intolerance later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0012] In another embodiment, the present disclosure is directed to a method of reducing long term adverse health effects later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0013] In another embodiment, the present disclosure is directed to a method of blunting the glycemic response of a pregnant woman. The method comprises administering to the pregnant woman a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide.

[0014] In another embodiment, the present disclosure is directed to a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises isomaltulose, maltodextrin having a DE of 9 to 16, fructooligosaccharides, and an insoluble dietary fiber.

[0015] It has now surprisingly been discovered that an improvement in glycemia and insulinemia in a woman during gestational and lactating periods can be obtained by administering to the woman a nutritional composition including a carbohydrate system that includes a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. Additionally, it has been discovered that the risk of the offspring developing adiposity, obesity, sarcopenia, and/or glucose intolerance or other long term adverse health effects later in life is also reduced when the mother consumes the carbohydrate system during pregnancy or during pregnancy and lactation. Surprisingly, it appears that these benefits are related to the complexity of

the carbohydrate system itself as opposed to the glycemic index or load of the diet of the mother.

BRIEF DESCRIPTION OF THE FIGURES

[0016] Figure 1 is a schematic representation of the experimental study of the Examples.

[0017] Figures 2A and 2B are birthweight and growth curves for the experimental study of the Examples.

[0018] Figure 3 shows offspring adipogenesis graphs for the experimental study of Example 1.

[0019] Figure 4 shows offspring adipogenesis graphs for the experimental study of Example 1.

[0020] Figure 5 shows offspring adipogenesis graphs for the experimental study of Example 1.

[0021] Figure 6 shows lean body mass graphs for the experimental study of Example 2.

[0022] Figure 7 shows lean body mass graphs for the experimental study of Example 2.

[0023] Figure 8 shows lean body mass graphs for the experimental study of Example 2.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0024] The nutritional compositions and methods of the present disclosure utilize a specific carbohydrate system. The carbohydrate system, which may include all of the carbohydrate components of the nutritional composition, or only a part of the overall carbohydrate component of the nutritional composition, includes the combination of a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. The nutritional compositions including the carbohydrate systems are administered to a pregnant woman, or a pregnant and then lactating woman, to not only improve glycemia and insulinemia in the woman during

gestational and lactating periods, but also to improve the lean body mass development and formation of the offspring and to prevent or reduce the incidence in the offspring of developing long term adverse health effects, including obesity, sarcopenia, sarcopenic obesity, glucose intolerance, and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension) later in life. The woman receiving the nutritional composition including the carbohydrate system may, in some cases, be an obese woman who may be diabetic or have gestational diabetes mellitus.

[0025] The methods of the present disclose using the carbohydrate systems as described herein provide an easy, convenient, and effective means for improving the health of the pregnant or pregnant and then lactating mother and for improving the long term health of the offspring by improving lean body mass development and formation and reducing the potential for long term adverse health effects in the offspring later in life. As diseases and conditions such as obesity, sarcopenia, and glucose intolerance continue to significantly impact the daily lives of more and more adolescents and adults, it becomes increasingly important to develop methods of programming offspring early in life so as to reduce the risk and/or incidence of these diseases and conditions later in life. The methods of the present disclosure allow offspring to be programmed early in life against long term adverse health effects later in life, including obesity, sarcopenia, sarcopenic obesity, glucose intolerance, and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension). Furthermore, the methods of the present disclosure allow a significant protective effect against detrimental metabolic and body composition changes induced by an obesogenic environment in adult life.

[0026] These and other optional features of the nutritional compositions and methods of the present disclosure, as well as some of the many other optional variations and additions, are described in detail hereafter.

[0027] The terms “retort” and “retort sterilized” 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 retort sterilized nutritional liquid product.

[0028] The terms “aseptic” and “aseptic sterilized” are used interchangeably herein and unless otherwise specified, refer 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.

[0029] The terms “nutritional formula” or “nutritional product” or “nutritional composition,” as used herein, are used interchangeably and, unless otherwise specified, refer to nutritional liquids, nutritional solids, nutritional semi-liquids, nutritional semi-solids, 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.

[0030] The term “nutritional liquid,” as used herein, unless otherwise specified, refers to nutritional products in ready-to-drink liquid form, concentrated form, and nutritional liquids made by reconstituting the nutritional powders described herein prior to use.

[0031] The term “nutritional powder,” as used herein, unless otherwise specified, refers to nutritional products in flowable or scoopable form that can be reconstituted with water or another aqueous liquid prior to consumption and includes both spray dried and drymixed/dryblended powders.

[0032] The term “nutritional semi-solid,” as used herein, unless otherwise specified, refers to nutritional products that are intermediate in properties, such as rigidity, between solids and liquids. Some semi-solids examples include puddings, gelatins, and doughs.

[0033] The term “nutritional semi-liquid,” as used herein, unless otherwise specified, refers to nutritional products that are intermediate in properties, such as flow properties, between liquids and solids. Some semi-liquids examples include thick shakes and liquid gels.

[0034] The term “later in life,” as used herein, refers to the period of life from weaning through elderly, including childhood, adolescence and adulthood.

[0035] 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.

[0036] 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.

[0037] 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.

[0038] 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.

[0039] The various embodiments of the nutritional compositions of the present disclosure may also be substantially free of any optional or selected ingredient or feature described herein, provided that the remaining nutritional compositions still contain all of the required ingredients or features as described herein. In this context, and unless otherwise specified, the term “substantially free” means that the selected nutritional compositions contain less than a functional amount of the optional ingredient, typically less than 1%, including less than 0.5%, including less than 0.1%, and also including zero percent, by weight of such optional or selected ingredient.

[0040] The nutritional compositions and methods of the present disclosure may comprise, consist of, or consist essentially of the essential elements of the products and methods as described herein, as well as any additional or optional element described herein or otherwise useful in nutritional compositions.

Product Form

[0041] The nutritional compositions as described herein for use in the methods of the present disclosure as noted below comprise a carbohydrate system that includes a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. The actual product form of the nutritional composition administered to the pregnant or lactating woman is not critical so long as the carbohydrate system is as described herein. As such, the product forms described herein should be viewed as exemplary and not limiting in any manner as other product forms not listed herein are within the scope of the present disclosure.

[0042] The nutritional compositions of the present disclosure may be formulated and administered in any known or otherwise suitable oral product form. Any nutritional solid, semi-solid, liquid, semi-liquid, or powder 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 carbohydrate system as described herein. In one specific embodiment, the nutritional composition is in the form of a bar, such as a nutritional bar, weight loss bar, or meal replacement bar.

