Abstract:

Title: HIGH ENERGY LIQUID ENTERAL NUTRITIONAL COMPOSITION

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High energy and high protein liquid nutrition enteral compositions are provided that contain micellar casein and caseinate.
HIGH ENERGY LIQUID ENTERAL NUTRITIONAL COMPOSITION

FIELD OF THE INVENTION

The present invention is in the field of liquid enteral nutritional compositions.

BACKGROUND OF THE INVENTION

The present invention relates in general to a liquid enteral composition for providing nutrition, either as a supplement, or as a complete nutrition, with a high energy content.

The human body requires energy to perform its vital functions, such as blood circulation, immune processes, respiration processes, etc. Energy can be supplied in the form of calories. Calories are typically supplied by the consumption of food. Calorie sources can be classified into three categories: proteins, fats, and carbohydrates. Proteins can provide the body with support for muscular activity, fats can provide the body with stored energy, and carbohydrates can supply the body with immediate energy. Essential vitamins and minerals are necessary to help regulate the processes of the human body.

A person should receive a proper balance of nutrients to sustain health, otherwise, malnutrition can result in a variety of physical complications. Moreover, it is imperative that the support provided be adapted to the needs of a person. For example, patients who are ill, require increased and specialized nutritional support. An increase in specific nutrients can help the body recover from a particular stress placed upon it, such as sport, emotional and labour stress, illness, medical surgery, malnutrition, etc.

Nutritional needs can also change with a person's age. For example, elderly persons show a decrease in the amount of energy their body requires from fat sources.

In this respect, it is submitted that in the context of this application, an elderly person is a person of the age of 50 or more, in particular of the age of 55 or more, more in particular of the age of 60 or more, more in particular of the age of 65 or more. This rather broad definition takes into account the fact that the average age varies between different populations, on different continents, etc. Most developed world countries have accepted the chronological age of 65 years as a definition of 'elderly' or older person (associated with the age at which one may begin to receive pension benefits), but like many westernized concepts, this does not adapt well to e.g. the situation in Africa. At the moment, there is no United
Nations (UN) standard numerical criterion, but the UN agreed cut-off is 60+ years to refer to the older population in Western world. The more traditional African definitions of an elder or 'elderly' person correlate with the chronological ages of 50 to 65 years, depending on the setting, the region and the country.

The decrease in the amount of energy is attributed to a decrease in the number of functioning cells in said elderly person. This is also attributed to a decrease in activity. Accordingly, an elderly person's nutritional requirements may be different than a young or middle aged person.

Because at least certain persons may not receive their required nutritional support from a normal diet, or may not be able to eat normal food, nutritional compositions, such as nutritional supplements and complete nutrition have been designed to provide nutritional support to persons in need thereof. This nutrition can be directed towards a particular type of nutritional support. For example, a supplement may provide a person with additional calories for increased energy. Although these supplements provide a certain amount of nutritional support, it is in the best interests to provide a nutritional composition having increased nutritional value for a specific nutritional requirement. In the above examples of elderly persons and ill patients, it is desired to provide nutritional liquid compositions having increased energy as well as increased protein per unit dosage.

In this regard, although an elderly person's energy needs may be reduced, their ability to consume products may also be diminished. For example, they may have difficulty consuming a product due to, e.g., swallowing difficulties, or due the too large amount of product they need to consume to meet the daily intake of nutrients. Hence, compliance is not optimal, and often, the intake is suboptimal, leading to suboptimal nourishment.

Further, certain disease states or conditions may require restrictions on the diet a patient consumes. For example, renal patients may have fluid restrictive diets.

Also, a number of patients need nutrition in the smallest volume of liquid. These patients may be cachectic patients or persons suffering from end-stage AIDS, cancer or cancer treatment, severe pulmonary diseases like COPD (Chronic Obstructive Pulmonary Disease), tuberculosis and other infection diseases or persons that experience severe surgery or trauma like burns.

Furthermore, persons suffering from disorders in the throat or mouth such as oesophageal cancer or stomatitis and persons having problems with swallowing like dysphagic persons,
require special liquid, low-volume nutrition. Also, persons suffering from reduced appetite and/or loss of taste will benefit from a low-volume liquid nutritional composition.

