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(54) Title: IMPROVEMENT OF MUSCULOSKELETAL HEALTH BY NUTRITION AND EXERCISE

(57) Abstract: The present invention provides a treatment or program comprising the administration of a nutritional composition and physical exercise, in particular in the frame of a regular exercise program, for ensuring healthy growth and improving the quality of life of children, for example. The invention addresses in particular children of compromised health and children with suboptimal nutrition. The treatment of the invention is suitable to improving the musculoskeletal health in a subject. In particular, the treatment of the invention is suitable to increase muscle strength, muscle power, muscle endurance, bone health, bone strength, and bone density.

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TITLE

"IMPROVEMENT OF MUSCULOSKELETAL HEALTH BY NUTRITION AND EXERCISE

BACKGROUND

[0001] The present invention relates to a composition, to a composition in combination with physical exercise for supporting growth of a subject, in particular of a child with compromised health. The invention further relates to uses and methods for supporting growth, of improving musculoskeletal health, and for obtaining further beneficial effects as reported in this specification.

[0002] Growth is the main characteristic of childhood and a well-known indicator of a child's health status. Interrelated to healthy growth is the integrity of the musculoskeletal system. Lean body mass is important to maintaining functional mobility and retaining optimal metabolic function. Furthermore, enhancing bone accretion in the pediatric population during the critical window opportunity of development is warranted in order to ensure long-term development. Indeed, by the age of 18 both boys and girls have achieved 90% of their peak bone mass. Thus patterns of growth early in life will impact health parameters in adulthood.

[0003] Optimal nutrition clearly plays a role in musculoskeletal development such as adequate intake of dairy calcium and vitamin D. On the other hand, the present invention seeks for further ways for ensuring healthy growth, in particular in human subjects having a fragile health status or suffering from compromised health. For example, children suffering from certain diseases may suffer from malnutrition or sub-optimal nutrition.

SUMMARY

[0004] It is an objective of the present invention to increase life quality in a subject.

[0005] It is an objective of the present invention to improve well-being of a subject.

[0006] It is an objective of the present invention to improve and/or support musculoskeletal health. It is an objective to improve the status and/or integrity of the musculoskeletal system.

[0007] It is an objective of the invention to increase muscle strength, muscle power and/or muscle endurance.

[0008] It is an objective to improve bone health, bone mineral density, bone mineral content, bone density, bone mineralization, bone microarchitectural morphology, bone turnover, bone elasticity, bone mechanical stiffness, and bone resistance to fracture and fissure.

[0009] It is an objective to improve body composition, such as body mass index, lean body mass, muscle mass, reduce fat portion in the body, and the like.

[0010] It is an objective to reduce insulin resistance.

[0011] It is also an objective of the invention to improve the blood lipid profile.

[0012] An objective of the present invention is to provide nutrition, and in particular to provide nutrition that is suitable to support healthy growth. The invention has the objective of providing nutrients, phytonutrients, antioxidents, vitamins and minerals that support a healthy growth even in subjects, in particular children, having impaired absorption of nutrients in the gastro-intestinal tract, subjects suffering from malnutrition of any kind and origin, and subjects that are weakened due to disease, and other subjects having a compromised health status.

[0013] The present invention addresses the objectives above, and provides methods, uses and composition for obtaining the health benefits set out above.

[0014] Interestingly, the invention is based on the finding that certain subjects, such as children having compromised health, do not sufficiently engage in physical activity, thereby negatively influencing the parameters that are necessary for healthy growth. The present invention has in particular the goal of disrupting the vicious circle that emerges in subjects with fragile health status and/or malnutrition. These subjects naturally reduce or completely avoid physical activity and/or exercises, partly due to lacking motivation and lack of energy, thereby further reducing their body's capacity to cope with reduced health and/or disease.

[0015] The present invention concerns a composition comprising one or more nutrients. The composition is suitable to achieve one or more beneficial effects in a subject, such as health effects, therapeutic effects and prophylactic effects, for example. The beneficial effects reported herein are generally referred to as "effects" or "effect". In

an aspect, the invention provides a combination of the composition of the invention and physical exercise for obtaining said effects in the subject. In an aspect, the invention provides a nutrition- and exercise-based treatment and/or program for obtaining the effects of the invention.

[0016] In general, the effects obtained in accordance with the invention (the effects of the invention) encompass an increase of life quality in general. Life quality is improved, according to an embodiment, by way of the further beneficial effects reported herein. Accordingly, an effect of the invention is that the invention improves well-being of a subject. A further effect of the invention is the improvement of health in general of a subject. An effect of the invention is that the invention ensures and/or supports growth in a subject, in particular a subject that is growing and/or not yet grown-up. An effect of the invention is the improvement and/or support of musculoskeletal health. An effect of the invention is the improvement and/or support of the status and/or integrity of the musculoskeletal system. An effect of the invention is to increase muscle and/or bone mass and/or formation. An effect of the invention is to increase muscle and/or bone accretion. An effect of the invention is the increase of one or more selected from muscle strength, muscle power, local muscle endurance and combinations thereof. An effect of the invention is the increase of one or more selected from bone health, bone density, bone strength, and/or combinations thereof. An effect of the invention is that it increases lean body mass. An effect of the invention is the reduction of the incidence of bone fracture and/or reducing the risk of bone fractures. An effect of the invention is the enhancement of motor skill performance. The invention further has the effect of increasing bone mineral density and/or bone mineral content. A further effect of the invention is the improvement of the body composition. A further effect of the invention is the improvement of insulin sensitivity. A further effect is that the invention improves the blood or serum lipid profile. The invention is suitable to achieve one or a combination of two or more of these effects. The reference to an "effect of the invention" or the "effects of the invention" refers to one or a combination of two or more or to all these effects and other effects reported elsewhere in this specification.

[0017] According to an embodiment, the effects of the invention are obtained in a subject. Preferably, the subject is a growing subject, in particular a child. According to an embodiment, the invention is directed to subjects, in particular children having

compromised health. Further indications with respect to the subject in which the effects of the invention are obtained are set forth elsewhere in this specification and in particular in the detailed description of the preferred embodiments.

[0018] In an aspect the present invention provides a composition comprising one or more nutrients for obtaining any one or more of the effects of the invention.

[0019] In an aspect, the present invention provides a composition comprising one or more nutrients and physical exercise for obtaining any one or more of the effects of the invention.

[0020] In an aspect, the present invention provides a composition comprising one or more nutrients in a treatment for obtaining any one or more of the effects of the invention, said treatment further comprising physical exercise.

[0021] In another aspect, the invention provides a treatment comprising (1) administration of nutrients and/or of a composition comprising nutrients and (2) physical exercise for obtaining any one or more of the effects of the invention.

[0022] In an aspect the present invention provides a treatment comprising (1) administration of nutrients and/or of a composition comprising nutrients and (2) the prescription and/or recommendation of physical exercise for obtaining any one or more of the effects of the invention.

[0023] In an aspect the present invention provides a composition comprising nutrients for increasing any one of the physical-exercise supported and/or stimulated effects of the invention.

[0024] In an aspect, the present invention provides a composition comprising nutrients for increasing the effects of the invention produced by physical exercise.

[0025] In an aspect the present invention provides a composition comprising nutrients for obtaining the effects of the invention in a subject undergoing physical exercise.

[0026] In an aspect the present invention provides a composition comprising nutrients for obtaining the effects of the invention between periods of physical exercise.

[0027] In an aspect the present invention provides a composition comprising nutrients for the preservation of the effects of the invention in a subject between periods of physical exercise.

[0028] In an aspect, the invention provides a method for obtaining any one or more of the effects of the invention, the method comprising the steps of administrating a composition comprising nutrients.

[0029] In an aspect, the invention provides a method for obtaining any one or more of the effects of the invention, the method comprising the steps of administrating a composition comprising nutrients and conducting physical exercise.

[0030] In an aspect, the invention provides a method of treatment and/or a method comprising a treatment, said treatment comprising the administration of a composition comprising nutrients and physical exercise for obtaining any one or more of the effects of the invention.

[0031] In an aspect, the invention provides a method for obtaining any one or more of the effects of the invention, the method comprising the steps of administrating a composition comprising nutrients and prescribing and/or recommending physical exercise.

[0032] In an aspect, the invention provides a method for obtaining any one or more of the physical exercise-supported and/or stimulated effects of the invention, the method comprising the step of administrating a composition comprising nutrients to a subject.

[0033] In an aspect, the invention provides a method for increasing any one or more of the effects of the invention produced by physical exercise, the method comprising the step of administrating the composition of the invention.

[0034] In an aspect, the invention provides a method for obtaining any one or more of the effects of the invention, the method comprising the step of administrating the composition comprising nutrients to a subject undergoing physical exercise.

[0035] In an aspect, the invention provides a method for obtaining any one or more of the effects of the invention, the method comprising the step of administrating the composition of the invention between periods of physical exercise by a subject.

[0036] In an aspect, the invention provides a method for preserving any one or more of the effects of the invention between periods of physical exercise, the method comprising the step of administrating a composition comprising nutrients by a subject.

[0037] In an aspect, the present invention provides a composition comprising one or more nutrients and physical exercise for improving life quality and/or supporting growth.

[0038] In an aspect, the present invention provides a composition comprising one or more nutrients in a treatment for improving life quality and/or supporting growth, said treatment further comprising physical exercise.

[0039] In an aspect, the invention provides a method for improving life quality and/or supporting growth, the method comprising the steps of administrating a composition comprising nutrients and conducting physical exercise.

[0040] In an aspect, the invention provides a method of treatment and/or a method comprising a treatment, said treatment comprising the administration of a composition comprising nutrients and physical exercise for improving life quality and/or supporting growth.

[0041] In an aspect, the present invention provides a composition comprising one or more nutrients and physical exercise for improving musculoskeletal state and/or health.

[0042] In an aspect, the present invention provides a composition comprising one or more nutrients in a treatment for improving musculoskeletal state and/or health, said treatment further comprising physical exercise.

[0043] In an aspect, the invention provides a method for improving musculoskeletal state and/or health, the method comprising the steps of administrating a composition comprising nutrients and conducting physical exercise.

[0044] In an aspect, the invention provides a method of treatment and/or a method comprising a treatment, said treatment comprising the administration of a composition comprising nutrients and physical exercise for improving musculoskeletal state and/or health.

[0045] In an aspect, the present invention provides a composition comprising one or more nutrients and physical exercise for increasing one or more selected from the group of muscle strength, muscle power, muscle endurance, and combinations thereof and/or one or more selected from the group of bone health, bone strength, bone density, bone mineral content and/or density, and combinations thereof.

[0046] In an aspect, the present invention provides a composition comprising one or more nutrients in a treatment for increasing one or more selected from the group of muscle strength, muscle power, muscle endurance, and combinations thereof and/or one or more selected from the group of bone health, bone strength, bone density, bone mineral content and/or density, and combinations thereof, said treatment further comprising physical exercise.

[0047] In an aspect, the invention provides a method for increasing one or more selected from the group of muscle strength, muscle power, muscle endurance, and combinations thereof and/or one or more selected from the group of bone health, bone strength, bone density, bone mineral content and/or density and combinations thereof, the method comprising the steps of administrating a composition comprising nutrients and conducting physical exercise.