[0043] The exact form of the nutritional composition of the present disclosure is not critical, although it is desirably formulated as dietary product forms, which are defined herein as those embodiments comprising the carbohydrate system as described herein in a product form that also contains at least one of fat and protein, and optionally, additional carbohydrates. The compositions 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 product for use in pregnant and/or lactating women afflicted with specific diseases or conditions or with a targeted nutritional benefit.

Nutritional Liquids

[0044] Nutritional liquids include both concentrated and ready-to-feed nutritional liquids. These nutritional liquids are most typically formulated as suspensions, emulsions or clear or substantially clear liquids.

[0045] 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.

[0046] The nutritional liquids may be and typically are shelf stable. The nutritional liquids 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%, of water by weight of the nutritional liquid. The nutritional liquids 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.

[0047] The nutritional liquid 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.

[0048] Although the serving size for the nutritional liquid can vary depending upon a number of variables, a typical serving size is generally 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 300 mL, including from about 100 mL to about 300 mL, from about 4 mL to about 250 mL, from about 150 mL to about 250 mL, from about 10 mL to about 240 mL, and from about 190 mL to about 240 mL.

Nutritional Powders

[0049] The nutritional powders are in the form of flowable or substantially flowable particulate compositions, or at least particulate compositions. Particularly suitable nutritional powder forms include spray dried, agglomerated or dryblended powder compositions, or combinations thereof, or powders prepared by other suitable methods. The compositions can easily be scooped and measured with a spoon or similar other device, wherein the compositions can easily be reconstituted with a suitable aqueous liquid, typically water, to form a nutritional liquid 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 or within 20 minutes of reconstitution.

Carbohydrate System

[0050] The methods of the present invention utilize a nutritional composition that includes a carbohydrate system as described herein. The carbohydrate system may include all of the carbohydrate components present in the nutritional composition such that the nutritional composition does not contain any other carbohydrates components, or may include only a portion of the carbohydrate components present in the nutritional composition; that is, in some embodiments there are additional carbohydrate components present in the nutritional composition in addition to the carbohydrate system as described herein such as, for example, lactose.

[0051] The carbohydrate systems as described herein comprise specific combinations of individual carbohydrates that have a low glycemic index, generally less than 55.

[0052] The carbohydrate systems of the present disclosure include a simple carbohydrate that has a slow rate of digestion. Simple carbohydrates include those carbohydrates that are comprised of monosaccharide sugars or disaccharide sugars. Carbohydrates that have a slow rate of digestion are those carbohydrates that are low glycemic and low insulinemic and are carbohydrates that generally provide a gradual, relatively low rise in blood glucose over time. Suitable simple carbohydrates that have a slow rate of digestion that are suitable for use in the carbohydrate system include isomaltulose, sucromalt, and combinations thereof. Sucromalt may be made from the enzymatic conversion of sucrose and maltose into a fructose and oligosaccharide liquid syrup. The oligosaccharide is comprised of glucoses linked together by alternating 1,3 and 1,6 linkages.

[0053] The simple carbohydrate that has a slow rate of digestion may be present in the carbohydrate system in an amount of from about 40% to about 80% by weight, including from about 40% to about 75% by weight, including from about 40% to about 70% by weight, including from about 45% to about 70% by weight, including from about 50% to about 70% by weight, including from about 55% to about 70% by weight, including from about 60% to about 70% by weight, including from about 65% to about 70% by weight. In some specific embodiments, the simple carbohydrate that has a slow rate of digestion may be present in the carbohydrate system in an amount of about 65% by

weight, or even about 66% by weight, or even about 67% by weight, or even about 68% by weight, or even about 69% by weight, or even about 70% by weight.

[0054] In addition to the simple carbohydrate that has a slow rate of digestion, the carbohydrate system includes a complex carbohydrate. Complex carbohydrates include those carbohydrates that are chains of three or more single sugar molecules linked together. Suitable complex carbohydrates for use in the carbohydrate system include, for example, maltodextrins. In some particularly desirable embodiments, the maltodextrins will have a Dextrose Equivalent of from 9 to 16. Other suitable complex carbohydrates in some embodiments include other sources of starches such as, for example, corn starch, rice starch, wheat starch, and the like.

[0055] The complex carbohydrate may be present in the carbohydrate system in an amount of from about 1% to about 15% by weight, including from about 2% to about 12% by weight, including from about 2% to about 10% by weight, including from about 3% to about 10% by weight, including from about 4% to about 10% by weight, including from about 5% to about 10% by weight, including from about 6% to about 10% by weight, including from about 7% to about 10% by weight, and including from about 8% to about 10% by weight. In some particularly desirable embodiments, the complex carbohydrate is present in the carbohydrate system in an amount of about 8% by weight, including about 9% by weight, including about 10% by weight.

[0056] In addition to the simple carbohydrate that has a slow rate of digestion and the complex carbohydrate, the carbohydrate systems as described herein additionally include at least one of: (1) a nonabsorbent carbohydrate; and (2) an indigestible oligosaccharide. In some embodiments of the present disclosure, the carbohydrate system will comprise, consist essentially of, or consist of a simple carbohydrate that has a slow rate of digestion, a complex carbohydrate, and a nonabsorbent carbohydrate. In other embodiments of the present disclosure, the carbohydrate system will comprise, consist essentially of, or consist of a simple carbohydrate that has a slow rate of digestion, a complex carbohydrate, and an indigestible oligosaccharide. In still other embodiments of the present disclosure, the carbohydrate system will comprise, consist essentially of, or consist of a simple carbohydrate that has a slow rate of digestion, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible carbohydrate. In some embodiments, as

noted above, one or more additional carbohydrates, such as lactose, may be present in addition to the carbohydrate system.

[0057] In some embodiments, the carbohydrate system includes a nonabsorbent carbohydrate. Nonabsorbent carbohydrates include fibers and other non-absorbable starches that are not substantially absorbed in the upper intestinal tract so that they pass through to the colon where bacteria ferment them into fatty acids that can be absorbed. These fatty acids may act to heal the lining of the colon. Suitable nonabsorbent carbohydrates include inulin, and insoluble dietary fibers, including Fibersol® fibers, including Fibersol® 2E, which is a digestion resistant maltodextrin, Nutriose®, amylose, or other insoluble fibers, and combinations thereof.