Therefore, a need exists for improved enteral compositions, with an increased amount of protein and calories per unit volume for an elderly person or ill patient.

However, increasing calories and/or proteins in a nutritional liquid composition may increase the overall viscosity of the composition. This can make the liquid nutritional composition difficult to consume or administer, and can also diminish the taste of the nutritional composition. Furthermore, technical difficulties exists in producing a stable, in particular a shelf-stable nutritional liquid composition having a high content of proteins.

The problem of the present invention is therefore to provide a stable, attractive, liquid enteral composition for providing nutrition, either as a supplement, or as a complete nutrition, with a high energy content, to a person, in particular to an elderly person or an ill patient.

A number of attempts have been made to solve this problem.

WO 02/098242 A1 (Nestle, 12 December 2002) discloses a calorically dense liquid oral supplement (2.25 kcal/ml) based on a (60:40) soy protein isolate/caseinate mixture with a protein level of 9 g/100 ml (16 En%), 12.25 g/100 ml of fat (49 En%), and 19.7 g/100 ml of carbohydrates (35 En%).

The commercially available product Resource 2.0 is a high calorie product from Novartis (2 kcal/ml), based on a mixture of calcium and sodium caseinate as protein source, comprising 9 g/100 ml of proteins, 9 g/100 ml of fat, and 22 g/100 ml of carbohydrates, and provided in a 237 ml unit dosage.

The commercially available product VHC 2.25 is a high calorie product from Nestle (2.25 kcal/ml), based on a mixture of calcium- and potassium caseinate and isolated soy protein as protein source, comprising 9 g/100 ml of proteins, and provided in a 250 ml unit dosage.

SUMMARY OF THE INVENTION

The present invention provides a liquid enteral nutritional composition with a high energy content, designed to meet the nutritional needs of persons in need thereof, in particular elderly and patients with certain disease states. The composition provides an increased amount of energy per unit volume while providing a sufficiently low viscosity to allow the composition
to be easily consumed orally or be administered by tube. In addition, the taste of the composition is not diminished.

To this end, in a first aspect of the present invention, a liquid enteral nutritional composition is provided comprising 6 to 14 g of protein per 100 ml of the composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml.

In particular, a liquid enteral nutritional composition is provided comprising protein that provides 10 % to 30 % of the total energy content of the composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml.

Micellar Casein, also named Micellar Casein Isolate (abbreviated as MCI) is a high quality milk protein, produced by a proprietary process that does not denature the proteins. Fresh skim milk is ultra filtered, in much the same process used to make whey protein, to produce a pure, undenatured and easily soluble milk protein with its native structure. The resulting material contains more than 95 % casein, the rest mainly being whey and other non-protein nitrogen and other constituents, such as lactose. This milk protein is probably the least processed of all milk proteins. It has an intrinsic low viscosity and a liquid composition comprising said MCI is therefore easy to drink. In contrast, casein, as it is used in the context of this application refers to the curd form of casein, having lost its native micellar structure.

Within the context of this application, it is understood that MCI may also be provided in the form of other materials, such as, for instance, Milk Protein Concentrate (MPC), which is a product comprising micellar casein and whey, typically in a ratio of 80:20. Although the composition of the present invention should not contain large amounts of proteins other than MCI and caseinate, the composition of the present invention may comprise up to about 15 weight% of whey.

A problem associated with the use of micellar casein in the production of liquid enteral nutritional compositions with a high protein content and further containing acids, in particular citric acid, is the formation of calcium-acid complexes, such as calcium citrate. In particular citric acid is added to the composition to adjust the pH and also to adjust Ca-ion activity. A certain Ca-ion activity is beneficial to maintain a desired viscosity of the composition during processing of the composition, e.g. during pasteurisation and/or sterilisation. Calcium, originating from the micellar casein tends to react with acid, in particular the citric acid, thus forming calcium citrate crystals, which precipitate when the acidity of the composition
increases over time (pH lowering), giving rise to a poor shelf stability. Already at a pH of 6.9, the formation of Ca-citrate crystals is progressing. On the other hand, a certain Ca-ion activity is beneficial to maintain a desired viscosity of the composition during processing of the composition, e.g. during pasteurisation and/or sterilisation. In particular a certain Ca-ion activity is beneficial to prevent a viscosity increase during heating. Thus, besides shelf stability, it is a problem to arrive at a proper viscosity when using micellar casein. These problems have now surprisingly been solved by the inventors by a mixture of micellar casein and caseinate. Surprisingly, the viscosity of the final composition is not increased as much as could be expected by the substitution of an amount of micellar casein by the same amount of caseinate, such that a composition is obtained with still a low viscosity, which is still very easy to drink or to administer by tubing, while at the same time no undesired Ca-acid precipitates are observed.