[0048] In an aspect, the invention provides a method of treatment and/or a method comprising a treatment, said treatment comprising the administration of a composition comprising nutrients and physical exercise for increasing one or more selected from the group of muscle strength, muscle power, muscle endurance, and combinations thereof and/or one or more selected from the group of bone health, bone strength, bone density, bone mineral content and/or density and combinations thereof.

[0049] In an aspect, the present invention provides a composition comprising one or more nutrients in combination with a program of physical exercise for improving the musculoskeletal state in a child having a fragile health status and/or compromised health.

[0050] In an aspect, the present invention provides a composition a comprising one or more nutrients in a treatment for improving the musculoskeletal state in a child having a fragile health status and/or compromised health, said treatment further comprising physical exercise.

[0051] In an aspect, the present invention provides a method for improving the musculoskeletal state in a child having a fragile health status and/or compromised health, said method comprising the steps of administrating a composition comprising nutrients and conducting physical exercise.

[0052] According to an embodiment, the invention provides a composition and/or a method for increasing one or more selected from the group of muscle strength,

muscle power, muscle endurance, and combinations thereof and/or one or more selected from the group of bone health, bone strength, bone density and combinations thereof.

[0053] According to an embodiment, said child is suffering from Crohn's disease, cystic fibrosis (CF), irritable bowel syndrome, allergy, and/or asthma, in particular chronic allergy.

[0054] According to an embodiment, said physical exercise may involve the use of electronically-assisted and/or computer-assisted games.

[0055] Further aspects and preferred embodiments of the invention are provided in the appended claims and are set out in more detail in the description herein below.

DETAILED DESCRIPTION

[0056] According to an embodiment, the present invention supports growth and/or improves the musculoskeletal health and/or improves the musculoskeletal state of a subject.

[0057] In general, the subject may be any individual subject, in particular a subject in need of the beneficial effects reported in this specification, such as an improvement of the musculoskeletal health, for example.

[0058] The subject is preferably a growing subject, such as subjects that are not yet fully grown. In particular, the invention addresses needs of children, and the subject is thus preferably a child. The subject may be a 3 to 5 year old child and/or a 5 to 6 year old child. The invention thus addresses the needs of preschool children and/or children in the kindergarten.

[0059] According to a preferred embodiment, the invention addresses the needs of children having an age of at least 7 or 8 years. The subject may thus have an age of 7 to 18 years, for example, for example 7 to 16 years, 7 to 14 years, 7 to 12 years or most specifically 7 to 10 years. In accordance with an embodiment of the present invention, the intake of the nutritional composition of the invention and also the physical exercise is preferably adapted to the age of the child. In particular, children are grouped in the age classes from 1-3 years, 4-8 years, 9-13 years, 14-18 years, for example. On the other hand, although the invention has the purpose of supporting growth of children or adolescents and teenagers, the treatment of the invention may also support and/or

improve the health of the musculoskeletal system of adults, in particular human subjects that are older than 18 years old.

[0060] Preferably, the subject is a subject having compromised health and/or a fragile health status, in particular children having compromised health and/or a fragile health status.

[0061] According to an embodiment, the invention addresses subjects that are at a risk of a lack of regular and/or necessary physical activity or physical exercise. Healthy children generally have a natural need or desire to exercise and play. Regular physical activity is believed, without wishing to be bound by theory, to increase the children's confidence to be physically active, which in turn may lead to a noticeable improvement in muscle strength, favourable changes in body composition, and an increase in regular physical activity.

[0062] On the other hand, children with fragile health status may lack motivation to be physically active, thereby entering a vicious circle: Lack of physical activity may lead to insufficient musculoskeletal growth, may dissuade from engaging in physical activity and may result in even more fragile health resulting possibly in a state of disease. The present invention is suitable to break this vicious circle by way of a combined exercise and nutrition program, as detailed elsewhere in this specification.

[0063] The subject is preferably a pediatric patient. According to an embodiment, the subject, in particular the child, is suffering from suboptimal nutrition and/or malnutrition. According to an embodiment, the subject, in particular the child, is selected from subjects suffering from Crohn's disease, cystic fibrosis (CF), inflammatory bowel disorders, and/or subjects suffering from asthma and/or allergy.

[0064] According to an embodiment, the subject is suffering from a disease or condition specified herein above and below or elsewhere in this specification.

[0065] According to an embodiment, the purpose or effect of the invention is to reduce and/or prevent deficiencies and/or deficiency symptoms in subjects having reduced absorption and/or absorption capacities, in particular reduced capacity of nutrient, for example mineral absorption capacities. The terms "absorption" and "absorption capacities" refer, in particular, to absorption in the gastro-intestinal tract, in particular in the intestines, for example the small and/or large intestine. In several situations and/or conditions, a subject the capacity of a subject's gastro-intestinal tract to

absorb one or more specific nutrients (in particular micronutrients) is compromised. This may lead to a lack or deficiency of the respective nutrient in the body of the subject. Such a situation or condition may be due to a specific disease, such as an infectious or a genetic disease, or due to other circumstances. For example, a subject may be less capable of absorbing vitamins and/or minerals in general, or less capable of absorbing one or several specific vitamins and/or minerals, for example particular calcium.

[0066] According to an embodiment, the child is a child that is under sub-optimal nutrition. In other words, the child does not receive all essential and/or nutrients that are necessary for healthy growth in sufficient amounts.

[0067] Although the invention is particularly adapted to children, the invention may also be used in non-human subjects. According to an embodiment, the subject is an animal, for example a mammal. According to an embodiment, the subject is selected from livestock and/or pet animals, such as cattle, including cows, goats, sheep, but also pigs, camels, or poultry animals, for example.

[0068] Furthermore, although the invention addresses in particular growing subjects, the invention may be used in grown-up subjects, such as adults, for example. The treatment in accordance with the invention may, for example, improve the musculoskeletal state of a grown-up subject, including patients suffering from reduced absorption in the gastro-intestinal tract as specified elsewhere in this specification, for example.

[0069] The present invention relates, in an aspect, to a composition. The composition is intended for oral administration and/or consumption. In this regard, the composition comprises and preferably consists of edible components and/or matter. The composition is thus preferably free of any toxic and/or unwholesome matter, which is not intended or suitable for oral administration to a human or animal.

[0070] Within the context of this specification the word “comprises” is taken to mean “includes, among other things”. It is not intended to be construed as “consists of only”.

[0071] The composition of the invention need not be but preferably is a nutritional composition comprising several nutrients. Nutrients may be selected from macronutrients, such as proteinogenic matter, available carbohydrates and sources of fatty acids and/or from micronutrients, such as vitamins, minerals and trace elements

and the like. Preferred nutrients of the nutritional composition are specified elsewhere in this specification.

[0072] A nutritional composition may be a food product intended for human consumption, for example, a beverage, a drink, a bar, a snack, an ice cream, a dairy product, for example a chilled or a shelf-stable dairy product, a fermented dairy product, a drink, for example a milk-based drink, a growing-up milk, a confectionery product, a chocolate-containing and/or a chocolate-based product, a chocolate, a cereal product such as a breakfast cereal, a sauce, a soup, an instant drink, a frozen product intended for consumption after heating in a micro-wave or an oven, a ready-to-eat product, a fast food or a nutritional formula. A "chilled product", is preferably a product that is stored at 1-10°C, preferably 2-8°C and most preferably 3-6°C before consumption, in particular in the time between the end of manufacturing and consumption.

[0073] A nutritional formula encompasses any nutritionally complete or supplementary formulation (a nutritional supplement, for example). As used herein, “nutritionally complete” are preferably nutritional products that contain sufficient types and levels of macronutrients (protein, fats and carbohydrates) and micronutrients to be sufficient to be a sole source of nutrition for the subject to which it is being administered to. Patients can receive 100% of their nutritional requirements from such complete nutritional compositions. According to an embodiment, the nutritional formula is a supplementary formulation providing supplementary nutrition. A "supplementary formula" may not be nutritionally complete, but preferably contains specific nutrients that are supportive, for example in combination with physical exercise, with further of the beneficial effects of the invention, and/or which address specific or additional needs of the subject.

[0074] The nutritional formula may be a generally applicable nutritional formula, for example adapted to subjects of a specific age, for example a formula for children of the age classes specified elsewhere in this specification, but it may also be a formula for elderly patients, for intensive care patients, or a specially adapted formula for patients suffering from a specific disease, for example. Any nutritional formula may be reconstitutable, that is, present in a substantially dried, for example powdered form, or ready-to-drink, in the form of liquid formulas, for example. The nutritional formula

may be a low-fat formula and/or a formula that can be consumed during any kind of diet. The formula may be low in lactose.

[0075] Alternatively, or in addition, the composition of the invention may be a pharmaceutical composition. It may be provided in the form of tablets, pills, capsules, for example gelatine capsules, effervescent tablets, and the like, for example.

[0076] Accordingly, the present invention provides the composition of the invention for use in therapeutic treatment, in particular as a medicament.

[0077] The composition of the invention is preferably orally administered. The term "administered" and/or "administration" preferably refers to oral ingestion, intake and/or consumption by the subject. Preferably, the composition is consumed by eating and/or drinking. In another embodiment, the composition is administered by tube feeding.

[0078] The present specification sets out exemplary and/or preferred amounts of specific nutrients that are preferably administered as part of the composition of the invention. It is noted that these amounts are preferably determined on the basis of complete nutrition, that is the composition of the invention is a complete nutritional formula and there is no other nutrition administered or consumed. In case a subject consumes normal food and the composition of the invention is a supplementary composition or a pharmaceutical composition, the administered amounts may in some instances need to be reduced, so as to avoid intakes that are substantially above the tolerable upper intake levels (ULs). On the other hand, in some instances some subjects have increased need of certain nutrients, for example due to reduced absorption in the gastro-intestinal tract. In these cases, the administered amounts as indicated in this specification apply, or possibly even higher amounts.

[0079] According to an embodiment, the composition of the invention is nutritionally complete, but may be used in combination with other and/ normal food, as a supplement. According to an embodiment, the nutritionally complete formula may be consumed in combination with other food, thus as to contribute to anything from 5-100%, for example 10-100%, preferably 20-100%, 40-100%, 50-100%, and/or 70-100% of the caloric needs of the subject.

[0080] The composition comprises at least one nutrient. Nutrients may be selected from macronutrients (proteinogenic matter, available carbohydrates and lipids,

in particular oils and/or fats), and from micronutrients, such as vitamins and minerals. According to an embodiment, the invention comprises selected macro- and micronutrients.

[0081] In an embodiment, the composition comprises one or more phytonutrients and/or antioxidants. Non-limiting examples of phytonutrients include flavonoids such as quercetin, curcuminoids such as curcumin and limonin. Antioxidants are molecules capable of slowing or preventing the oxidation of other molecules. Non-limiting examples of antioxidants include vitamin A, carotenoids, vitamin C, vitamin E, selenium, flavonoids, lactowolfberry, wolfberry, polyphenols, lycopene, lutein, lignan, coenzyme Q10 ("CoQ10"), hesperidine and glutathione.

[0082] The composition may also comprise nucleotides.

