

**USE OF SPECIFIC CARBOHYDRATE SYSTEMS DURING PREGNANCY FOR
PREVENTING FAT ACCUMULATION IN PREGNANT WOMEN**

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and any benefit of European Patent Application No. EP 13382090.2 filed March 15, 2013, the entire contents of which are incorporated by reference in its entirety.

FIELD OF THE DISCLOSURE

[0002] The present disclosure is directed to the administration of specific carbohydrate systems to a pregnant woman for improving preventing fat accumulation in the pregnant woman, as well as for preventing the risk of metabolic complications related to fat accumulation during pregnancy, later in life. More specifically, the present disclosure is directed to the administration of a carbohydrate system comprising a slow rate of digestion simple carbohydrate, a complex carbohydrate, and a non-absorbent carbohydrate and/or an indigestible carbohydrate to a pregnant woman. In one aspect, such administration may both prevent fat accumulation as well as reduce long term adverse effects associated with fat accumulation which may occur after pregnancy later in life.

BACKGROUND OF THE DISCLOSURE

[0003] The prevalence of obesity and overweight 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, obese, and/or diabetic will also increase. In normal pregnancies, glucose homeostasis is maintained, in spite of insulin resistance, by a concomitant compensatory increase in insulin secretion. The increase in insulin secretion is associated with hypertrophy and hyperplasia of the b-cells. For this reason, pregnancy, especially in obese women, is classified as an insulin resistance stage. In obese pregnant women,

gestational-related fat is predominantly accumulated centrally, and represents a combination of truncal fat and visceral fat. Excess central fat is strongly associated with adverse metabolic outcomes either during pregnancy (i.e., gestational diabetes mellitus and preeclampsia) or in adult life (i.e., hypertension, cardiovascular disease and diabetes). During pregnancy, fat accumulation in excess of healthy amounts can result in the condition of overweight or obesity, leading to adverse outcomes during pregnancy and/or later in life.

[0004] 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. 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 reduce the incidence or prevent fat accumulation and resulting weight gain in a pregnant woman, thereby preventing and/or reducing 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) that may affect the mother, and/or the offspring, later in life.

[0006] The present disclosure is directed to methods for preventing fat accumulation in a pregnant woman during the gestational period, so as to avoid one or more of the adverse consequences described above.

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 preventing fat accumulation and thereby improving the health of the woman and/or offspring during and/or after pregnancy. 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 to improve the health of the woman, and, in other aspects, reduce long term adverse health effects, such as obesity, glucose intolerance, and related co-morbidities associated to metabolic syndrome (cardiovascular disease and hypertension).

[0008] Thus, in embodiments, the present disclosure is directed to a method of reducing and/or preventing excessive fat accumulation in a pregnant woman during gestation. The method comprises administering to the pregnant woman during and/or before the gestational period a nutritional composition comprising a carbohydrate system. The carbohydrate system may comprise a slow rate of digestion simple carbohydrate, a complex carbohydrate, a nonabsorbent carbohydrate, and an indigestible oligosaccharide. In one aspect, the carbohydrate system may be administered to a woman prior to pregnancy. In one aspect, the carbohydrate system is administered to a woman during pregnancy.

[0009] In embodiments, the present disclosure is directed to a nutritional composition comprising a carbohydrate system. The carbohydrate system comprises isomaltulose, maltodextrin, fructooligosaccharides, and an insoluble dietary fiber.

[0010] It has now surprisingly been discovered that by administration of 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 to a woman during gestation, excessive fat accumulation can be prevented or reduced.

BRIEF DESCRIPTION OF THE FIGURES

[0011] Figure 1 is a schematic representation of the experimental study of the Examples.

[0012] Figures 2A and 2B show maternal body weight and food intake curves during the gestational period for the experimental study of the Examples. Values are expressed as mean $\pm$ SEM.

[0013] Figure 3A shows the average percentage of fat per group before mating. Figure 3B shows the gestational fat weight gain in the pregnant rats during the gestational periods. Values are expressed as mean $\pm$ SEM.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0014] 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/or an indigestible oligosaccharide. The nutritional compositions including the carbohydrate systems may be administered to a pregnant woman, or a woman prior to pregnancy, to prevent or reduce the occurrence of fat accumulation in the woman, as well as to prevent adverse short and long term health effects associated with fat accumulation. 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.

[0015] The methods of the present disclose using the carbohydrate systems as described herein may provide an easy, convenient, and effective means for improving the health of the pregnant mother and reducing the potential for long term adverse health effects of the mother later in life by preventing or limiting fat accumulation during pregnancy. As diseases and conditions such as overweight and obesity continue to significantly impact the daily lives of more and more adults, it becomes increasingly important to develop methods of preventing fat accumulation during pregnancy so as to reduce the risk and/or incidence of conditions associated with overweight and obesity during and post pregnancy.