A liquid enteral nutritional composition consisting essentially of native micellar casein is exemplified in EP 0 686 396 Bl. The problem as described in the present application, has not been disclosed, nor the compositions with a high protein content according to the present invention are disclosed.

In a second aspect, the present invention concerns a method of providing nutrition to a person in need thereof, comprising the steps of administering to said person the nutritional composition according to the present invention.

In a third aspect, the present invention concerns the use of a mixture of micellar casein and caseinate in the manufacture of a liquid nutritional composition according to the present invention for providing nutrition to a person.

The invention will now be further elucidated by describing the preferred embodiments of the present invention.

**DETAILED DESCRIPTION OF THE INVENTION**

**Protein**

According to one embodiment of the present invention, a liquid enteral nutritional composition is provided comprising 6 to 14 g of protein per 100 ml of the composition, preferably 8 to 12 g/100 ml of the composition, more preferably at least 9 g/100 ml of the
composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml.

According to another embodiment of the present invention, the protein provides 10 % to 30 %, preferably 12 % to 20 %, more preferably 14 % to 18 %, at least 15 % of the total energy content of the composition. The % of total energy is also abbreviated as En%; En% is thus short for energy percentage and represents the relative amount that a constituent contributes to the total caloric value of the composition. In another embodiment of the present invention, the protein provides at least 16 % of the total energy content. The high levels of protein are beneficial for patients who may not be physically capable of receiving a large volume, for example, fluid restricted patients. Such patients can be given a reduced level of fluid while still receiving a required amount of nutritional support per day.

In the context of this application, the term "at least" also includes the starting point of the open range. For example, an amount of "at least 95 weight%" means any amount equal to 95 weight % or above.

In the context of this application, enteral means orally or by tube.

In one embodiment of the present invention, the composition has an energy density of at least 2.0 kcal/ml, preferably at least 2.2 kcal/ml, more preferably at least 2.3 kcal/ml, even more preferably at least 2.4 kcal/ml. Although the composition has a high energy density, it also has a sufficiently low viscosity to allow it to be consumed by persons that may have difficulty swallowing products or those that are tube fed.

In one embodiment of the present invention, the combined amount of micellar casein and caseinate in the liquid nutritional composition according to the invention is at least 85 weight%, more preferably at least 90 weight %, more preferably at least 95 weight% of the total protein present in the liquid nutritional composition.

As aforementioned, the composition of the present invention should not contain large amounts of proteins other than MCI and caseinate. In a further embodiment of the present invention, the composition may comprise up to about 15 weight% of whey, preferably less than or equal to 10 weight% of whey, more preferably, less than or equal to 5 weight% of whey of the total protein present in the liquid nutritional composition.

In one embodiment of the present invention, Na-caseinate, Mg-caseinate, K-caseinate or any mixture thereof or combinations thereof such as Na/K-caseinate and Na/Mg caseinate are used as the source of caseinate. Preferably, Ca-caseinate, or a caseinate comprising Ca is not
used, as the micellar casein already contains a sufficient amount of calcium, and the formation of further calcium crystals should be avoided.

In one embodiment of the present invention, the weight ratio of micellar casein to caseinate ranges from 90:10 to 55:45. Preferably, the weight ratio of micellar casein to caseinate is equal to 65:35.

The composition according to the invention is designed to either supplement a person's diet or to provide complete nutritional support. Hence, the composition according to the invention may further comprise at least fat and/or carbohydrate and/or a source of vitamins and minerals and/or a source of prebiotics. Preferably, the composition according to the invention is a nutritionally complete composition.

Fat

In one embodiment of the present invention, the liquid nutritional composition according to the invention further comprises fat, said fat providing between 20 to 40 % of the total energy content of the composition. For a 2.0 kcal/ml composition, this amounts to 40 to 80 kcal per 100 ml.