[0083] Preferred components selected from macronutrients, micronutrients (vitamins and/or minerals), nucleotides, antioxidants and/or phytonutrients that may be used in the composition in accordance with the present invention, and/or preferred amounts of such components, are discussed in further detail elsewhere in this specification.

[0084] According to an embodiment, the composition of the invention comprises proteinogenic matter. For the purpose of the present specification, the expressions "a source of protein", "protein" and "a source of proteinogenic matter" and "proteinogenic matter" in general encompass any proteinogenic matter. These expressions thus encompass proteinogenic amino acids, in particular free amino acids, dipeptides, oligopeptides, polypeptides, proteins, and the like, and mixtures of the aforementioned. The expression "source of protein" also encompasses protein hydrolysates, for example. According to an embodiment, the composition comprises milk protein or a milk protein hydrolysate and free amino acids, for example whey protein as disclosed elsewhere in this specification and free amino acids.

[0085] Protein sources may be of plant, fungal or animal origin, for example. Protein or proteinogenic matter may thus be selected, for example, from milk protein, egg protein, meat protein, and plant protein. Plant protein may, for example, be selected independently from soy protein, pea protein, canola protein, wheat and fractionated wheat proteins, corn proteins, proteins from cereals in general, carob protein, zein proteins, rice proteins, oat proteins, potato proteins, peanut proteins, green pea powder,

green bean powder, proteins derived from vegetables, proteins derived from leguminosae, beans, lupins, mesquite, lentils, and pulses, or combinations thereof.

[0086] According to an embodiment, the nutritional composition comprises proteinogenic matter originating from milk protein. Milk protein may be obtained from any animal mammalian species, such as cattle, for example cows, buffalos, sheep, goats, but also from horses and camels, for example. Preferably, the composition of the invention comprises milk protein. The composition may comprise any one selected from casein, casein hydrolysates, caseinates, whey, whey hydrolysates, milk protein concentrate, milk protein isolate, and combinations thereof. Preferably, the composition comprises casein and/or whey, for example intact and/or hydrolysed casein and/or whey.

[0087] According to an embodiment, the composition comprises casein. For example hydrolyzed casein may be used. Preferably, the composition comprises casein comprising active TGF-β2. Casein rich in TGF-β2 as disclosed in US 2004/0102377, which is entirely incorporated herein by reference, is particularly preferred. Preferably, the composition comprises from 0.2 to 10 μg, preferably 0.5 to 2 μg TGF-β2 per g of casein. For example, the TGF-β2 may be in a form that can be/is activated during passage through the digestive tract, preferably in accordance to the teaching of US 2004/0102377.

[0088] The composition may comprise, for example, any whey protein or a mixture of different whey proteins. The composition may comprise proteinogenic matter derived, for example, from sweet whey obtained as a by-product in cheese manufacture, acid whey obtained as a by-product in acid casein manufacture, native whey obtained by milk microfiltration or rennet whey obtained as a byproduct in rennet casein manufacture may be used as the whey protein.

[0089] According to an embodiment, the composition comprises any one or more of proteinogenic matter based on β-lactoglobulin, α-lactalbumin, serum albumin, each independently in intact or hydrolyzed form, for example, and a combination of two or more of the aforementioned, besides possibly other proteinogenic matter.

[0090] According to a preferred embodiment, the composition comprises whey protein micelles. Whey protein micelles, their fabrication and beneficial properties, as well as numerous food products comprising whey protein micelles are

disclosed in US 2009/0035437 A1, filed August 21, 2008, WO2007110421, filed March 27, 2007, and WO2007110411, filed March 26, 2007, which are entirely incorporated herein by reference. These references also disclose a process for obtaining whey protein micelles of advantageous properties, such as a particular size distribution. These whey protein micelles may be obtained from whey protein of the prior art and from whey protein fractions as disclosed elsewhere in this specification.

[0091] Preferably, the whey proteins, in particular as comprised in the whey protein micelles, are arranged in such a way that the hydrophilic parts of the proteins are oriented towards the outer part of the agglomerate and the hydrophobic parts of the proteins are oriented towards the inner "core" of the micelle. This energetically favorable configuration offers good stability to these structures in a hydrophilic environment. As such, the micelles consist essentially of spherical agglomerates of denatured whey protein. The micelles are particularly characterized by their regular, spherical shape. Due to their dual character (hydrophilic and hydrophobic), this denatured state of the protein seems to allow interaction with a hydrophobic phase, e.g., a fat droplet or air, and a hydrophilic phase. The whey protein micelles therefore have perfect emulsifying and foaming properties.

[0092] Whey protein micelles preferably have a mean micelle diameter that is smaller than 1 micron, preferably being in the range of 100 nm and 900 nm, more preferably 100-770 nm, most preferably 200 and 400 nm. Preferably, the size distribution is such that more than 50%, preferably more than 80% of the micelles produced will have a size as indicated above. The (mean) diameter of the micelles can be determined using transmission electron microscopy, for example as disclosed in the above-indicated references.

[0093] In general, the whey protein micelles may be obtained by a process comprising the preparation of an aqueous solution of at least partially demineralised but preferably non-hydrolysed whey protein is prepared; adjustment of the pH and/or ionic strength of the solution to values that result in the formation of whey micelles of the desired size and, thereafter, preferably conducting a heat treatment of the solution. For the purpose of the present specification, the term "solution" also encompasses emulsions, suspensions, dispersions and slurries, for example. The pH adjustment is

generally conducted in dependence of the overall charge of the micelles at the end and in dependence of the ionic strength of the solution, as disclosed in the above references.

[0094] With respect to whey protein micelles, it is preferable that the whey protein does not undergo any hydrolysis step prior to micelle formation. Thus, the whey protein is preferably not subjected to any enzymatic treatment prior to micellization.

[0095] According to an embodiment, the content of divalent cations in the whey protein for the preparation of the whey protein micelles concentrate may be less than 2.5%, more preferably less than 2%, even more preferably less than 0.2%. In an embodiment, the whey proteins are completely demineralized.

[0096] Following adjustment of pH, the whey protein aqueous solution comprising micelles is generally subjected to the heat treatment. It is preferred to have the temperature in the range of from about 70°C to below 95°C. Once the desired temperature has been reached, it is kept at this temperature for a minimum of 10 seconds and a maximum of 2 hours, preferably, 12 to 25 minutes.

[0097] As disclosed in US 2009/0035437 A1, WO2007110421, and WO2007110411 cited above, the pH-adjusted and heat-treated aqueous solution comprising whey micelles is preferably concentrated, and may be used as such or may be dried, yielding a whey protein micelles powder. Before concentrating and/or before drying it is possible to conduct one or more purification steps, so as to increase the yield of micelles in the final preparation. Furthermore, whey protein micelles may be further treated and/or modified. For example, the whey protein micelles may be coated with an emulsifier, with peptides, proteins, gums, in order to modify the functionality and/or taste of the whey protein micelles.

[0098] According to an embodiment, the composition comprises only casein and is substantially free of whey protein. According another embodiment, the composition comprises only whey protein and is substantially free of casein. According to another embodiment, the composition comprises substantial amounts of both, casein and whey protein, for example, 10-90, preferably 20-80wt.-% casein and 90-10, preferably 80-20wt.-% of whey protein. Percentages are percent by weight of dry matter of total protein content of the composition.

[0099] According to an embodiment, proteinogenic matter provides 5-100% of the caloric energy of macronutrients of the composition. Preferably, proteinogenic

matter provides 8-50%, more preferably 10-40%, 11-30%, even more preferably 12-25%, 13-20% and most preferably 14-18% of the energy (provided by macronutrients) of the composition. This may apply in particular if the composition is nutritionally complete.

[00100] According to an embodiment, the composition of the invention comprises antioxidants, vitamins and/or minerals. In an embodiment, the comprises a antioxidant selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium, or combinations of two or more thereof.

[00101] In an embodiment, the product may include a vitamin selected from the group consisting of vitamin A , vitamin B1, vitamin B2, vitamin B3, vitamin B5, vitamin B6, vitamin B7, vitamin B9, and vitamin B12, vitamin C, vitamin D, in particular D3, vitamin E, vitamin K, folic acid, biotin, or combinations of two or more thereof.

[00102] In an embodiment, the product may include a mineral selected from the group consisting of boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc, or combinations of two or more thereof.

[00103] Any one or all vitamins and/or minerals may be present in the composition in accordance with recommended daily intakes or Dietary Reference Intakes (RDIs) (*Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals*, Food and Nutrition Board, Institute of Medicine, National Academies, 2004, www.nap.edu). The dietary reference intakes are specified in accordance with the age of human subjects, in particular for the age classes 1-3, 4-8, 9-13, 14-18, 19-30, 31-50, 51-70 and subjects that are older than 70 years. As from the age class 9-13 years and upwards, RDIs are generally also gender specific.

[00104] In the composition of the invention, vitamins and minerals may be present in dependence of the type of formula (supplemental and/or complete nutrition). Alternatively, as mentioned elsewhere in this specification, a specific formula may be suitable for complete nutrition, but may also be used in combination with normal or ordinary food and thereby be used as a supplementary nutrition.

[00105] According to an embodiment, some, several or all vitamins and/or minerals are present in amounts that correspond about to the RDI values, for example if

it is assumed that the composition is used as complete nutrition. According to an embodiment, some, several or all vitamins and/or minerals are present in amounts that exceed the RDI values, Preferably, however, amounts are close to or below the tolerable upper intake level (UL), as established in the context of the RDIs (same reference as above). In certain cases, such as in case of a subject suffering from a specific disorder resulting in reduced absorption or uptake, the amount of one or several minerals and/or vitamins may be above the RDIs, for example about, at, slightly below or slightly above the ULs. "Slightly", in particular as used in the expressions "slightly above" and "slightly below" refer preferably to 20% or less, preferably 15% or less, more preferably 10% or less of the respective amount. The expression "about" refers to ±20%, preferably ±15%, more preferably ±10%, even more preferably ±5% and most preferably ±3% of the indicated value, in case a value is indicated.

[00106] It is noted that exact administered doses may be dependent on the specific condition from which the subject is suffering. Daily administered doses above the RDIs and even above the ULs may be contained in the composition of the invention so as to account for increased needs of certain subjects with compromised health. It is noted that RDI and UL amounts are generally applicable to healthy individuals. For many micronutrients UL amounts are not available.

[00107] According to an embodiment, the nutritional composition comprises macronutrients such as proteinogenic matter, carbohydrates, lipids, minerals and vitamins, wherein the amount of some, several or all vitamins and/or minerals exceeds or corresponds to the RDIs. For children of 1-3 years, this applies in case 1000 kcal of the composition is administered per day. For children of 4-8 years, this applies in case 1500 kcal of the composition is administered per day. For children of 9-13 years, this applies in case 1800 kcal of the composition is administered. For children of 14-18 years, this applies in case about 2000 kcal per day of the composition is administered. For example, the amount of the vitamins some, several or all vitamins and/or minerals corresponds about to the UL value.

[00108] According to an embodiment, the composition of the invention comprises from about 800 to about 1200 kcal, preferably about 900 to about 1100 kcal, for example about 1000kcal per daily administered dose to a child of 1 to 3 years.