[0058] The nonabsorbent carbohydrate may be present in the carbohydrate system in an amount of from about 5% to about 25% by weight, including from about 5% to about 20% by weight, including from about 5% to about 19% by weight, including from about 5% to about 18% by weight, including from about 5% to about 17% by weight, including from about 5% to about 16% by weight, including from about 7.0% to about 16% by weight, including from about 7.0% to about 15.5% by weight. In some embodiments, the nonabsorbent carbohydrate is present in the carbohydrate system in an amount of about 7.0% by weight. In another embodiment, the nonabsorbent carbohydrate is present in the carbohydrate system in an amount of about 15.5% by weight.

[0059] In some embodiments, the carbohydrate system includes an indigestible carbohydrate. Indigestible carbohydrates are carbohydrates, including some fibers, that travel through the colon undigested so as to promote digestion and a healthy bowel. Suitable indigestible carbohydrates include fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof.

[0060] The indigestible carbohydrate may be present in the carbohydrate system in an amount of from about 1.0% to about 18% by weight, including from about 2% to about 17% by weight, including from about 2% to about 15% by weight, including from about 3% to about 15% by weight, including from about 3% to about 14% by weight, including from about 3% to about 13% by weight, including from about 3% to about 12% by weight. In one particularly desirable embodiment, the indigestible carbohydrate is present in the carbohydrate system in an amount of about 3.5% by weight. In another

particularly desirable embodiment, the indigestible carbohydrate is present in the carbohydrate system in an amount of about 12% by weight.

[0061] In a particularly desirable embodiment, the carbohydrate system comprises about 68% by weight isomaltulose, about 8.0% by weight maltodextrin having a DE of 9 to 16, about 12% by weight fructooligosaccharides, about 7.0 % by weight Fibersol 2E insoluble dietary fiber, and a maximum of 5.0% by weight lactose.

[0062] In another particularly desirable embodiment, the carbohydrate system comprises about 68% by weight isomaltulose, about 8.0% by weight maltodextrin having a DE of 9 to 16, about 3.5% by weight fructooligosaccharides, about 15.5 % by weight Fibersol 2E insoluble dietary fiber, and a maximum of 5.0% by weight lactose.

Macronutrients

[0063] The nutritional compositions including the carbohydrate systems as described herein may further comprise one or more optional additional macronutrients. The optional macronutrients include proteins, lipids, and carbohydrates in addition to the carbohydrate system described above, and combinations thereof. In some embodiments, the nutritional compositions are formulated as dietary products containing all three macronutrients for the pregnant or lactating woman.

[0064] Macronutrients suitable for use herein include any protein, lipid, or carbohydrate (in addition to the carbohydrate system) or source thereof that is known for or otherwise suitable for use in an oral nutritional composition, provided that the optional macronutrient is safe and effective for oral administration and is otherwise compatible with the other ingredients in the nutritional composition.

[0065] The concentration or amount of optional lipid, carbohydrate (including the carbohydrate system described herein), and protein in the nutritional compositions can vary considerably depending upon the particular product form (e.g., bars or other solid dosage forms, milk or soy-based liquids or other clear beverages, reconstitutable powders, etc.) and the various other formulations and targeted dietary needs. These optional macronutrients are most typically formulated within any of the embodied ranges described in the following tables.

Nutrient % Total Cal.	Embodiment A	Embodiment B	Embodiment C
Carbohydrate	0-98	2-96	10-75
Protein	0-98	2-96	5-70
Lipid	0-98	2-96	20-85
	Embodiment D	Embodiment E	Embodiment F
Carbohydrate	30-50	25-50	25-50
Protein	15-35	10-30	5-30
Lipid	35-55	1-20	2-20

Each numerical value preceded by the term “about”

Carbohydrate

[0066] Optional carbohydrates suitable for use in the nutritional compositions, in addition to the carbohydrate systems described herein, may be simple, complex, or variations or combinations thereof. Non-limiting examples of suitable carbohydrates include hydrolyzed or modified starch or cornstarch, maltodextrin, isomaltulose, sucromalt, glucose polymers, sucrose, corn syrup, corn syrup solids, rice-derived carbohydrate, glucose, fructose, lactose, high fructose corn syrup, honey, sugar alcohols (e.g., maltitol, erythritol, sorbitol), and combinations thereof.

[0067] Optional carbohydrates suitable for use herein also include soluble dietary fiber, non-limiting examples of which include gum Arabic, fructooligosaccharides (FOS), sodium carboxymethyl cellulose, guar gum, citrus pectin, low and high methoxy pectin, oat and barley glucans, carrageenan, psyllium, and combinations thereof. Insoluble dietary fiber is also suitable as a carbohydrate source herein, non-limiting examples of which include oat hull fiber, pea hull fiber, soy hull fiber, soy cotyledon fiber, sugar beet fiber, cellulose, corn bran, and combinations thereof.

Protein

[0068] Optional proteins suitable for use in the nutritional compositions include hydrolyzed, partially hydrolyzed or non-hydrolyzed proteins or protein sources, and can be derived from any known or otherwise suitable source such as milk (e.g., casein, whey), animal (e.g., meat, fish, egg albumen), cereal (e.g., rice, corn), vegetable (e.g., soy, pea, potato), or combinations thereof. The proteins for use herein can also include, or be entirely or partially replaced by, free amino acids known for use in nutritional products, non-limiting examples of which include L-tryptophan, L-glutamine, L-tyrosine, L-methionine, L-cysteine, taurine, L-arginine, L-carnitine, and combinations thereof.

Lipid

[0069] Optional lipids suitable for use in the nutritional composition include coconut oil, fractionated coconut oil, soy oil, corn oil, olive oil, safflower oil, high oleic safflower oil, high GLA-safflower oil, MCT oil (medium chain triglycerides), sunflower oil, high oleic sunflower oil, palm and palm kernel oils, palm olein, canola oil, flaxseed oil, borage oil, cottonseed oils, evening primrose oil, blackcurrant seed oil, transgenic oil sources, fungal oils, algae oils, marine oils (e.g., tuna, sardine), and so forth.

Other Optional Ingredients

[0070] The nutritional compositions as described herein may further comprise other optional ingredients that may modify the physical, chemical, aesthetic or processing characteristics of the products 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.

[0071] Non-limiting examples of such optional ingredients include preservatives, anti-oxidants, emulsifying agents, buffers, human milk oligosaccharides and other prebiotics, probiotics, nucleotides, carotenoids, pharmaceutical actives, additional nutrients as described herein, colorants, flavors, thickening agents and stabilizers, emulsifying agents, lubricants, and so forth, and combinations thereof.