The fat may include medium chain triglycerides (MCT, mainly 8 to 10 carbon atoms long), long chain triglycerides (LCT) or any combination of the two types. MCTs are beneficial because they are easily absorbed and metabolized in a metabolically-stressed patient. Moreover, the use of MCTs will reduce the risk of nutrient malabsorption. LCT sources, such as canola oil, rapeseed oil, or corn oil are preferred because they can reduce immune suppression associated with certain types of fatty acids concentrated in the body.

Preferably, the fat comprises 30 to 60 weight% of animal or algal fat, 40 to 70 weight% of vegetable fat and optionally 0 to 20 weight% of MCTs based on total fat of the composition.

The animal fat preferably comprises a low amount of milk fat, i.e. lower than 6 weight%, especially lower than 3 weight%. In particular, a mixture of corn oil, egg oil, and/or canola oil and specific amounts of marine oil are used. Egg oils, fish oils and algal oils are a preferred source of non-vegetable fats. Especially for compositions that are to be consumed orally, in order to prevent formation of off-flavours and to decrease a fishy after-taste, it is recommended to select ingredients that are relatively low in docosahexanoic acid (DHA), i.e. less than 6 weight%, preferably less than 4 weight% of the fat. Marine oils containing DHA are preferably present in the composition according to the invention in an amount lower than
25 weight\%, preferably lower than 15 weight\% of the fat. On the other hand, inclusion of eicosapentanoic acid (EPA) is highly desirable for obtaining the maximum health effect. The amount of EPA ranges preferably between 4 weight\% and 15 weight\%, more preferably between 8 weight\% and 13 weight\% of the fat. The weight ratio EPA:DHA is advantageously at least 6:4, for example between 2:1 and 10:1.

Also, the liquid nutritional composition according to the invention may beneficially comprise an emulsifier. Commonly known emulsifiers may be used and generally the emulsifier contributes to the energy content of the fat in said composition.

Carbohydrate

In one embodiment of the present invention, the liquid nutritional composition according to the invention further comprises carbohydrate, said carbohydrate providing between 30 to 60 \% of the total energy content of the composition. For a 2.0 kcal/ml composition, this amounts to 80 to 120 kcal per 100 ml. Preferably, the carbohydrate provides at least 40 \% of the total energy content of the composition according to the invention.

The composition of the carbohydrate preferably is such that high viscosities, excessive sweetness, excessive browning (Maillard reactions) and excessive osmolarities are avoided. Acceptable viscosities and osmolarities may be achieved by adjusting the average chain length (average degree of polymerisation, DP) of the carbohydrates between 1.5 and 6, preferably between 1.8 and 4. In order to avoid excessive sweetness, the total level of sucrose and fructose is less than 52 \% and preferably less than 40 \% of the weight of the carbohydrate, especially of the digestible carbohydrate. Long-chain digestible carbohydrates such as starch, starch fractions and mild starch hydrolysates (DP \geq 6, DE < 20), may also be present, preferably in an amount of less than 25 weight\%, especially less than 15 weight\% of the carbohydrate, and less than 6 g/100 ml, preferably less than 4 g/100 ml of the total liquid enteral composition according to the invention.