[00109] According to an embodiment, the composition of the invention comprises from about 1250 to about 1750 kcal, preferably about 1350 to about 1650 kcal, for example about 1500kcal per daily administered dose to a child of 4 to 8 years.

[00110] According to an embodiment, the composition of the invention comprises from about 1550 to about 2250 kcal, preferably about 1650 to about 1950 kcal, for example about 1800kcal per daily administered dose to a child of 9 to 13 years.

[00111] According to an embodiment, the composition of the invention comprises from about 1850 to about 2150 kcal, preferably about 1900 to about 2100 kcal, for example about 2000 kcal per daily administered dose to a child of 9 to 13 years.

[00112] According to an embodiment, the composition has about 70-30 g dry matter, preferably 80 to 120 g, more preferably 90-110 g, 95-105 g, for example about 100 g dry matter per 500 kcal of the composition. This applies in particular for nutritionally complete composition and/or for composition comprising all macronutrients (proteinogenic matter, lipids and carbohydrates), or compositions that are nutritionally complete with respect to macronutrients. From these amounts, in combination with caloric intake per day and age class, the weight-amount (e.g. g, mg, µg) of the respective nutrient (macro-, micronutrient, nucleotides, antioxidants and phytonutrient, in as far as applicable) in the composition of the invention may be determined.

[00113] According to an embodiment, the composition comprises about 200 g dry matter per daily administered dose to a child of 1-3 years. According to an embodiment, the composition comprises about 300 g dry matter per daily administered dose to a child of 4-8 years. According to an embodiment, the composition comprises about 360 g per daily administered dose to a child of 9-13 years. According to an embodiment, the composition comprises about 400 g per daily administered dose to a human subject that is 14 years old or older. These amounts apply, in particular, if the composition is nutritionally complete and/or is nutritionally complete with respect to all macronutrients.

[00114] According to an embodiment, the composition is not nutritionally complete, but is a supplement or a pharmaceutical composition, for example in the form of a tablet, pill, and so forth. In this case, the composition preferably has about 1 g to about 200 g per daily administered dose, about 1.5 g to about 100 g, preferably about

2-50 g, 3-40 g, 4-40 g, 5- 30 g, 6-20 g, 7-10 g per daily administered amount of the composition. Again the weight-amounts of the specific components of the composition (macro-, micronutrient, nucleotides, antioxidants and phytonutrient, in as far as applicable) may be determined from indications elsewhere in this specification with respect to daily administered doses.

[00115] According to an embodiment, the composition comprises vitamin K. For example, the composition comprises any one selected from vitamin K_1 (also known as phylloquinone, phytomenadione or phytonadione), vitamin K_2, (a series of vitamers also known as menaquinones or menatetranones, see below), or synthetic vitamin K forms, such as vitamin K_3, vitamin K_4, vitamin K_5, or combinations of the aforementioned. Preferably, the composition comprises vitamin K_2 and/or vitamin K_1.

[00116] According to an embodiment, the composition comprises vitamin K_2. Vitamin K_2 is a group of compounds called menaquinones ("MK") having side chains composed of a variable number of unsaturated isoprenoid residues generally designated as MK-n, where n specifies the number of isoprenoids. The most common MKs are MK-4 and MK-7. MK-4 is typically synthesized by animal organs and muscle, while MK-7 is typically synthesized by bacteria during fermentation. Accordingly, MK-7 is particularly abundant in fermented products including cheese, curd cheese and natto (fermented soybeans) and has a particularly long half-life when compared to vitamin K_1. Without wishing to be bound by theory, it is believed that vitamin K_2 provides better absorption and more stable serum levels through a longer half-life. The improved bioavailability of vitamin K_2 to extrahepatic tissue may also allow for a greater impact on bone health (i.e. mineralization, microarchitecture and strength) during normal growth and development. Therefore, vitamin K_2 provides for a more potent form of the vitamin in which its enhanced bioavailability can impact bone health during normal growth and development.

[00117] Without wishing to be bound by theory, it is believed that administering exogenous vitamin K_2 as part of the composition of the invention will improve osteocalcin carboxylation and improve indices of bone health during normal growth and development in children. Additionally, vitamin K_2 supplementation can also promote bone growth and bone quality in pediatric patients with underlying medical conditions in which bone growth and bone quality may be compromised. As a result,

administration of exogenous vitamin K_2 is believed to increase bone density and improves bone tissue microarchitecture in pediatric patients, thereby reducing the incidence for fracture risk. The effects of vitamin K_2 may be seen directly on bone quality such that this form of vitamin K modulates formation of proteins in the organic matrix of the bone involved in microarchitectural morphology, mineralization, density, elasticity and mechanical stiffness, as measured by peripheral quantitative computer tomography ("pQCT") or Dual Energy X-ray absorptiometry ("DEXA"), for example.

[00118] According to an embodiment, the composition comprises at least 25 μg vitamin K (any one or a combination of the aforementioned) or more per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 30 μg or more, at least or about 50 μg, at least or about 70 μg, at least or about 90 μg, at least or about 100 μg, at least or about 110 μg, at least or about 120 μg vitamin K or more per daily administered dose for a one to 3 year old child.

[00119] According to an embodiment, the composition comprises at least 45 μg vitamin K (any one or a combination of the aforementioned) or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 55 μg, at least or about 90 μg, at least or about 110 μg, at least or about 130 μg, at least or about 140 μg, at least or about 150 μg, at least or about 160 μg, at least or about 170 μg or more vitamin K per daily administered dose for a 4 to 8 year old child.

[00120] According to an embodiment, the composition comprises at least 50 μg vitamin K or more (any one or a combination of the aforementioned) per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 60 μg, at least or about 100 μg, at least or about 120 μg, at least or about 130 μg, at least or about 150 μg, at least or about 170 μg, at least or about 190 μg, at least or about 200 μg or more vitamin K per daily administered dose for a 9 to 13 year old child. These amounts preferably also apply if the subject is a human subject that is 14 years or older. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00121] According to an embodiment, the composition of the invention comprises a curcuminoid, for example curcumin. For example, the composition may comprise 20 mg or more curcuminoids per daily administered dose. According to an embodiment, the composition comprises ≥50 mg, ≥80 mg, ≥100 mg, ≥150 mg, ≥130 mg, ≥140 mg, ≥160 mg, ≥180 mg, ≥200 mg, ≥220 mg, ≥240 mg curcuminoid per daily administered dose.

[00122] The sign "≥", as used in the present specification, means "more than or about equal to" (the indicated value), preferably, "more than or equal to". The sign "≤", as used in the present specification, means "less than or about equal to" (the indicated value), preferably, "less than or equal to".

[00123] According to an embodiment and in accordance with the above amounts as applicable of curcuminoid, the composition preferably comprises not more than 500 mg, preferably not more than 400 mg, more preferably not more than 300 mg per daily administered dose. If the subject is a child that is 13 years old or younger the daily administered dose is preferably not more than 200 mg, preferably not more than 150 mg curcuminoid per daily administered dose.

[00124] A curcuminoid is a curcumin or a derivative of a curcumin with different chemical groups that have been formed to increase solubility of curcumins and make them suitable for drug formulation. Examples of curcumimoids include curcumin itself IUPAC name (1*E*,6*E*)-1,7-bis (4-hydroxy-3-methoxyphenyl) -1,6-heptadiene-3,5-dione; also called diferuloylmethane), demethoxycurcumin, bisdemethoxycurcumin, keto and enol forms of the aforementioned and mixtures thereof. Preferably the curcuminoid is curcumin, in particular natural curcumin or nature-identical, such as curcumin isolated from plants.

[00125] According to an embodiment, the composition comprises flavonoles, more preferably flavonoids, such as, for example, quercetin (also called xanthaurin or 3,3',4',5,7-pentahydroxyflavon, for example). According to an embodiment, the composition comprises ≥50 mg, ≥60 mg ≥70 mg, ≥80 mg ≥90 mg ≥100 mg ≥110 mg, ≥120 mg, ≥130 mg, ≥140 mg, ≥150 mg, ≥160 mg, ≥170 mg, ≥180 mg, ≥190 mg, ≥200 mg, ≥220 mg, ≥240 mg flavonoles, preferably flavonoids, in particular quercetin per daily administered dose. According to an embodiment and in accordance with the above amounts as applicable of flavonoles, preferably flavonoids (in particular

quercetin), the composition preferably comprises not more than 600 mg, preferably not more than 500 mg and most preferably not more than 400 mg of flavonoles per daily administered dose. If the composition is administered to a child that is 13 years or younger, the daily administered dose is preferably ≤250 mg, more preferably ≤200 mg and even more preferably ≤175 mg flavonoles, preferably flavonoids, in particular quercetin per daily administered dose.

[00126] According to an embodiment, the composition of the invention comprises calcium (Ca^{2+}). There are many forms in which calcium may be added, in particular calcium salts, such as calcium stearate, calcium lactate, calcium citrate, calcium phosphate and/or calcium gluconate, just to mention a few examples.

[00127] According to an embodiment, the composition comprises at least 450 mg calcium or more per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least 500 mg, at least 800 mg, at least 900 mg, at least 1000 mg, at least 1100 mg, at least 1200 mg, at least 1800 mg or more calcium per daily administered dose for a one to 3 year old child.

[00128] According to an embodiment, the composition comprises at least 750 mg calcium per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 800 mg, at least or about 1500 mg, at least or about 1600 mg, at least or about 1700 mg, at least or about 1750 mg, at least or about 1800 mg, at least or about 2000 mg or more calcium per daily administered dose for a 4 to 8 year old child.

[00129] According to an embodiment, the composition comprises at least 1200 mg or more calcium per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 1300 mg, at least or about 1700 mg, at least or about 1800 mg, at least or about 1900 mg, at least or about 2000 mg, at least or about 2050 mg, at least or about 2100 mg, at least or about 2200 mg or more calcium per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00130] According to an embodiment, the composition comprises vitamin D (including vitamin D_2 and D_3). According to an embodiment, the composition

comprises at least 5 μg or more vitamin D per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 10 μg, at least or about 25 μg, at least or about 28 μg, at least or about 30 μg, at least or about 40 μg, at least or about 50 μg, at least or about 50 μg or more vitamin D per daily administered dose for a one to 3 year old child.

[00131] According to an embodiment, the composition comprises at least 5 μg vitamin D or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 15 μg, at least or about 25 μg, at least or about 30 μg, at least or about 40 μg, at least or about 30 μg, at least or about 35 μg, at least or about 40 μg, at least or about 50 μg or more vitamin D per daily administered dose for a 4 to 8 year old child.

[00132] According to an embodiment, the composition comprises at least 5 μg vitamin D or more per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 10 μg, at least or about 30μg, at least or about 33 μg, at least or about 35 μg, at least or about 38 μg, at least or about 40 μg, at least or about 45 μg, at least or about 55 μg or more vitamin D per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00133] According to an embodiment, the composition of the invention comprises phosphorous. According to an embodiment, the composition comprises at least 460 mg or more phosphorous per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 650 mg, at least or about 700 mg, at least or about 750 mg, at least or about 770 mg, at least or about 780 mg, at least or about 900 mg, at least or about 1000 mg or more phosphorous per daily administered dose for a one to 3 year old child.