[0072] 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 product 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 composition.

[0073] A stabilizer may also be included in the nutritional compositions. Any stabilizer that is known or otherwise suitable for use in a nutritional product 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.

[0074] The nutritional composition may further comprise any of a variety of vitamins, non-limiting examples of which include vitamin A, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, pyridoxine, vitamin B12, niacin, folic acid, pantothenic acid, biotin, vitamin C, choline, inositol, salts and derivatives thereof, and combinations thereof.

[0075] The nutritional composition may also further comprise any of a variety of minerals known or otherwise suitable for use in nutritional compositions, non-limiting examples of which include phosphorus, magnesium, calcium as described hereinbefore, zinc, manganese, copper, iodine, sodium, potassium, chloride, selenium, and combinations thereof.

Methods of Manufacture

[0076] The nutritional compositions for use in the nutrition systems 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.

[0077] The nutritional compositions 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 two separate slurries are prepared, that are later blended together, heat treated, standardized, and either terminally sterilized to form a retort composition or aseptically processed and filled to form an aseptic composition. Alternately, the slurries can be blended together, heat treated, standardized, heat treated a second time, evaporated to remove water, and spray dried to form a powder composition.

[0078] The slurries formed may include a carbohydrate-mineral (CHO-MIN) slurry and a protein-in-fat (PIF) slurry. Initially, the CHO-MIN slurry is formed by dissolving selected carbohydrates (e.g., carbohydrate system, etc.) in heated water with agitation, followed by the addition of minerals (e.g., potassium citrate, magnesium chloride, potassium chloride, sodium chloride, choline chloride, etc.). The resulting CHO-MIN slurry is held with continued heat and moderate agitation until it is later blended with the other prepared slurries.

[0079] The PIF slurry is formed by heating and mixing the oil (e.g., high oleic safflower oil, soybean oil, coconut oil, monoglycerides, etc.) and emulsifier (e.g., soy lecithin), and then adding oil soluble vitamins, mixed carotenoids, protein (e.g., whey protein, casein protein, etc.), carrageenan (if any), calcium carbonate or tricalcium phosphate (if any), and ARA oil and DHA oil (in some embodiments) with continued heat and agitation. The resulting PIF slurry is held with continued heat and moderate agitation until it is later blended with the other prepared slurries.

[0080] Water was heated and then combined with the CHO-MIN slurry, nonfat milk (if any), and the PIF slurry under adequate agitation. The pH of the resulting blend was adjusted to 6.6-7.0, and the blend was held under moderate heated agitation. ARA oil and DHA oil is added at this stage in some embodiments.

[0081] The composition is then subjected to high-temperature short-time (HTST) processing, during which the composition is heat treated, emulsified and homogenized, and then cooled. Water soluble vitamins and ascorbic acid are added, the pH is adjusted to the desired range if necessary, flavors (if any) are added, and water is added to achieve the desired total solid level. For aseptic compositions, the emulsion receives a second heat treatment through an aseptic processor, is cooled, and then aseptically packaged into suitable containers. For retort compositions, the emulsion is packaged into suitable containers and terminally sterilized. In some embodiments, the emulsions can be optionally further diluted, heat-treated, and packaged to form a desired ready-to-feed or concentrated liquid, or can be heat-treated and subsequently processed and packaged as a reconstitutable powder, e.g., spray dried, dry mixed, agglomerated.

[0082] The spray dried composition or dry-mixed composition may be prepared by any collection of known or otherwise effective techniques, suitable for making and formulating a nutritional powder. For example, when the powder composition 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 powder composition. Following drying, the finished powder may be packaged into suitable containers. Dryblending or drymixing may also be used to prepare the nutritional compositions of the present disclosure.

Methods of Use

[0083] In some embodiments, the nutritional composition including the carbohydrate system as described above is administered to a pregnant woman to provide advantageous benefits to the woman during pregnancy and also to the offspring (baby) after delivery and later in life. In other embodiments, the nutritional composition including the carbohydrate system as described above is administered to the pregnant woman and

additionally administered to the woman during lactation such that the suckling offspring and the mother continue to derive additional benefits as noted herein.

[0084] In one embodiment, the nutritional composition including the carbohydrate system as described herein is administered to the pregnant woman to blunt the glycemic response of digestible glucose polymers in the woman and to improve glycemia and insulinemia during the gestational period. In some embodiments, the pregnant woman may be diabetic and/or obese, and/or may have gestational diabetes mellitus, or may be at risk of being diabetic and/or obese or having gestational diabetes mellitus. As such, in some embodiments, the offspring of the mother may be at increased risk of obesity, glucose intolerance, and the like later in life.

[0085] In another embodiment, the nutritional composition including the carbohydrate system as described herein is administered to the pregnant woman and to the woman during lactation to blunt the glycemic response of digestible glucose polymers in the woman and to improve glycemia and insulinemia during the gestational and lactation periods. In some embodiments, the pregnant woman may be diabetic and/or obese, or may have gestational diabetes mellitus, or may be at risk of being diabetic and/or obese or having gestational diabetes mellitus. As such, in some embodiments, the offspring of the mother may be at increased risk of obesity, glucose intolerance, and the like later in life. Although generally less desirable, the nutritional composition including the carbohydrate system as described herein may be administered to the woman only during the lactation period and not during pregnancy.

[0086] In other embodiments, the nutritional composition including the carbohydrate system as described herein is administered to the pregnant woman, and optionally to the lactating woman, to improve the lean body mass development and formation of the offspring so as to prevent, or reduce the incidence of, or reduce the risk of, or reduce the extent or occurrence of, sarcopenia and sarcopenic obesity later in the life of the offspring. The improvement in lean body mass development and formation includes an increase in lean muscle mass and strength and enhanced peak muscle mass accretion. By improving the lean muscle mass development and formation of the offspring, the incidence of sarcopenia and sarcopenic obesity later in the life of the offspring may be reduced.

[0087] In other embodiments, the nutritional composition including the carbohydrate system is administered to the pregnant woman, and optionally to the lactating

woman, to prevent or reduce the incidence of long term adverse health effects in the offspring later in life. The methods of the present disclosure are effective for preventing or reducing the incidence of, reducing the risk of, or reducing the extent or occurrence of, numerous long term adverse health effects in the offspring later in life, including adiposity, hyperphagia, obesity, diabetes, glucose intolerance, cardiovascular disease, hypertension and non alcoholic fatty liver disease (NAFLD).