In one embodiment of the present invention, the carbohydrate includes maltodextrinose with a high DE (dextrose equivalent). In one embodiment the carbohydrate includes maltodextrinose with a DE of \geq 20, preferably \geq 30 or even \geq 40, such as a DE of about 47. Surprisingly, the use of maltodextrinose leads to few or no Maillard reaction products upon heating. Without being bound to any explanation, this effect might be attributed to the fact that the compact micellar structure of the micellar casein offers few lysine reaction sites for a Maillard
reaction. In one embodiment of the present invention, the carbohydrate includes maltodextrine with a high DE in an amount of at least 35 weight%, preferably at least 50 weight%, preferably at least 65 weight%, preferably at least 90 weight% of the total weight of carbohydrate. In one embodiment of the present invention, the carbohydrate includes maltodextrine with a low DE of 2 to 20. In one embodiment of the present invention, the carbohydrate includes maltodextrine with a low DE of 2 to 10, preferably with a low DE of about 2. In one embodiment of the present invention, the carbohydrate includes maltodextrine with a low DE in an amount of less than 35 weight%, preferably less than 20 weight%, preferably less than 10 weight% of the carbohydrate. Maltodextrine with a low DE may also be referred to as maltodextrine. In another embodiment of the present invention, the carbohydrate includes maltodextrine with a high DE, preferably a DE of > 20, preferably > 30 or even > 40, most preferably a DE of about 47 in combination with maltodextrine with a low DE, preferably a low DE of 2 to 20, more preferably a low DE of 2 to 10, most preferably with a low DE of about 2. As is known, maltodextrine with a low DE, such as of about 2, gives rise to a high viscosity. Maltodextrine with a high DE, such as of about 47 gives rise to a low viscosity, but is very sweet. The combination of both maltodextrines optimizes the balance between sweetness and viscosity. In one embodiment of the present invention, the carbohydrate includes at least 65 weight%, preferably at least 90 weight%, based on total weight of carbohydrate of maltodextrine with a DE > 40, preferably with a DE of about 47 and 0 to 10 weight% of maltodextrine with a DE 2 to 10, preferably with a DE of about 2.

In another embodiment of the present invention, the carbohydrate includes trehalose. As was indicated, it is one of the main objects of the invention to provide a nutritional composition with a low viscosity. Sucrose is very well suited for such purpose, but gives rise to very sweet compositions, which are in general disliked by the consumer. Maltodextrine with a low DE, such as of about 2, does not suffer from the latter drawback, but gives rise to a high viscosity. Maltodextrine with a high DE, such as of about 47 gives rise to a low viscosity, but is again very sweet, and gives further rise to the undesired Maillard reactions. Trehalose is a preferred choice of carbohydrate, as it gives rise to a low viscosity, no undesired Maillard reactions and it has a sweetness about half of that of sucrose. In one embodiment of the present invention, the carbohydrate includes trehalose in an amount of 20 % to 60 % of the weight of the carbohydrate, in an amount of 20 % to 45 %, more preferably in an amount of 25 % to 45 % of the weight of the carbohydrate.
Vitamins and minerals

The composition according to the invention may contain a variety of vitamins and minerals. Overall, the composition according to the invention preferably includes at least 100% of the United States Recommended Daily Allowance (USRDA) of vitamins and minerals in a one litre portion.

In one embodiment of the present invention, the composition according to the invention provides all necessary vitamins and minerals. For example, the composition according to the invention preferably provides 6 mg of zinc per 100 ml of the composition which is beneficial for tissue repair in a healing patient. Preferably, the composition according to the invention (also) provides 25 mg of vitamin C per 100 ml of the composition to aid patients with more severe healing requirements. Further, preferably, the composition according to the invention (also) provides 2.25 mg iron per 100 ml of the composition. Iron is beneficial in maintaining bodily fluids as well as circulatory system functions in an elderly patient.

In another embodiment of the present invention, the amount of divalent ions ranges between 170 mg/100 ml and 230 mg/100 ml and preferably between 180 mg/100 ml and 220 mg/100 ml. Preferably, the amount of calcium ranges between 155 mg/100 ml and 185 mg/100 ml and preferably between 160 mg/100 ml and 180 mg/100 ml. The phosphorus content can be above 10 mg per g of protein, with a calcium to phosphorus weight ratio between 1.0 and 2.0, preferably between 1.1 and 1.7. Carnitin may advantageously be present in an amount of 8 mg/100 ml to 1000 mg/100 ml, preferably 10 mg/100 ml to 100 mg/100 ml of composition; it may have the form of carnitin, alkyl camitin, acyl carnation or mixtures thereof. Organic acids are preferably present at a level of between 0.1 g/100 ml to 0.6 g/100 ml, especially 0.25 g/100 ml to 0.5 g/100 ml. These acids include short fatty acids such as acetic acid, hydroxy acids such as lactic acid, gluconic acid, and preferably polyvalent hydroxy acids, such as malic acid and citric acid. In one embodiment of the present invention, the present composition also comprises citric acid.