[0016] 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.

[0017] 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.

[0018] 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.

[0019] 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.

[0020] 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.

[0021] 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.

[0022] 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.

[0023] 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.

[0024] The term “later in life,” as used herein, refers to the period of life from weaning through elderly, including childhood, adolescence and adulthood.

[0025] 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.

[0026] 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.

[0027] 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.

[0028] 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.

[0029] 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.

[0030] 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

[0031] 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/or an indigestible oligosaccharide. The actual product form of the nutritional composition administered 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.

[0032] 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.

[0033] 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 women afflicted with specific diseases or conditions or with a targeted nutritional benefit.

Nutritional Liquids

[0034] 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.

[0035] 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.

[0036] 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.

[0037] 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.

[0038] 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

[0039] 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

[0040] 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.

[0041] The carbohydrate systems as described herein may comprise specific combinations of carbohydrates (CHO) that provide a low glycemic load, generally less than about 55, or less than about 50, or less than about 40, or less than about 35, or less than about 30, or less than about 28, or about 27. As used herein, the experimental glycemic load is determined experimentally by feeding human test subjects 50 g of available CHO comprising 5.5% lactose + 8.8% maltodextrin DE 9-16 +75% Isomaltulose + 10.7% Fibersol 2E after an overnight fast, expressed as a percentage of the response after 50 g anhydrous glucose was taken by the same subject. This procedure is described in Wolever et al, Measuring the Glycemic Index of Foods: Interlaboratory Study, Am J Clin Nutr. 2008 Jan;87(1):247S-257S. This is in contrast to the “daily glycemic load” or “DGL” of the experimental rodent diet, in which DGL is determined theoretically considering the amount

of each individual carbohydrate contained in the CHO mixture, the glycemic index of the CHO mixture and the total dietary intake.

[0042] 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.

[0043] 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.

[0044] 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 about 5 to about 25, or about 9 to about 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.

[0045] 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.

[0046] 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/or (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.

[0047] 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.

[0048] 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.

[0049] 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.

[0050] 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.

[0051] 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.

[0052] 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

[0053] 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.

[0054] 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.

[0055] 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

Nutrient % Total Cal.	Embodiment A	Embodiment B	Embodiment C
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

[0056] 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.

[0057] 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

[0058] 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

[0059] 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

[0060] 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.

[0061] 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.

[0062] 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.

[0063] 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.

[0064] 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.

[0065] 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

[0066] 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.

[0067] 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.

[0068] 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.

[0069] The PIF slurry may be 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.

[0070] Water is 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 is adjusted to 6.6-7.0, and the blend is held under moderate heated agitation. ARA oil and DHA oil is added at this stage in some embodiments.

[0071] 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.

[0072] 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

[0073] In some embodiments, the nutritional composition including the carbohydrate system as described above is administered to a pregnant woman to prevent fat accumulation to provide advantageous benefits to the woman during pregnancy and, in some instances, later in life. In a yet further aspect, the nutritional composition may be administered to a woman prior to pregnancy, particularly where the risk of weight gain during pregnancy is high, or in instances in which other conditions, such as diabetes, make avoidance of weight gain particularly important to the health of the mother and/or offspring, during and/or after the gestational period.

[0074] In one embodiment, the nutritional composition including the carbohydrate system as described herein is administered to the pregnant woman to reduce fat accumulation during the gestational period so as to prevent, or reduce the incidence of, or reduce the risk of, or reduce the extent or occurrence of, disorders or conditions associated with fat accumulation and/or obesity. 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.

[0075] 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 woman prior to pregnancy. 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.

[0076] In one specific embodiment, the present disclosure is directed to a method of preventing fat accumulation in a pregnant woman. 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.

[0077] In another specific embodiment, 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.

[0078] 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.

EXAMPLES

[0079] 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

[0080] 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 weight gain of rats during gestation.

Materials and Methods

[0081] *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 (Reference group) 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 two experimental obesogenic HF-diets, containing different types of carbohydrates with different GI, (Table 1 set forth below).

[0082] **Table 1.** 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.