[0088] As noted herein, the nutritional composition including the carbohydrate system described herein may be administered to a pregnant woman, or may be administered to a pregnant woman and then further to the woman during lactation. When the nutritional composition including the carbohydrate system described herein is administered to a pregnant woman, it is generally administered for a period of at least 1 month, including at least 2 months, including at least 3 months, including at least 4 months, including at least 5 months, including at least 6 months, including at least 7 months, including at least 8 months, and including substantially during the entire pregnancy. In a desirable embodiment, the nutritional composition including the carbohydrate system described herein is administered in a continuous, day to day manner, although administration in a manner other than day to day or every day is within the scope of the methods of the present disclosure. When the nutritional composition of the present disclosure including the carbohydrate system as described herein is administered to a lactating woman, it may be administered for the entire period of lactation, or for a lesser period of time, although it is generally desirable to administer the nutritional composition for the entire period of lactation. In a desirable embodiment, the nutritional composition including the carbohydrate system described herein is administered during lactation in a continuous, day to day manner, although administration in a manner other than day to day or every day is within the scope of the methods of the present disclosure.

[0089] In one specific embodiment, the present disclosure is directed to a method of reducing obesity later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system comprising about 68% by weight isomaltulose, about 8.0% by weight maltodextrin having a DE of 9 to 16, about 12% by weight fructooligosaccharides, about 7.0% by weight Fibersol 2E insoluble dietary fiber, and about 5.0% by weight lactose.

[0090] In another specific embodiment, the present disclosure is directed to a method of reducing obesity later in the life of an offspring. The method comprises administering to a pregnant woman a nutritional composition comprising a carbohydrate system comprising about 68% by weight isomaltulose, about 8.0% by weight maltodextrin having a DE of 9 to 16, about 3.5% by weight fructooligosaccharides, about 15.5% by weight Fibersol 2E insoluble dietary fiber, and about 5.0% by weight lactose.

[0091] The carbohydrate system as described herein for administration to the pregnant woman may be administered to the woman such that the daily intake is from about 20 grams to about 175 grams, including from about 50 grams to about 175 grams, including from about 75 grams to about 150 grams, including from about 75 grams to about 125 grams, including from about 90 grams to about 125 grams, and further including from about 100 grams to about 125 grams. When the carbohydrate system is administered to the lactating woman, it may be administered such that the daily intake is from about 20 grams to about 210 grams, including from about 50 grams to about 210 grams, including from about 75 grams to about 210 grams, including from about 100 grams to about 210 grams, including from about 125 grams to about 200 grams, and further including from about 150 grams to about 175 grams.

Exemplary patent claims relating to the above-disclosed subject matter include the following. 1. A method of reducing sarcopenia later in the life of an offspring, the method comprising administering to a pregnant woman a nutritional composition comprising a carbohydrate system, the carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. 2. The method of claim 1 further comprising administering the nutritional composition to the woman during a period of lactation. 3. The method of claim 1 wherein the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof. 4. The method of claim 1 wherein the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof. 5. The method of claim 4 wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16. 6. The method of claim 1 wherein the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof.

7. The method of claim 1 wherein the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof. 8. The method of claim 1 wherein the nutritional composition is administered daily for at least the last three months of the pregnancy. 9. The method claim 1 wherein the nutritional composition is administered daily for at least the last six months of the pregnancy. 10. The method of claim 1 wherein the woman consumes from about 20 to about 175 grams of the carbohydrate system per day. 11. The method of claim 1 wherein the woman consumes from about 90 to about 125 grams of the carbohydrate system per day. 12. The method of claim 1 wherein the carbohydrate system is comprised of from about 40% to about 80% by weight slow rate of digestion simple carbohydrate, from about 1% to about 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from about 1% to about 20% by weight indigestible carbohydrate. 13. The method of claim 1 wherein the carbohydrate system is comprised of from about 60% to about 70% by weight slow rate of digestion simple carbohydrate, from about 6% to about 10% by weight complex carbohydrate, from about 5% to about 20% by weight nonabsorbent carbohydrate, and from about 2% to about 15% by weight indigestible carbohydrate. 14. A method of improving the lean body mass development and formation of an offspring, the method comprising administering to a pregnant woman a nutritional composition comprising a carbohydrate system, the carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. 15. The method of claim 14 further comprising administering the nutritional composition to the woman during a period of lactation. 16. The method of claim 14 wherein the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof. 17. The method of claim 14 wherein the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof. 18. The method of claim 17 wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16. 19. The method of claim 14 wherein the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof. 20. The method of claim 14 wherein the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof. 21. The method of claim 14 wherein the

nutritional composition is administered daily for at least the last three months of the pregnancy. 22. The method claim 14 wherein the nutritional composition is administered daily for at least the last six months of the pregnancy. 23. The method of claim 14 wherein the woman consumes from about 20 to about 175 grams of the carbohydrate system per day. 24. The method of claim 14 wherein the woman consumes from about 90 to about 125 grams of the carbohydrate system per day. 25. The method of claim 14 wherein the carbohydrate system is comprised of from about 40% to about 80% by weight slow rate of digestion simple carbohydrate, from about 1% to about 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from about 1% to about 20% by weight indigestible carbohydrate.

Exemplary patent claims relating to the above-disclosed subject matter further include the following: 1. A method of reducing obesity later in the life of an offspring, the method comprising administering to a pregnant woman a nutritional composition comprising a carbohydrate system, the carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. 2. The method of claim 1 further comprising administering the nutritional composition to the woman during a period of lactation. 3. The method of claim 1 wherein the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof. 4. The method of claim 1 wherein the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof. 5. The method of claim 4 wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16. 6. The method of claim 1 wherein the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof. 7. The method of claim 1 wherein the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof. 8. The method of claim 1 wherein the nutritional composition is administered daily for at least the last three months of the pregnancy. 9. The method claim 1 wherein the nutritional composition is administered daily for at least the last six months of the pregnancy. 10. The method of claim 1 wherein the woman consumes from about 20 to about 175 grams of the carbohydrate system per day. 11. The method of claim 1 wherein the woman consumes from about 90 to about 125 grams of the carbohydrate system per day. 12. The