[00134] According to an embodiment, the composition comprises at least 500 mg phosphorous or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 850 mg, at least or about 900 mg, at least or about 1000 mg, at least or about 1100 mg, at least or about 1150 mg, at least or about 1170m, at least or

about 1180 mg, at least or about 1300 mg or more phosphorous per daily administered dose for a 4 to 8 year old child.

[00135] According to an embodiment, the composition comprises at least 1250 mg phosphorous or more per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 950 mg, at least or about 100 mg, at least or about 1200 mg, at least or about 1300 mg, at least or about 1350 mg, at least or about 1400 mg, at least or about 1410 mg, at least or about 1500 mg or more phosphorous per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00136] According to an embodiment, the composition comprises iron. According to an embodiment, the composition comprises at least 7 mg or more iron per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 8 mg, at least or about 9 mg, at least or about 10 mg, at least or about 10.5 mg, at least or about 11 mg, at least or about 12 mg, at least or about 15 mg or more iron per daily administered dose for a one to 3 year old child.

[00137] According to an embodiment, the composition comprises at least 10 mg iron or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 12 mg, at least or about 13 mg, at least or about 14 mg, at least or about 15 mg, at least or about 15.5 mg, at least or about 16 m, at least or about 18 mg, at least or about 20 mg or more iron per daily administered dose for a 4 to 8 year old child.

[00138] According to an embodiment, the composition comprises at least 8 mg iron or more per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 13 mg, at least or about 14 mg, at least or about 16 mg, at least or about 17 mg, at least or about 18 mg, at least or about 19 mg, at least or about 20 mg, at least or about 25 mg or more iron per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00139] According to an embodiment, the composition comprises zinc. According to an embodiment, the composition comprises at least 3 mg or more zinc per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 4 mg, at least or about 5 mg, at least or about 6 mg, at least or about 7 mg, at least or about 8 mg, at least or about 9 mg, at least or about 9.5 mg or more zinc per daily administered dose for a one to 3 year old child.

[00140] According to an embodiment, the composition comprises at least 5 mg zinc or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 6 mg, at least or about 7 mg, at least or about 8 mg, at least or about 9 mg, at least or about 10 mg, at least or about 11 m, at least or about 12 mg, at least or about 14 mg or more zinc per daily administered dose for a 4 to 8 year old child.

[00141] According to an embodiment, the composition comprises at least 8 mg zinc or more per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 10 mg, at least or about 13 mg, at least or about 14 mg, at least or about 15 mg, at least or about 16 mg, at least or about 17 mg, at least or about 20 mg, at least or about 22 mg or more zinc per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00142] According to an embodiment, the composition comprises copper. According to an embodiment, the composition comprises at least 340 μg or more copper per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 700 μg, at least or about 800 μg, at least or about 900 μg, at least or about 930 μg, at least or about 950 μg, at least or about 970 μg, at least or about 1000 μg or more copper per daily administered dose for a one to 3 year old child.

[00143] According to an embodiment, the composition comprises at least 440 μg copper or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 1000 μg, at least or about 1200 μg, at least or about 1300 μg, at least or about

1350 μg, at least or about 1400 μg, at least or about 1450 μg, at least or about 1475 μg, at least or about 1500 μg, at least or about 2000 μg or more copper per daily administered dose for a 4 to 8 year old child.

[00144] According to an embodiment, the composition comprises at least 700 μg or more copper per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 1300 μg, at least or about 1400μg, at least or about 1500 μg, at least or about 1600 μg, at least or about 1700 μg, at least or about 1750 μg, at least or about 4000 μg, at least or about 5000 μg or more copper per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00145] According to an embodiment, the composition comprises magnesium. According to an embodiment, the composition comprises at least 80 mg or more magnesium per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 100 mg, at least or about 140 mg, at least or about 160 mg, at least or about 170 mg, at least or about 180 mg, at least or about 200 mg, at least or about 230 mg or more magnesium per daily administered dose for a one to 3 year old child.

[00146] According to an embodiment, the composition comprises at least 130 mg magnesium or more per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 180 mg, at least or about 200 mg, at least or about 220 mg, at least or about 240 mg, at least or about 260 mg, at least or about 280 mg, at least or about 300 mg, at least or about 310 mg or more magnesium per daily administered dose for a 4 to 8 year old child.

[00147] According to an embodiment, the composition comprises at least 240 mg or more magnesium per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 280 mg, at least or about 300 mg, at least or about 320 mg, at least or about 330 mg, at least or about 340 mg, at least or about 350 mg, at least or about 360 mg, at least or about 370 mg or more magnesium per daily administered dose for a 9 to 13 year old child. These or higher amounts, preferably in accordance with

RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00148] According to an embodiment, the composition comprises manganese. According to an embodiment, the composition comprises at least 1.2 mg or more manganese per daily administered dose of the composition, in particular if administered to a 1 to 3 year old child. Preferably, the composition comprises at least or about 1.4 mg, at least or about 1.5 mg, or about at least or about 1.6 mg, at least or about 1.7 mg, at least or about 1.8 mg, at least or about 1.9 mg, at least or about 2 mg or more manganese per daily administered dose for a one to 3 year old child.

[00149] According to an embodiment, the composition comprises at least 1.5 mg or more manganese per daily administered dose of the composition, in particular if administered to a 4 to 8 year old child. Preferably, the composition comprises at least or about 2 mg, at least or about 2.3 mg, at least or about 2.5 mg, at least or about 2.6 mg, at least or about 2.7 mg, at least or about 2.8 m, at least or about 2.9 mg, at least or about 3 mg or more manganese per daily administered dose for a 4 to 8 year old child.

[00150] According to an embodiment, the composition comprises at least 1.9 mg manganese or more per daily administered dose of the composition, in particular if administered to a 9 to 13 year old child. Preferably, the composition comprises at least or about 2.5 mg, at least or about 3.0 mg, at least or about 3.2 mg, at least or about 3.4 mg, at least or about 3.5 mg, at least or about 4 mg, at least or about 5 mg, at least or about 6 mg or more manganese per daily administered dose, in particular for a 9 to 13 year old child or a human subject who is older than that. These or higher amounts, preferably in accordance with RDIs and ULs, preferably also apply if the subject is a human subject that is 14 years or older.

[00151] According to a preferred embodiment, the composition of the invention comprises further nutrients. In particular, the composition comprises further macronutrients, besides proteinogenic matter, so as to provide a nutritionally balanced blend of nutrients, or a blend of nutrients that is possibly adapted to the need of the subject.

[00152] The composition of the invention preferably comprises available carbohydrates. "Available carbohydrates" represents that fraction of carbohydrate that can be digested by human enzymes, is absorbed and enters into intermediary

metabolism. Available carbohydrates do not include dietary fibre. Available carbohydrates may be selected from monosaccharides, such as glucose, fructose, mannose, and galactose; disaccharides, such as saccharose (sucrose), lactose, maltose, trehalose, isomaltose; trisaccharides, such as maltotriose; oligosaccharides in general (2-10 monosaccharadie units), and polysaccharides (more than 10 monosaccharide units), and mixtures thereof, just to mention a few common examples. Examples of available polysaccharide carbohydrates are in particular starches, such as those from corn, wheat, tapioca, rice, and potato, including amylose and amylopectin. The starches can be natural or modified or gelatinized. Preferably the composition is free of modified starch. Available carbohydrates thus also include also include honey, maple syrup, glucose (dextrose), corn syrup, corn syrup solids, high fructose corn syrups, crystalline fructose, juice concentrates, and crystalline juice, which may also be used as sweetening agents. The composition may comprise dextrins, such as maltodextrin, which is obtained from starch by hydrolysis. Dextrins typically contain a mixture of saccharides of different chain length. The source of available starch may be selected from any one or still other available carbohydrates, and from combinations thereof.

[00153] The monosaccharde units of the mono-, di-, tri-, oligo-, and polysaccharides may be selected from all different types of saccharides that can be used in food, such as trioses, tetroses, pentoses, hexoses, deoxy sugars, and so forth.

[00154] Cereals are a preferred source of carbohydrates.

[00155] The composition of the invention may contain lactose. According to another embodiment, the composition of the invention is low in lactose or substantially lactose free. "Low in lactose" preferably means that less than 40%, preferably less than 30%, less than 20%, less than 10%, preferably less than 5%, most preferably less than 3% by weight of available carbohydrates being provided by lactose. In case there are no other available carbohydrates in the composition, "low in lactose" means that less that 10% by weight of the composition, preferably less than 5%, more preferably less than 3% and most preferably less than 2% by weight of the composition is lactose." Substantially lactose free" means that lactose preferably provides less than 2%, preferably less than 1% and most preferably less than 0.5% of the weight of available carbohydrates of the composition. In case there are no other available carbohydrates than lactose in the composition, "substantially lactose free" means that less than 1%,

preferably less than 0.5% most preferably less than 0.3% by weight of the composition are provided by lactose. Percent by weight are percent by weight of dry matter for the purpose of this specification, unless otherwise indicated.

[00156] According to an embodiment, available carbohydrates provide about 30-75%, preferably 35-70%, more preferably 40-65%, most preferably 45-60%, for example 45-55% of the total caloric energy of the composition. These amounts may apply in particular if the composition is nutritionally complete.

[00157] The composition of the invention preferably comprises lipids. Suitable sources of lipids include those that are useful for human nutrition and may be of any suitable origin, such as vegetal and animal oils or fat, for example. Animal oils include milk fat and fish oil, for example. Lipid sources include lipids obtained from milk, fish, eggs, seeds, nuts, fungi, microorganisms such as yeast and bacteria, for example. Lipid sources include sources containing phospholipids, mono- di-, triglycerides, fatty acids, sterol-related compounds such as cholesterol, sphingosines, ceramides, glycosphingolipids, gangluiosides and the like. Preferred sources of lipids are milk, vegetal oils and fish oil.

[00158] According to an embodiment, the composition of the invention comprises polyunsaturated fatty acids (PUFAs), which may be selected, independently, for example, from omega-3 and from omega-6 fatty acids. According to an embodiment, the composition of the invention comprises omega-3 fatty acids.

[00159] According to an embodiment, the composition of the invention comprises one selected from eicosapentaenoic acid (EPA, 20:5, ω-3), docosahexaenoic acid (DHA, 22:6, ω-3), α-linolenic acid (ALA: 18:3 ω-3), docosapentaenoic acid (DPA, 22:5, ω-3), arachidonic acid (ARA, 20:4, ω-6), and linoleic acid (LA: 18:2, ω-6), and combinations thereof.

[00160] Preferably, the composition comprises at least 0.7 g of omega-3 fatty acids per daily administered dose, in particular if the subject is a 1-3 year old child.

[00161] Preferably, the composition comprises at least 0.9 g of omega-3 fatty acids per daily administered dose, in particular if the subject is a 4-8 year old child.

[00162] Preferably, the composition comprises at least 1.3 g of omega-3 fatty acids per daily administered dose, in particular if the subject is a 9-13 year old child.

[00163] Preferably, the composition comprises at least 70 mg of EPA per daily administered dose, in particular if the subject is a 1-3 year old child.