Prebiotics

The liquid enteral nutritional composition according to the invention may be fortified with a prebiotic, for example, with non-digestible carbohydrates (dietary fibres), such as fructo-oligosaccharides or inulin. In an embodiment of the present invention, the composition according to the invention comprises 0.5 g/100 ml to 6 g/100 ml of non-digestible
carbohydrates. The dietary fibres include non-digestible oligosaccharides having a DP of 2 to 20, preferably 2 to 10. More preferably, these oligosaccharides do not contain substantial amounts (less than 5 weight%) of saccharides outside these DP ranges, and they are soluble. These oligosaccharides may comprise fructo-oligosaccharides (FOS), trans-galacto-oligosaccharides (TOS), xylo-oligosaccharides (XOS), soy oligosaccharides, and the like. Optionally, also higher molecular weight compounds such as inulin, cellulose, resistant starch and the like may be incorporated in the composition according to the invention. The amount of insoluble fibre such as cellulose is preferably lower than 20 weight% of the dietary fibre fraction of the composition according to the invention, and/or below 0.4 g/100 ml. The amount of thickening polysaccharides such as carrageenans, xanthans, pectins, galactomannans and other high molecular weight (DP > 50) indigestible polysaccharides is preferably low, i.e. less than 20% of the weight of the fibre fraction, or less than 1 g/100 ml. Instead, hydrolysed polysaccharides such as hydrolysed pectins and galactomannans can advantageously be included.

A preferred fibre component is an indigestible oligosaccharide with a chain length (DP) of 2 to 10, for example Fibersol® (resistant oligoglucose), in particular hydrogenated Fibersol®, or a mixture of oligosaccharides having a DP of 2 to 10, such as fructo-oligosaccharides or galacto-oligosaccharides, which may also contain a small amount of higher saccharides (e.g. with a DP of 11 to 20). Such oligosaccharides preferably comprise 50 weight% to 90 weight% of the fibre fraction, or 0.5 g/100 ml to 3 g/100 ml of the composition according to the invention. Other suitable fibre components include saccharides that have only partial digestibility.

Viscosity and osmolality

In one embodiment of the present invention, the viscosity of the liquid enteral nutritional composition is lower than 50 mPa.s at 20 °C at a shear rate of 100 s⁻¹, preferably between 20 and 45 mPa.s. The viscosity may be determined using a rotational viscosity meter using a cone/plate geometry. In a further embodiment of the present invention, the protein consists of a blend of micellar casein and caseinate in a ratio of 65:35. The latter embodiment of the present invention has a viscosity of approximately about 40 mPa.s. This is ideal for orally administering the liquid enteral nutritional composition according to the invention because a person may easily consume a serving having a low viscosity such as that displayed by the present invention. This is also ideal for unit dosages that are tube fed.
In one embodiment of the present invention, the osmolality of the composition is preferably lower than 900 mOsm/l, more preferably lower than 800 mOsm/l, most preferably lower than 700 mOsm/l.

In one embodiment of the present invention, the density of the composition ranges between 1.05 g/ml and 1.20 g/ml, especially between 1.10 g/ml and 1.18 g/ml.

**Dosage unit**

The liquid enteral nutritional composition according to the invention may have the form of a complete food, i.e. it can meet all nutritional needs of the user. As such, it preferably contains 1200 to 2500 kcal per daily dosage. The daily dosage amounts are given with respect to a daily energy supply of 2000 kcal to a healthy adult having a body weight of 70 kg. For persons of different condition and different body weight, the levels should be adapted accordingly. It is understood that the average daily energy intake preferably is about 2000 kcal. The complete food can be in the form of multiple dosage units, e.g. from 4 (250 ml/unit) to 20 (50 ml/unit) per day for an energy supply of 2000 kcal/day using a liquid enteral nutritional composition according to the invention of 2.0 kcal/ml.

The liquid enteral nutritional composition can also be a food supplement, for example to be used in addition to a non-medical food. Preferably as a supplement, the liquid enteral nutritional composition contains per daily dosage less than 1500 kcal, in particular as a supplement, the liquid enteral nutritional composition contains 400 to 1000 kcal per daily dose. The food supplement can be in the form of multiple dosage units, e.g. from 2 (250 ml/unit) to 10 (50 ml/unit) per day for an energy supply of 1000 kcal/day using a liquid enteral nutritional composition according to the invention of 2.0 kcal/ml.