method of claim 1 wherein the carbohydrate system is comprised of from about 40% to about 80% by weight slow rate of digestion simple carbohydrate, from about 1% to about 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from about 1% to about 20% by weight indigestible carbohydrate. 13. The method of claim 1 wherein the carbohydrate system is comprised of from about 60% to about 70% by weight slow rate of digestion simple carbohydrate, from about 6% to about 10% by weight complex carbohydrate, from about 5% to about 20% by weight nonabsorbent carbohydrate, and from about 2% to about 15% by weight indigestible carbohydrate. 14. A method of reducing glucose intolerance later in the life of an offspring, the method comprising administering to a pregnant woman a nutritional composition comprising a carbohydrate system, the carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. 15. The method of claim 14 further comprising administering the nutritional composition to the woman during a period of lactation. 16. The method of claim 14 wherein the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof. 17. The method of claim 14 wherein the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof. 18. The method of claim 17 wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16. 19. The method of claim 14 wherein the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof. 20. The method of claim 14 wherein the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof. 21. The method of claim 14 wherein the nutritional composition is administered daily for at least the last three months of the pregnancy. 22. The method claim 14 wherein the nutritional composition is administered daily for at least the last six months of the pregnancy. 23. The method of claim 14 wherein the woman consumes from about 20 to about 175 grams of the carbohydrate system per day. 24. A method of reducing long term adverse health effects later in the life of an offspring, the method comprising administering to a pregnant woman a nutritional composition comprising a carbohydrate system, the carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. 25. The method of claim 24 further

comprising administering the nutritional composition to the woman during a period of lactation. 26. A nutritional composition comprising a carbohydrate system, the carbohydrate system comprising isomaltulose, maltodextrin having a DE of 9 to 16, fructooligosaccharides, and an insoluble dietary fiber.

EXAMPLES

[0092] 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.

Example 1

[0093] In this Example, a well established rat model of developmental programming (the “maternal over-nutrition” model) was used to evaluate the effect of maternal nutritional intervention, using various carbohydrate systems with a low glycemic index (GI), during gestation on the offspring glycemic control as a nutritional strategy to prevent the risk of developing adiposity later in life in the offspring.

Materials and Methods

[0094] *Animal maintenance and experimental procedures.* Female Sprague-Dawley virgin rats (10-wk-old) were obtained from Charles River Laboratories (Orleans Cedex, France). Protocols for all experimental procedures were conducted in accordance with the ethical guidelines for animal experimentation at the Spanish National Research Council (RD 1201/2005 October 10). Rats were housed individually with free access either to the control standard AIN 93M (American Institute of Nutrition) diet or the highly palatable obesogenic lard diet (HF). The AIN 93M diet contained 4% fat, 12.9% protein, 70% carbohydrates and 5% fiber, while the HF diet consisted of 20.5% fat, 24.2% protein, 41.5% carbohydrates and 7.9% fiber. After 6 weeks of eating these diets, the rats were bred with 13 week old male AIN 93M-fed Sprague Dawley rats. After mating, and only during gestation period ($\approx$ 21 days), the dams fed with HF diet were then randomly assigned to one of four experimental obesogenic HF-diets, containing different types of carbohydrates with different GI, (Table 1 set forth below).

[0095] Table 1

	Standard control and obesogenic rodent diets			Experimental obesogenic rodent diets			
	AIN93G	AIN93M	HF	GL241	GL256	GL362	GL625
Total Protein	18.30	12.89	24.19	24.19	24.19	24.19	24.19
Calcium caseinate	97.60	98.41	97.81	97.74	97.65	97.81	97.81
Total Fat	7.00	4.10	20.50	20.50	20.50	20.50	20.50
Lard fat	0.00	0.00	99.99	99.96	98.46	99.99	99.99
Total HC	64.59	71.19	49.42	49.2	49.11	49.42	49.42
Maltodextrin (GI=95)	18.97	20.53	24.43	7.76	7.76	0.01	24.43
Lactose (GI=46)	----	----	----	5.16	5.15	65.85	----
Isomaltulose (GI=32)	----	----	----	67.88	67.88	----	----
Sucrose (GI=65)	14.37	13.91	36.07	0.74	0.33	16.09	36.07
Glucose (GI=100)	----	----	----	0.08	0.08	----	----
Cornstarch (GI=85)	59.48	58.54	16.00	----	----	----	16.00
Fibersol 2E (GI=5)	----	----	----	6.99	15.47	----	----
FOS (GI=0)	----	----	----	11.98	3.49	18.97	----
Cellulose (GI=0)	7.18	7.02	7.90	----	----	----	7.90
Glycemic Load (GL)	910	927	625	241	256	362	625

Total glycemic load (GL) was calculated by first multiplying the amount of each carbohydrate contained in a daily dietary intake by its glycemic index (with the use of glucose as the reference food), then by summing the values from all CHO sources. Daily dietary glycemic load thus represents the quality and quantity of carbohydrate intake and the interaction between the two.

[0096] Meanwhile, the dams fed with AIN 93M diet continued on AIN 93 G diet, (consisted of 7% fat, 18.3% protein, 57.4% carbohydrates and 7.2% fiber), during the gestation period. Body weight was monitored at least weekly and food intake was measured 3 times per week by weighing the diet in the feed containers. After delivery and throughout the lactation period ($\approx$ 21 days), regardless of the diets consumed during pre- and pregnancy periods, all dams were fed with the control standard AIN 93G diet. Within 24 hours of birth, litter size was adjusted to 8 male pups per litter. After weaning, the dams were euthanized and the male pups were weaned onto standard AIN 93G and multi-housed in cages until 6 weeks of age. During the growing period until the adolescence (90-days-old), offspring rats were housed individually with free access to the control standard AIN 93M diet. To investigate whether a hypercaloric diet will worsen the adipose-metabolic phenotype of the adult progeny, at age of 13 weeks, all offspring rats, regardless of the diet consumed by their mothers, were fed with the obesogenic HF diet for 4 weeks. During adolescence and adult periods, offspring body weight and food intake were assessed at least weekly. Figure 1 displays a scheme of the experimental design used in the present Example.

[0097] *Body composition analysis.* Fat body composition was assessed via two independent methods, post-mortem dissected weights of retroperitoneal, perirenal, and gonadal fat pads from rats and by Echo MRI. Echo MRI is a quantitative magnetic resonance body composition analyzer that utilizes the resonance energy of hydrogen nuclei in a magnetic field to compute the density of the tissue. MRI was performed in conscious unanesthetized rats, at delivery, weaning adolescence and adult periods. Each MRI measurement takes ~1 min/rat, and all measurements were performed in duplicate. Index of % fat was derived using this technique.

Results

[0098] *Offspring: birthweight and growth curves.* At delivery the average body weights of the offspring did not significantly differ among study groups (Figure 2A). In addition to body weight at birth, there were no significant differences in the offspring body weight gain after eating the standard AIN 93 (G/ M) diets, during the growing period, or the HF diet during adulthood period (Figure 2B).