[00164] Preferably, the composition comprises at least 90 mg of EPA per daily administered dose, in particular if the subject is a 4-8 year old child.

[00165] Preferably, the composition comprises at least 0.13 g of EPA per daily administered dose, in particular if the subject is a 9-13 year old child.

[00166] According to an embodiment, the composition of the invention comprises medium chain fatty acids (MCFA) and/or long chain fatty acids (LCFA). Medium chain fatty acids, for the purpose of the present specification, are fatty acids have 6 to 14 carbons (C6-C14). Myristic acid, for the purpose of this specification, is thus considered a MCFA. LCFA, for the purpose of this specification, have more than 14 carbons (>C14).

[00167] According to an embodiment, the composition of the invention comprises medium chain triglycerides (MTC). MTC, for the purpose of the present specification, are triglycerides that comprise substantial amounts, preferably 30%, 40%, 50%, 60%, 70% or more of MCFAs. For example, the lipids of the composition of the invention may comprise from 0 to 70%, preferably 1 to 60%, more preferably 2 to 50%, even more preferably, from 3 to 40% of MTC, in percent by weight of all lipids present in the composition.

[00168] According to an embodiment, lipids provide 15-55%, preferably 20-50%, more preferably 25-45%, most preferably 30-40% of the caloric energy of macronutrients of the composition. These mounts are particularly preferred if the subject is a 1-3 year old child. Furthermore, these amounts apply in particular if the composition is nutritionally complete.

[00169] According to an embodiment, lipids provide 10-50%, preferably 15-45%, more preferably 20-40%, most preferably 25-35% of the caloric energy of macronutrients of the composition, if the subject is a 4-9 year old child, or if the subject a human subject that is older than that. Furthermore, these amounts apply in particular if the composition is nutritionally complete.

[00170] According to an embodiment, the composition of the invention comprises nucleotides. As used herein, a “nucleotide” is understood to be a subunit of deoxyribonucleic acid (“DNA”) or ribonucleic acid (“RNA”). It is an organic compound

made up of a nitrogenous base, a phosphate molecule, and a sugar molecule (deoxyribose in DNA and ribose in RNA). Individual nucleotide monomers (single units) are linked together to form polymers, or long chains. Exogenous nucleotides are specifically provided by dietary supplementation. The exogenous nucleotide can be in a monomeric form such as, for example, 5'-Adenosine Monophosphate ("5'-AMP"), 5'-Guanosine Monophosphate ("5'-GMP"), 5'-Cytosine Monophosphate ("5'-CMP"), 5'-Uracil Monophosphate ("5'-UMP"), 5'-Inosine Monophosphate ("5'-IMP"), 5'-Thymine Monophosphate ("5'-TMP"), or combinations thereof. The exogenous nucleotide can also be in a polymeric form such as, for example, an intact RNA. There can be multiple sources of the polymeric form such as, for example, yeast RNA According to an embodiment, the composition comprises ≥5 mg, preferably ≥6 mg, ≥7 mg, ≥8 mg, ≥9 mg, and ≥10 mg of nucleotides per 100 g of dry matter of the composition. According to an embodiment, the composition comprises ≥2.5 mg, preferably ≥3 mg, ≥3.5 mg, ≥4 mg, ≥4.5 mg, and ≥5 mg of nucleotides per daily administered dose of the composition.

[00171] According to an embodiment, the composition of the invention comprises one or more components selected from the macronutrients (proteinogenic matter, lipids, available carbohydrates), vitamins, minerals, nucleotides, phytonutrients and/or antioxidants selected from flavonoids, curcuminoids, limonins, carotenoids, lactowolfberry, wolfberry, polyphenols, lycopene, lutein, lignan, coenzyme Q10 ("CoQ10"), hesperidine and glutathione and combinations thereof and combinations thereof.

[00172] According to an embodiment, the composition of the invention comprises one or more selected from the macronutrients selected from proteinogenic matter, in particular whey protein, lipids, in particular lipids comprising omega-3 fatty acids, vitamins, minerals, nucleotides, phytonutrients and/or antioxidants (selected from flavonoids, curcuminoids, limonins, carotenoids, lactowolfberry, wolfberry, polyphenols, lycopene, lutein, lignan, coenzyme Q10 ("CoQ10"), hesperidine and glutathione and combinations thereof, for example) and combinations thereof.

[00173] According to an embodiment, the composition of the invention comprises one or more selected from the macronutrients selected from proteinogenic matter, in particular whey protein, lipids, in particular lipids comprising omega-3 fatty

acids (in particular EPA), vitamins selected from vitamin K, vitamin D, calcium, phosphorous, iron, zinc, copper, magnesium, manganese, flavonoids, in particular quercetin, curcuminoids, in particular curcumin, and combinations thereof.

[00174] According to an embodiment, the composition of the invention comprises one or more selected from whey protein, lipids comprising omega-3 fatty acids (in particular EPA), vitamins selected from vitamin K, vitamin D, calcium, phosphorous, iron, zinc, copper, magnesium, manganese, flavonoids, in particular quercetin, curcuminoids, in particular curcumin and combinations thereof, for example at the amounts as specified elsewhere in this specification.

[00175] According to an embodiment, the composition of the invention comprises one or more selected from whey protein, lipids comprising omega-3 fatty acids (in particular (EPA), vitamins selected from vitamin K, vitamin D, calcium, iron, zinc, magnesium, manganese, quercetin, curcumin and combinations thereof.

[00176] According to an embodiment, the composition of the invention comprises one or more components and/or ingredients selected from whey protein, vitamin K, curcumin, quercetin, eicosapentaenoic acid (EPA), and nucleotides.

[00177] According to an embodiment, the subject consuming the composition of the invention, and/or the subject to whom the composition is administered conducts physical exercise.

[00178] According to an embodiment, the physical exercise refers to physical exercise that is part of a program. Preferably, the program is specifically adapted to the subject. Alternatively, the program starts at a very low intensity level and exercise intensity or frequency is increased in accordance with the subject's capacities and evolution. Accordingly, the term "exercise" or "physical exercise", for the purpose of the present specification, refers to exercise that is part of an exercise program in accordance with the invention.

[00179] According to an embodiment, the exercise is described, prescribed or recommended to the subject. Furthermore, the exercise program is preferably specifically defined. In particular, the individual elements of the exercise are specifically described and/or defined and adapted to the subject.

[00180] In order to adapt exercises to the subject, there is preferably a step of evaluating physical status (such abilities to perform physical exercises and the like,

force, endurance, and the like) and possibly health and/or bone status. According to an embodiment, evaluation may be performed by a health-care assistant or another trained person having experience in physical training and/or physical exercises, such as, for example, a physical therapist or a trainer. For example, the anaerobic threshold may be determined as described elsewhere in this specification for evaluating status of a subject.

[00181] According to another embodiment, an evaluation of the physical status of the subject is performed in any kind of automated way, for example by way of a questionnaire to be filled in, which may be on paper or computer assisted, for example on-line or via a computer program.

[00182] The physical exercises in accordance with the invention are defined or determined and distinguish in this way from other kind of activity, such as normal playing or sports taking place outside the frame of the present invention. The physical exercise is defined in terms of one or more selected from actual, specific elements of physical exercise that are performed, quantity of exercises, frequency, regularity and period of treatment, during which the exercise program is conducted, and combinations thereof. It is possible and even preferred that some parameters of physical activity evolve in the course of the exercise program. In particular, it is expected that physical capacities (muscle strength, endurance, and so forth) develop in a positive way and that frequency and/or intensity of exercise can be increased, or that further, additional exercises can be added in the course of the program. Without wishing to be bound by theory, it is envisaged that motivation, health status, musculoskeletal status and so forth are increased.

[00183] According to an embodiment, the step of conducting physical exercise in accordance with the invention involves one or more selected from motivating, instructing and/or inciting said child to perform exercises that are specifically adapted to the physical capacities of said child.

[00184] The physical exercise program is preferably designed so as to avoid repetitions that could be experienced as boring. The physical exercise program preferably avoids non-compliance by the subject, for example due to repetitions or because the program is not adapted to the subject.

[00185] The physical exercise may be of any form. According to an embodiment, the exercise program comprises anaerobic exercise. Without wishing to be

bound by theory, the inventors believe that in the context of the invention anaerobic exercise, also referred to resistance exercise, is suitable to provide an effective osteogenic stimulus. Specifically, the overload stimulus of resistance exercise and contraction of skeletal muscle during exercise provides loading forces to the underlying bones. Additionally, the resistance exercise promotes anabolism, for example for lean mass accretion. The physical exercise may also comprise aerobic exercise, and a combination of both anaerobic and aerobic exercise.

[00186] Without wishing to be bound by theory, it is also noted that the increased physical activity may be used to help to minimize excessive adiposity and/or obesity in some subjects. Furthermore, the optimization of body composition to increase lean body mass (with nutrition plus exercise) will have a positive impact on glucose control/insulin sensitivity.

[00187] According to an embodiment, the step of conducting physical exercise in the method and/or treatment of the invention comprises demonstrating a physical exercise to a child and/or preparing physical exercises with said child.

[00188] The physical exercise or exercise program may include the use of any device, tool and/or toy or may not make use of devices, tools and/or toys. According to an embodiment, the exercise includes games. According to an embodiment, the physical exercise involves the use of weight machines. According to an embodiment, the physical exercise involves the use of free weights or weight units that can be attached to the body of the subject. According to an embodiment, the physical exercise involves the use of any kind of resilient device, which can be actuated by a subject whit the aid of muscular strength and which, by way of its resilience, returns to an original state once muscular effort is reduced. For example, the physical exercise involves the use of elastic bands, for example therabands. For example, the physical exercise involves the use of a hand-grip. According to an embodiment, the physical exercise involves the use of any kind of resilient device, which can be actuated by a subject whit the aid of muscular strength and which, by way of its resilience, returns to an original state once muscular effort is reduced. According to an embodiment, the physical exercise involves the use of medicine balls. According to an embodiment, the physical exercise comprises the use of a combination of one or more of the aforementioned.

[00189] According to an embodiment, the physical exercise involves the use of electronically-assisted and/or computer-assisted games. In particular, the physical exercise preferably involves games that make use of motion sensors, such as sensors of acceleration, slowing down or change of direction and/or orientation, such as gyroscopes, for example. Another example of electronically- or computer-assisted games involves tactile devices, for example a tactile carpet, panel, pad and/or covering. For example, a carpet-like tactile device can sense where a subject touches the carpet, for example by his feet or hands, and process the data to yield a specific result, for example in a game. Typical examples of electronically- and/or computer-assisted games and devices involving the physical exercise are Wii stations, for example using force plates and the like. Other examples include PlayStation™ and X-Box™, which may be used and/or adapted for the purpose of conducting physical exercise in accordance with the present invention.

[00190] According to an embodiment, the physical exercise comprises free exercises, which do not require any further instrument or device, such as push-ups, squats, semi-squats, and so forth.

[00191] According to an embodiment, the physical exercises are home based, that is they can be performed at home by the subject.