	Standard control rodent diets		Experimental obesogenic rodent diets	
	AIN93G	AIN93M	HF Low GI	HF
Total Protein	18.30	12.89	24.19	24.19
Calcium caseinate	97.60	98.41	97.65	97.81
Total Fat	7.00	4.10	20.50	20.50
Lard Fat	0.00	0.00	98.46	99.99
Total HC	64.59	71.19	49.11	49.42
Maltodextrin (GI=95)	18.97	20.53	7.76	24.43
Lactose (GI=46)	--	--	5.15	--
Isomaltulose (GI=32)	--	--	67.88	--
Sucrose (GI=65)	14.37	13.91	0.33	36.07
Glucose (GI=100)	--	--	0.08	--
Cornstarch (GI=85)	59.48	58.54	--	31.60
Fibersol 2E (GI=5)	--	--	15.47	--
FOS (GI=0)	--	--	3.49	--
Cellulose (GI=0)	7.18	7.02	--	7.90
Glycemic Load (GL)	910	927	256	625

[0083] Meanwhile, the dams fed with AIN 93M diet continued on AIN 93G diet (consisting of 7% fat, 18.3% protein, 57.4% carbohydrates and 7.2% fiber), during the gestation period. Body weight and body composition (determined by Magnetic Resonance Imaging, “MRI”) were monitored at least weekly and food intake was measured 3 times per week by weighing the diet in the feed containers. Figure 1 displays a scheme of the experimental design used in the present Example.

Results

[0084] No differences were found in the weight increase along gestation among HF, HF Low GI and Reference groups (Figure 2A). Food intake during gestation was similar for both HF and HF Low GI groups until the last recorded day, when the HF Low GI rats took significantly less food than the HF rats (Figure 2B).

[0085] Figure 3A displays percentage of body fat, assessed by Echo MRI, for mothers before mating. Fat mass was not significantly different among groups. However, higher body adiposity was evident in mothers fed with HF diet for 6 weeks. During the pregnancy period (Figure 3B), dams fed with HF diet had increased gestational fat.

Interestingly, dams from the HF/Low GI group, whose diet contained mixtures of slow digested carbohydrates (such as isomaltulose), complex carbohydrates (such as maltodextrin), resistant starches (such as Fibersol) and fiber (such as FOS), did not show an increase in fat mass over the same period. Rather, the gestational fat was significantly lower as compared with dams from the HF group during the pregnancy period.

[0086] A low GI diet containing the carbohydrate system according to the embodiments disclosed herein during pregnancy may prevent unhealthy fat accumulation and/or obesity in pregnant women during gestation.

WHAT IS CLAIMED IS:

1. A method of preventing fat accumulation in a woman during gestation, the method comprising administering to said pregnant woman a nutritional composition comprising a carbohydrate system, said 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 said nutritional composition to a non-pregnant woman prior to pregnancy.

3. The method of either claim 1 or claim 2 wherein said woman is of normal weight.

4. The method of any preceding claim, wherein said woman has a condition selected from the group consisting of overweight, obesity, diabetes, gestational diabetes, or combinations thereof.

5. The method of any preceding claim, wherein the slow rate of digestion simple carbohydrate is selected from the group consisting of isomaltulose, sucromalt, and combinations thereof.

6. The method of any preceding claim, wherein the complex carbohydrate is selected from the group consisting of a maltodextrin, corn starch, rice starch, wheat starch, and combinations thereof.

7. The method of any preceding claim, wherein the complex carbohydrate comprises maltodextrin having a Dextrose Equivalent of from 3 to 25.

8. The method of any preceding claim, wherein the complex carbohydrate comprises maltodextrin having a Dextrose Equivalent of from 9 to 16.

9. The method of any preceding claim wherein the nonabsorbent carbohydrate is selected from the group consisting of inulin, insoluble dietary fibers, digestion resistant maltodextrins, and combinations thereof.

10. The method of any preceding claim wherein the indigestible oligosaccharide is selected from the group consisting of fructooligosaccharides, galactooligosaccharides, trans-galactooligosaccharides, xylooligosaccharides, and combinations thereof.

11. The method of any preceding claim wherein the nutritional composition is administered daily for at least the last three months of the pregnancy, preferably at least the last six months of the pregnancy.

12. The method of any preceding claim wherein the woman consumes from 20 to 175 grams of the carbohydrate system per day.

13. The method of any preceding claim wherein the woman consumes from 90 to 125 grams of the carbohydrate system per day.

14. The method of any preceding claim wherein the carbohydrate system comprises from 40% to 80% by weight slow rate of digestion simple carbohydrate, from 1% to 15% by weight complex carbohydrate, from about 5% to about 25% by weight nonabsorbent carbohydrate, and from 1% to 20% by weight indigestible carbohydrate.

15. The method of any preceding claim wherein the carbohydrate system comprises from 60% to 70% by weight slow rate of digestion simple carbohydrate, from 6% to 10% by weight complex carbohydrate, from 5% to 20% by weight nonabsorbent carbohydrate, and from 2% to 15% by weight indigestible carbohydrate.