[0099] *Offspring adipogenesis.* Figure 3 displays percentage body fat, assessed by Echo MRI, for offspring at delivery, weaning and adolescence periods. Fat mass was not significantly different among groups at birth and at weaning. However, higher body adiposity was evident in adolescent offspring of HF mothers as compared to adolescent offspring of lean dams fed AIN93 diet. A novel finding of the present Example was that a low GI diet on a high-fat diet background may exert measurable benefits on offspring adipogenesis later in life as compared to high GI diet depending on the carbohydrates profiling. Interestingly, offspring born from dams that consumed HF diet containing the carbohydrates mixture with the high GL (GL 625) had lower adiposity compared with offspring of HF dams fed with a carbohydrates system with a lower GL (GL 362). Low GI foods are not necessarily healthier. In fact, it is known that increased consumption of food with a low GI, containing high amount of refined sugars (fructose or sucrose), may be detrimental in terms of adiposity, dyslipidemia, insulin resistance by direct alterations on the lipid metabolism and insulin action. In the present Example, the HF with the GL 362 contained in its carbohydrate composition the highest amount of refined sugars (81%), meanwhile the HF with the GL 625 only contained 36.1 % of refined sugars in its composition. If the adipogenesis data are displayed taking into account not the GI of HF diet but considering the complexity grade of carbohydrate system contained in the high fat

diet, we observe that the HF diets with low GI (GL 241 and 256) containing mixtures of slow digested carbohydrates (such as isomaltulose), complex carbohydrates (such as maltodextrin), resistant starches (such as fibersol) and fiber (such as FOS) induced a significant reduction in the percentage of body fat of adolescent offspring of HF mothers, being very similar to those of lean mothers (Figure 4).

[00100] An important aspect of the present Example was that the dietary carbohydrate systems, consumed by the HF mothers during the pregnancy period, may also exert a significant protective effect against the detrimental effects induced by a HF diet in the adult progeny (Figure 5). As expected, consumption of HF diet, for 4 weeks, induced an increase in body adipogenesis in the adult progeny of lean mothers. However, the groups that consumed the HF diet with low GI (GL 241 and 256) contain mixtures of slow digested carbohydrates (such as isomaltulose), complex carbohydrates (such as maltodextrin), resistant starches (such as fibersol) and fiber (such as FOS), for the same 4 weeks did not show this increase in fat mass. These data suggest that the effects promoted by the carbohydrates mixtures (GL 241 and 256) during pregnancy prevent an obesogenic challenge later in life (such as in adulthood).

Conclusions

[00101] Maternal nutritional intervention using different carbohydrate systems during pregnancy did not affect body weight gain of their offspring from neonatal to adult periods.

[0102] Adipogenesis programming was not directly associated to the GI of the diet consumed by the insulin resistant rats during the pregnancy period.

[0103] Adipogenesis programming was associated to a combination of the low GI and the complexity of CHO system of the diet consumed by the insulin resistant rats during the pregnancy period.

[0104] A diet with a low GI and complex CHO system as described herein consumed by the insulin resistant rats during the pregnancy period, also exerted in the offspring a significant protective effect against obesogenic environment later in life.

Example 2

[0105] In this Example, a well established rat model of developmental programming (maternal over-nutrition model), was utilized to study the effect of maternal nutritional intervention, using different carbohydrates system with low glycemic index (GI), during gestation on the offspring glycemic control as a nutritional strategy to prevent impaired skeletal muscle development that are normally associated with maternal obesity/insulin resistance in their offspring.

Materials and Methods

[0106] *Animals maintenance and experimental procedures.* Ten week old Female Sprague-Dawley virgin rats were obtained from Charles River Laboratories (Orleans Cedex, France). Protocols for all experimental procedures were conducted in accordance with the ethical guidelines for animal experimentation at the Spanish National Research Council (RD 1201/2005 October 10). Rats were housed individually with free access either to the control standard AIN 93M diet or the highly palatable obesogenic lard diet (HF). The AIN 93M diet contained 4% fat, 12.9% protein, 70% carbohydrates and 5% fiber, while the HF diet consisted of 20.5% fat, 24.2% protein, 41.5% carbohydrates and 7.9% fiber. After 6 wks of eating these diets, rats were bred with 13-wk-old male AIN 93M-fed Sprague Dawley rats. After mating, and only during gestation period (≈ 21 days), the dams fed with HF diet were then randomly assigned to one of four experimental obesogenic HF-diets, containing different types of carbohydrates with different GI, (shown in Table 1 of Example 1). Meanwhile, the dams fed with AIN 93M diet continued on AIN 93 G diet, (consisted of 7% fat, 18.3% protein, 57.4% carbohydrates and 7.2% fiber), during the gestation period. Body weight was monitored at least weekly and food intake was measured 3 times per week by weighing the diet in the feed containers. After delivery and throughout the lactation period (≈ 21 days), regardless of the diets consumed during pre- and pregnancy periods, all dams were fed with the control standard AIN 93G diet. Within 24 h of birth, litter size was adjusted to 8 male pups per litter. After weaning the dams were euthanized and the male pups were weaned onto standard AIN 93G and multi-housed in cages until 6 week of age. During the growing period until adolescence (90-day-old), offspring rats were housed individually with free access to the control standard AIN 93M diet. To investigate whether a hypercaloric diet will worsen the adipose-metabolic phenotype of the adult progeny, at age of 13 weeks all offspring rats, regardless of the diet consumed by their mothers, were fed with the obesogenic HF diet for 4 weeks. During adolescence and adult periods, offspring body weight and food intake were assessed at least

weekly. Figure 1 displays a scheme of the experimental design used in the present Example.

[0107] *Body composition analysis.* Lean body mass measurements were determined by Echo MRI. Echo MRI is a quantitative magnetic resonance body composition analyzer that utilizes the resonance energy of hydrogen nuclei in a magnetic field to compute the density of the tissue. MRI was performed in conscious unanesthetized rats, at delivery, weaning adolescence and adult periods. Each MRI measurement takes ~1 min/rat, and all measurements were performed in duplicate. Index of % muscle mass was derived using this technique.

[0108] *Statistical analysis.* To evaluate differences in the body weight gain, we performed two-way ANOVA, considering the terms treatment and time. Statistical evaluation of the offspring lean body mass were analyzed using one-way ANOVA. A posteriori post hoc tests were carried out between treatments at each time point using Tukey test. The probability level at which the differences were considered significant was set at $p < 0.05$.