[00192] According to an embodiment, the actually conducted exercises by the subject are recorded and/or tracked. The method and/or treatment of the invention thus preferably comprises the step of tracking physical exercise performed by the subject. In particular, any one selected from progress, compliance with the program and exercise progression is tracked and/or recorded. Exercises performed by the subject can be noted on paper, but are preferably stored in a database. According to an embodiment, the actual exercises and associated parameters such as time spent with an exercise, number of repetitions, intensity, and the like are registered by way of a computer-assisted device, in particular a computer. The actually performed exercises may be entered into the database by the subject her-/himself or by another person, such as an assistant or by parents, for example. According to an embodiment, exercises involving a computer are tracked automatically during exercising.

[00193] According to an embodiment, the exercise program involves an interactive, computer-based and/or computer-assisted device comprising input and

output elements. Preferably, the exercise program involves visual out- and/or inputs. For example, the subject (or another person) may enter performed exercises via a input device, such as a joy-stick, a computer mouse, a keypad, but preferably via a visual input device, such as, for example, tactile screen. According to an embodiment, the computer-assisted device recording and/or tracking the exercises of a subject comprises a computer pad or a so-called smart tablet with a tactile screen, of the iPad or Motorola Xoom-type, for example.

[00194] Preferably, the subject can enter achievements in terms of the physical exercise program and preferably an output is generated. The output preferably contains messages and/or images that are motivating, congratulating and/or encouraging the subject to continue exercises, and/or that show achievements, progress, and the like.

[00195] According to an embodiment, a exercise device, for example for conducting resistance exercises, measures forces imparted on the body and a visual feedback corresponding to the force, for example on a monitor or screen, is created. For example, input signals can be determined using therabands and/or force plates, for example measuring force. In this case, it is not necessary that the user (the subject) enters him/herself the results or outcome of an exercise, but the data are automatically stored and visualized by connecting the exercise device with a computer-assisted device.

[00196] According to an embodiment, the computer-assisted or computer-based device involves an on-line system, where date and information with respect to physical exercises and progress can be introduced and possibly commented. Furthermore, there may be on-line feedback, for example mediated by the internet. Furthermore, there may be interactions between subjects in accordance with the invention over said computer-based device. There may also be group activities and games between subjects belonging, preferably, to the same age group.

[00197] According to an embodiment, the physical exercise is regular, or the exercise program involves regular exercise. The expression "regular exercise" does not imply that exactly the same exercise is conducted regularly, but also encompasses different exercises or a series of different exercises that is repeated. Preferably, exercises are conducted at regular intervals. For example, exercises are conducted one, two or three times a day, every day, every other day, every three days, every four days, and so

forth. According to an embodiment, exercises are conducted once a week, twice a week, three times a week, four times a week, five times a week, six times a week, seven times a week, eight times a week, nine times a week, or more often per week.

[00198] It is noted that the expression "physical exercise" or "exercise" is preferably different from physical activity in general, the latter term referring to physical activity of a subject taking place outside the context of the invention, and in particular activity that is not part of the exercise program of the invention, for example as specified herein. Physical activity refers generally to aerobic activity.

[00199] The exercise are preferably conducted over a certain minimum period, the minimum period being, for example, a week, 2, 3, 4, 5, 6, 7, 8, 9, 10 weeks, one month, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 months, a year or over a total period that is more than one year. Of course, the individual elements of exercise (for example a specifically developed game certain of a Wii station) may be regularly adapted to the subject in the course of the period covered by the exercise program. Adaptation involves reduction and/or increase of the intensity or frequency of exercise, in dependency of progress being made or general health status of the subject. The period of treatment is thus preferably the minimum period.

[00200] According to an embodiment, the physical exercise is conducted in the frame of an exercise program adapted to physical capacities of said child, wherein said exercise program comprises different exercise elements and wherein the same or different exercise elements are conducted after periods of time over a treatment period.

[00201] In accordance with the invention, the beneficial effects reported in this specification are obtained in a subject that consumes the composition of the invention and that also undergoes exercise as disclosed elsewhere in this specification. In order to obtain the effects of the invention, the composition is consumed repeatedly over a certain time, preferably regularly, and the exercise is also conducted repeatedly over the time span of the treatment, preferably regularly. The composition is preferably administered several times a day, daily, every other day, every three days, at least 7 times or more per week, 6 times or more per week, 5, 4, 3, 2, or on 1 day or more per week, in particular during the treatment period.

[00202] The treatment thus preferably encompasses administration of the composition and physical exercise. The composition is preferably administered in the

same overall period as the exercises are conducted. The duration of the treatment period corresponds in general to the period, for example the minimum period specified with respect to the exercise or exercise program. According to an embodiment, the composition as defined elsewhere in this specification is administered for a longer or shorter overall period than the period for exercise. For example, the composition may be administered before the start of the physical exercise program, or vice versa. Similarly, the composition may be administered even beyond the period of physical exercise, or the exercise program may be continued while administration of the composition is stopped.

[00203] The term treatment, for the purpose of the present specification, may have different meanings. The term "treatment" and "treat" are used to refer to the obtainment of the beneficial effects of the invention. In this regard, the term "treatment" refers to improvement of life and/or health status in a subject, for example by stopping or improving a disease or an unhealthy condition, slowing down progress of a disease state or of an unhealthy condition. In this context, the term "treatment" thus may refer to medical treatment, therapy and/or prophylactic treatment.

[00204] On the other hand, the term "treatment" is generally used in this specification to refer to the nutrition and/or exercise program of the present invention. The treatment, in this regard, thus refers to the administration of the composition of the invention in combination with conducting the physical exercise, in particular a physical exercise program, for example as exemplified in this specification. In this context, the term "treatment" could possibly be replaced or defined by the terms "program", "process", "procedure", "accomplishment", "execution" and the like.

[00205] The administration of the composition of the invention, preferably in combination with physical exercise, provides several important health benefits In particular, the teaching of the present invention is suitable to improve life quality, to improve well-being, to support growth, to ensure healthy growth, improves and/or supports musculoskeletal state and/or health, to increase muscle and/or bone mass, density, formation and/or mineral content, and further benefits as reported elsewhere in this specification.

[00206] According to an embodiment, the invention comprises monitoring and/or assessment of the effects of the invention, progress of the subject in terms of the

effects of the invention. For example, the musculoskeletal state, muscle strength, bone density, bone mineral content, and the like are assessed, preferably several times during the exercise or treatment period, for example at the beginning, in the curse of, and at the end of the treatment period.

[00207] For example, the effect of the treatment in accordance with the invention is assessed and/or monitored.

[00208] The quality of life, for example, may be assessed employing the validated Medical Outcomes Study 36-item Short-Form General Health Survey. The questionnaire consists of 36 questions, is self administered and assesses quality of life and wellbeing in 8 multi item scales regarding physical functioning and perception of physical role, vitality, general and mental health, perception of emotional role, social functioning and bodily pain. The quality of life may also and/or alternatively be assessed using measures of self-confidence.

[00209] The effects of the present invention may, generally, be assessed by measures of physical performance (muscle strength, power and/or balance), by biomarkers of bone turnover (e.g. NTx, osteocalcin) and inflammation (e.g. TNFα, CRP, IL-6), quantification of lean body mass (Bod Pod, BIA, MRI), bone growth (Micro Computed Tomography, Magnetic Resonance Imaging-MRI), analyses of whole blood cells (gene microarray for network genes with respect to musculoskeletal areas.

[00210] Increased muscle strength and other effects of the invention may be obtained using the following exercises and/or protocols, which are in particular also used for assessing the presence of the effects of the invention, that is, the progress of the subject in accordance with the effects of the invention.

[00211] According to an embodiment, hand grip strength is improved, assessed and/or monitored. Hand grip strength may, for example, be measured in the non-dominant hand with a Digimax electronic dynamometer (Mechatronic Hamm GmbH, Germany). The subject performs the test while sitting comfortably with shoulder adducted and neutrally rotated, the elbow supported on a table and flexed to 90 degrees, forearm and wrist in neutral position. The subject will be instructed to perform a maximal isometric contraction. The test will be repeated within 30 seconds and the highest value was recorded.

[00212] According to an embodiment, isokinetic peak torque and isometric strength of muscles is improved, assessed and/or monitored. This may be made using an isokinetic dynamometer. Such devices may be used for a variety of muscles, such as for example, flexors and extensors of limps and/or articulations. For example, an isokinetic dynamometer may be used to assess isokinetic peak torque and isometric strength of knee or elbow flexors and extensors.

[00213] According to an embodiment, the physical activity, in particular during the exercises of the program in accordance with the invention, is monitored. Physical activity is, for example, monitored in order to assess and/or compare the combined effects of the administration of the composition and the physical exercise in accordance with the invention. The effects may be compared to effects obtained in subjects that do not consume the composition of the invention. Or activity levels in general may be compared of subjects that undergo the combined treatment of specific nutrition and physical exercise in accordance with the invention with subjects that do not undergo the treatment of the invention.

[00214] According to an embodiment, physical activity may objectively measured, assessed and/or evaluated by way of accelerometry. Accelerometry may be performed, for example, using the Actigraph Model GT3X (Manufacturing Technology Inc., FL, USA). The actigraph is generally worn superior to the iliac crest in a custom pouch, secured to the subject's belt by a plastic fastening. Assessments can be made at baseline and 6 months. These accelerometers are small enough to be unobtrusive and produce little interference with normal physical activity. Subjects will be instructed to wear the actigraph for a 7-day period during waking hours and remove it for sleep and bathing only. Activity is preferably recorded using 1-second epochs. In general, accelerometry allows objective measurement of physical activity by the use of a motion sensor which records both the number and magnitude of vertical accelerations generated by a subject's movement. Both the volume and intensity of physical activity can be quantified.

[00215] According to an embodiment, physical performance is increased, assessed and/or monitored. For example, the "Short Physical Performane Battery (SPPB) is a test and/or physical exercise for training and/or assessing force, strength, endurance, balance and speed in particular of the muscles and/or musculoskeletal

system of the lower limps. The test comprises the subtests of 1.) 4 meter walk 2) five timed chair rises. 3) one or more simple balance tests. Results from each subtest are ranked using a 0-4 scale and the composite score is summed. Guralnik, et al.: A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. In: J Gerontol. 49. 1994, 2, M85-M94.

[00216] The anaerobic power of the muscles and/or musculoskeletal system of the lower body may be increased, measured, assessed and/or monitored using, for example, the Wingate anaerobic cycling test (WANT). An arm ergometer can be used for improving and/or assessing upper body anaerobic power. Eur J Appl Physiol (1983) 51: 409-417.

[00217] The aerobic power of muscle and/or of the musculoskeletal system may be increased, measured, evaluated, assessed and/or monitored using, for example, one or more grade exercise tests (GXT) to assess peak oxygen uptake, for example. Such a test may be used to evaluate an subject's physiological response (e.g. heart rate, blood pressure, and oxygen consumption) to exercise, the intensity of which is increased in stages. These tests can be performed using a bench (for step-ups), a cycle ergometer, or a treadmill. A typical test on a treadmill starts with a subject walking gently on a revolving belt, which is accelerated at three minute intervals until the subject is running at maximum pace or until the subject experiences any discomfort or irregularities (e.g. of heartbeat). Heart rate and oxygen consumption are monitored continuously. Blood pressure is measured at rest, during exercise, and after exercise. GXTs provide estimates of the ability of the lungs, heart, and blood vessels to deliver oxygen to respiring tissue; therefore they are measurements of aerobic fitness or power or cardiorespiratory fitness. This test may be used, for example, for assessing the anaerobic threshold in a subject.