Results

[0109] *Offspring: birthweight and growth curves.* At delivery the average body weights of the offspring did not significantly differ among study groups (Figure 2A). In addition to body weight at birth, there were not significant differences in the offspring body weight gain after eating the standard AIN 93 (G/ M) diets, during the growing period, or the HF diet during adulthood period (Figure 2B).

[0110] *Offspring skeletal muscle mass.* Figure 6 displays percentage lean body mass, assessed by Echo MRI, for offspring at delivery, weaning and adolescence periods. Lean body mass, was not significantly different among groups at birth and at weaning. However, lower muscle mass was evident in adolescent offspring of HF mothers as compared to adolescent offspring of lean dams fed AIN93 diet. A novel finding of the present study was that a low GI diet on a high-fat diet background may exert measurable benefits on offspring lean body mass as compared to high GI diet depending on the carbohydrates profiling. Interestingly, offspring born from dams that consumed HF diet containing the carbohydrates mixture with the high GL (GL 625) had higher lean body mass compared with offspring of HF dams fed with a carbohydrates system with a lower

GL (GL 362). Low GI foods are not necessarily healthier. In fact, it is known that increased consumption of food with a low GI, containing high amount of refined sugars i.e. fructose or sucrose, may be detrimental in terms of adiposity, dyslipidemia, insulin resistance by direct alterations on the lipid metabolism and insulin action. In the present study, the HF with the GL 362 contained in its carbohydrate composition the highest amount of refined sugars (81%), meanwhile the HF with the GL 625 only contained 36.1% of refined sugars in its composition. If the lean body mass data are displayed taking into account not the GI of HF diet but considering the complexity grade of carbohydrate system contained in the high fat diet, it can be observed that the percentages of lean body mass of adolescent offspring of HF mothers fed with low GI (GL 241 and 256) [containing mixtures of slow digested carbohydrates (such as isomaltulose), complex carbohydrates (such as maltodextrin), resistant starches (such as Fibersol) and fiber (such as FOS) were very similar to those of lean mothers (Figure 7).

[0111] An important aspect of the present study was that the dietary carbohydrate systems, consumed by the HF mothers during the pregnancy period, may also exert a significant protective effect against the detrimental effects induced by a HF diet in the adult progeny (Figure 8). As expected, consumption of HF diet, for 4 weeks, induced a reduction in lean body mass in the adult progeny of lean mothers. However, the groups that consumed the HF diet with low GI (GL 241 and 256) contain mixtures of slow digested carbohydrates (such as isomaltulose), complex carbohydrates (such as maltodextrin), resistant starches (such as Fibersol) and fiber (such as FOS), for the same 4 weeks did not show this reduction in lean body mass. These data suggest that the effects promoted by the carbohydrates mixtures (GL 241 and 256) during pregnancy might prevent from the lost of lean body mass associated to an obesogenic challenge at adulthood life.

Conclusions

[0112] Maternal nutritional intervention using different CHO systems during pregnancy, did not affect body weight gain of their offspring from neonatal to adult periods.

[0113] Programming of muscle development was not directly associated to the GI of the diet consumed by the insulin resistant rats during the pregnancy period.

[0114] Programming of muscle development was associated to a combination of the low GI and the complexity of CHO system of the diet consumed by the insulin resistant rats during the pregnancy period.

[0115] A diet with a low GI and complex CHO system consumed by the insulin resistant rats during the pregnancy period, also exerted in the offspring a significant protective effect against muscle mass lost induced by obesogenic environment later in life.

WHAT IS CLAIMED IS:

1. The combination of a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide for use in a method of treating a pregnant woman wherein the method results in an improvement in the health of the offspring of the pregnant woman.
2. The combination according to claim 1, wherein the improvement in the health of the offspring is a reduction in at least one long term adverse health effect.
3. The combination according to claim 2, wherein the long term adverse health effect comprises one or more of sarcopenia, obesity, and glucose intolerance.
4. The combination according to claim 1, wherein the improvement in the health of the offspring is an improvement in lean body mass development and formation of the offspring.
5. The combination according to any of claims 1-4, wherein the method includes administration of the combination to the woman during a period of lactation.
6. The combination according to claim 1 wherein at least one of the following is met:
 - (a) the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof,
 - (b) the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof,
 - (c) the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof,
 - (d) the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof.

7. The combination according to claim 6, wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16.
8. The combination according to claim 1, wherein the use includes daily administration of the combination for at least the last three months of the pregnancy.
9. The combination according to claim 1, wherein the use includes consumption of from about 20 to about 175 grams of the combination per day.
10. The combination according to claim 1, comprising from about 40% to about 80% by weight slow rate of digestion simple carbohydrate, from about 1% to about 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from about 1% to about 20% by weight indigestible carbohydrate.
11. The combination according to any one of claims 1-10, wherein the combination is incorporated into a nutritional composition suitable for oral consumption.
12. Use of the combination of a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide for the manufacture of a medicament for use in the treatment of a pregnant woman wherein the treatment results in an improvement in the health of the offspring of the pregnant woman.
13. Use according to claim 12, wherein the improvement in the health of the offspring is a reduction in at least one long term adverse health effect.
14. Use according to claim 13, wherein the long term adverse health effect comprises one or more of sarcopenia, obesity, and glucose intolerance.
15. Use according to claim 12, wherein the improvement in the health of the offspring is an improvement in lean body mass development and formation of the offspring.
16. Use according to claim 12, wherein the treatment includes administering the medicament to the woman during a period of lactation.
17. Use according to claim 12, wherein at least one of the following is met:

- (a) the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof,
- (b) the nonabsorbent carbohydrate is selected from the group consisting of inulin, dietary insoluble fibers, digestion resistant maltodextrins, and combinations thereof,
- (c) the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof,
- (d) the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof.

18. Use according to claim 17, wherein the maltodextrin has a Dextrose Equivalent of from 9 to 16.

19. Use according to claim 12, wherein the medicament is administered daily for at least the last three months of the pregnancy.

20. Use according to claim 12, wherein about 20 to about 175 grams of the combination is consumed by the woman per day.

21. Use according to claim 12, wherein the combination comprises from about 40% to about 80% by weight slow rate of digestion simple carbohydrate, from about 1% to about 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from about 1% to about 20% by weight indigestible carbohydrate.

22. Use according to any one of claims 12-21, wherein the medicament is a nutritional composition suitable for oral consumption.