[00218] According to an embodiment, the invention is suitable to increase bone health in an individual. More specifically, the invention is suitable to improve bone microarchitectural morphology, bone mineralization, bone density, bone elasticity and mechanical stiffness of bones. These parameters may be assessed, for example, by peripheral quantitative computer tomography ("pQCT") or Dual Energy X-ray absorptiometry ("DEXA"). Generally speaking, bone density is expressed as the relationship between bone mass (expressed as the degree of photon attenuation through

the bone, or bone mineral content (BMC)) and the image of the bone on a film (i.e., the area) (expressed as BMC/cm^2). Additionally, pQCT is a procedure that evaluates peripheral bone in 3 dimensions (volumetric) and is commonly applied to the forearm or tibia. A radiation source (typically x-rays) and a sensor revolve around the bone under examination, which is them reconstructed on the computer screen in a three-dimensional (3-D) image. pQCT is an optimal technique for evaluating bone geometry even though sensitivity varies with the site under evaluation. Unlike most other techniques, pQCT measures true bone density (volumetric mineral bone density) because it normalizes the bone mineral content derived not from the projected area but rather from the volume of the examined bone. pQCT can also be used to calculate the SSI, an index of bone resistance to torsion. The index takes into account bone geometry and the bone's mineral characteristics. See, Geometry and bone density, Radetti, G., et al., Panminerva Med 2006; 48:181-6. DEXA is based on x-ray spectrometry and its fundamental principle is based on the degree of attenuation of x-rays emitted from 2 different sources of energy. DEXA is normally used to evaluate lumbar or proximal femoral bone mineralization. DEXA has an accuracy of 4-10% and a coefficient of variation of 1-1.5%.

[00219] Examples

[00220] The following examples are illustrative of some of the products and methods of making the same falling within the scope of the present invention. They are not to be considered in any way limitative of the invention. Changes and modifications can be made with respect to the invention. The skilled person will recognize many variations in these examples to cover a wide area of formulas, ingredients, processing and mixtures to rationally adjust the nutrients and other elements of the invention for a variety of applications.

[00221] Example 1:

[00222] A powdered nutritional composition is prepared in a conventional manner using powdered whey protein micelles as disclosed in US 2009/0035437, Example 13, as only protein source, glucose syrup, sucrose, milk fat, medium chain triglycerides (MCT oil), corn oil, soy lecithin as emulsifier, potassium citrate, calcium phosphate, sodium citrate, calcium carbonate, magnesium chloride, acidity regulator: potassium hydroxide, potassium chloride, vitamins: C, E, niacin, panthothenic acid, B6,

thiamin (B1), A, riboflavin (B2), D, folic acid, K, biotin, B12,; choline bitatrtrate, ferrous sulphate, zinc sulphate, magnesium oxide, manganese sulphate, copper sulphate, sodium molybdate, potassium iodide, chromium chloride, sodium selenate. The detailed nutritional composition is given in Table 1 below:

[00223] **Table 1:** Nutrients in the composition of the invention

Nutrient	Unit	Per 100 ml	Per 100g powder
Total energy	Kcal	100	491
Total fat (42% TEI)	g	4.7	23.08
Total protein (14% TEI)	g	3.58	17.58
Total carbohydrate (44% TEI)	g	11	54.01
Minerals (Ash)	g	0.51	2.50
Sodium	mg	35	171.85
Potassium	mg	120	589.20
Chloride	mg	75	368.25
Calcium	mg	91	446.81
Phosphorous	mg	61	299.51
Magnesium	mg	20	98.20
Iron	mg	1.1	5.40
Zinc	mg	0.96	4.71
Copper	mg	0.1	0.49
Manganese	mg	0.2	0.98
Fluoride	mg	<0.2	<1
Chromium	µg	5.1	25.04
Molybdenum	µg	7.5	36.83
Selenium	µg	3.5	17.19
Iodine	µg	10	49.1
Vitamin A	µg RE (IU)	84 (280)	412
Vitamin D	µg (IU)	1.0 (40)	4.91

Vitamin E	mg α-TE (IU)	1.3 (2.0)	6.38
Vitamin K	µg	5.5	27.01
Vitamin C	mg	9.7	47.63
Thiamin (Vit. B2)	mg	0.12	0.59
Riboflavin (vit. B2)	mg	0.13	0.64
Pantothenic acid	mg	0.5	2.46
Vitamin B6	mg	0.17	0.83
Vitamin B12	µg	0.32	1.57
Niacin	mg (mg NE)	1.2 (2.0)	5.9
Folic acid	µg	24	117.84
Biotin	µg	3.2	15.71
Choline	mg	7.2	35.35
Inositol	mg	4.1	20.13

[00224] A serving size of the composition is prepared by mixing 50 g of the powder with about 210 ml with clean water (e.g. non-carbonated mineral water), so as to yield about 250 ml.

[00225] Prophetic Example

[00226] A 9 year old boy suffering from cystic fibrosis and is underweight. The boy lacks motivation for playing with his friends. The boy will be asked to participate in a combined nutrition and exercise program in accordance with the present invention and agrees. Together with a healthcare specialist, the physical capacities of the boy will be assessed by the aid of computer games involving physical activity such as dancing and adapted exercises, as well as exercises involving medicinal balls and free weights and typical exercises that can be performed without any equipment, such as push-ups and squats. On the basis of the assessment outcome, a specific exercise program involving different types of exercise elements will be set up. The exercise program will involve exercises every day for a determined time and at least every other day there will be anaerobic exercises. At the same time the boy will receive the nutritional composition according to Example 1 of which at least one serving per day

should be consumed, but possibly more, in particular up to 1800kcal per day in case no other, habitual food is or can be consumed.

[00227] Every day, the defined exercises are conducted in accordance with the program and accomplishment will subsequently entered by the boy himself in a user-friendly database using a computer with a tactile screen and graphic interface (an iBook), where the boy will immediately indicate the exercise conducted by touching the corresponding symbol on the screen and indicating the number of repetitions and/or exercises conducted. The computer will generate an output in dependence of the input in order to motivate and encourage the boy to increase exercise intensity and/or frequency or to simply reward the boy for the exercises that were achieved. The boy will be free to continue exercises beyond the program schedule if he feels like.

[00228] After four weeks of treatment, the boy will have become more active and participates again in playing with friends. Muscle strength, endurance and bone density will be determined and will be shown to be increased. In general, a detailed assessment will show that musculoskeletal health is increased, as well as well-being. There will be indications showing good development in body weight and size, suggesting healthy growth.

[00229] It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present subject matter and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

CLAIMS

The invention is claimed as follows:

1. A composition comprising one or more nutrients in combination with a program of physical exercise for improving the musculoskeletal state in a child having a fragile health status and/or compromised health.

2. A composition comprising one or more nutrients in a treatment for improving the musculoskeletal state in a child having a fragile health status and/or compromised health, said treatment further comprising physical exercise.

3. A composition of claim 1, for increasing at least one characteristic selected from the group of muscle strength, muscle power, muscle endurance, bone health, bone strength, bone density and combinations thereof.

4. A composition of claim 1, the composition comprising at least one component selected from the group consisting of macronutrients (proteinogenic matter, lipids, available carbohydrates), vitamins, minerals, nucleotides, phytonutrients and/or antioxidants (selected from flavonoids, curcuminoids, limonins, carotenoids, lactowolfberry, wolfberry, polyphenols, lycopene, lutein, lignan, coenzyme Q10 ("CoQ10"), hesperidine and glutathione and combinations thereof) and combinations thereof.

5. The composition of claim 1, the composition comprising one or more components selected from the group consisting of whey protein, vitamin K, curcumin, quercetin, eicosapentaenoic acid (EPA), and nucleotides.

6. The composition of claim 1, which is a nutritionally complete formula or a nutritional supplement.

7. The composition of claim 1, wherein the physical exercise comprises anaerobic exercise.

8. The composition of claim 1, wherein the physical exercise is conducted in the frame of an exercise program adapted to physical capacities of the

child, wherein the exercise program comprises different exercise elements and wherein the same or different exercise elements are conducted after periods of time over a treatment period.

9. The composition of claim 1, wherein the child is a child under sub-optimal nutrition and/or suffers from malnutrition.

10. The composition of claim 1, wherein the child suffers from reduced nutrient absorption in the gastrointestinal tract.

11. The composition of claim 1, wherein the child is suffering from a condition selected from the group consisting of Crohn's disease, cystic fibrosis (CF), irritable bowel syndrome, allergy, in particular chronic allergy and asthma.

12. The composition of claim 1, wherein the physical exercise involves the use of electronically-assisted and/or computer-assisted games.

13. A method for improving the musculoskeletal state in a child having a fragile health status and/or compromised health, the method comprising the steps of administering to a child in need of same a composition comprising nutrients and conducting physical exercise.

14. The method of claim 13, wherein the step of conducting physical exercise involves one or more actions selected from the group consisting of motivating, instructing and/or inciting the child to perform exercises that are specifically adapted to the physical capacities of the child.

15. The method of claim 13, wherein the step of conducting physical exercise involves demonstrating a physical exercise to a child and/or preparing physical exercises with said child.

16. The method of claim 13, wherein the composition comprises one or more components selected from the group consisting of macronutrients (proteinogenic matter, lipids, available carbohydrates), vitamins, minerals, nucleotides, phytonutrients and/or antioxidants (selected from flavonoids, curcuminoids, limonins, carotenoids, lactowolfberry, wolfberry, polyphenols, lycopene, lutein, lignan, coenzyme Q10

("CoQ10"), hesperidine and glutathione and combinations thereof) and combinations thereof.

17. The method of claim 13, for increasing at least one characteristic selected from the group of muscle strength, muscle power, muscle endurance, bone health, bone strength, bone density and combinations thereof.

18. The method of claim 13, wherein the composition comprises one or more components selected from the group consisting of whey protein, vitamin K, curcumin, quercetin, eicosapentaenoic acid (EPA), and nucleotides.

19. The method of claim 13, wherein the composition is a nutritionally complete formula or a nutritional supplement.

20. The method of claim 13, wherein the physical exercise comprises anaerobic exercise.

21. The method of claim 13, wherein the physical exercise is conducted in the frame of an exercise program adapted to physical capacities of the child, wherein the exercise program comprises different exercise elements and wherein the same or different exercise elements are conducted after periods of time over a treatment period.

22. The method of claim 13, wherein the child is a child under sub-optimal nutrition and/or suffers from malnutrition.

23. The method of claim 13, wherein the child suffers from reduced nutrient absorption in the gastrointestinal tract.

24. The method of claim 13, wherein the child is suffering from a condition selected from the group consisting of Crohn's disease, cystic fibrosis (CF), irritable bowel syndrome, allergy, in particular chronic allergy and asthma.

25. The method of claim 13, wherein the physical exercise involves the use of electronically-assisted and/or computer-assisted games.