In one embodiment of the present invention, a unit dosage comprises any amount of the liquid enteral nutritional composition according to the invention between 10 ml and 250 ml, the end values of this range included, preferably any amount between 25 ml and 200 ml, the end values of this range included, more preferably any amount between 50 ml and 150 ml, the end values of this range included, most preferably about 125 ml. For example, a person receiving 50 ml unit dosages can be given 10 unit dosages per day to provide nutritional support using a liquid enteral nutritional composition according to the invention of 2.0 kcal/ml. Alternatively a person receiving 125 ml unit dosages can be given 4 or 5 or 6 or 7 or 8 unit dosages per day.
to provide nutritional support using a liquid enteral nutritional composition according to the invention of 2.0 kcal/ml. Such small dosage units are preferred because of better compliance.

In one embodiment of the present invention, the composition is provided in a ready to use liquid form and does not require reconstitution or mixing prior to use. The composition according to the invention can be tube fed or administered orally. For example, the composition according to the invention can be provided in a can, on spike, and hang bag. However, a composition may be provided to a person in need thereof in powder form, suitable for reconstitution using an aqueous solution or water such that the composition according to the invention is produced. Thus in one embodiment of the present invention, the present composition is in the form of a powder, accompanied with instructions to dissolve or reconstitute in an aqueous composition or water to arrive at the liquid nutritional enteral composition according to the present invention. In one embodiment of the present invention, the present liquid nutritional enteral composition may thus be obtained by dissolving or reconstituting a powder, preferably in an aqueous composition, in particular water.

In one embodiment of the present invention, the composition according to the invention is packaged. The packaging may have any suitable form, for example a block-shaped carton, e.g. to be emptied with a straw; a carton or plastic beaker with removable cover; a small-sized bottle for example for the 80 ml to 200 ml range, and small cups for example for the 10 ml to 30 ml range. Another suitable packaging mode is inclusion of small volumes of liquid (e.g. 10 ml to 20 ml) in edible solid or semi-solid hulls or capsules, for example gelatine-like coverings and the like. Another suitable packaging mode is a powder in a container, e.g. a sachet, preferably with instructions to dissolve or reconstitute in an aqueous composition or water.

**Preparation**

The liquid enteral nutritional composition according to the invention may be prepared by first preparing the liquid protein composition. This may be done by sequentially or simultaneously dissolving micellar casein in powder form and caseinate in powder form in water. It is also possible to use micellar casein in a wet form, directly prepared from milk. It may even be advantageous to prepare the micellar casein as a part of a continuous process to prepare the composition according to the invention. The latter may be done in the same production facility to prepare the composition according to the invention.
Furthermore, if the liquid enteral nutritional composition is to contain further components, a nutritional product may be prepared by subsequently adding the carbohydrates to the protein composition, followed by adding the water-soluble vitamins and other components in one or two stages, mixing, adjusting the resulting composition to the desired viscosity, adding the fat, including fat-soluble vitamins, homogenizing, subjecting the resulting solution to a heat-treatment (pasteurization, sterilisation) and packaging the resulting product. In this respect, it is noted that the acidity of the composition is very important during the heat-treatment. The pH should be between about 6.6 and 7.2 for the pasteurisation and sterilisation. Typical pasteurisation times are 30 sec at 85 °C. Typical sterilisation times are 4 minutes at 124 °C.

Effectivity

The present invention also concerns a method of providing nutrition to a person in need thereof, comprising the steps of administering to said person the nutritional composition according to the present invention. Said person may be an elderly person, a person that is in a disease state, a person that is recovering from a disease state, or a person that is malnourished.

In a further aspect, the present invention also concerns the simultaneous or sequential use of micellar casein and caseinate in the manufacture of a liquid nutritional composition according to the present invention for providing enteral nutrition to a person in need thereof. In one particular embodiment of the present invention, said composition provides 6 to 14 g of protein per 100 ml of composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml. In another particular embodiment of the present invention, said protein provides 10 % to 30 % of the total energy content of the composition, the composition having an energy density of at least 2.0 kcal/ml.

In one embodiment, the present invention concerns a liquid enteral nutritional composition comprising:

a) about 9.6 g of protein per 100 ml of the composition of a mixture of micellar casein and caseinate with a weight ratio of about 65:35, said protein providing about 16 % of the total energy content of the composition;

b) fat providing about 35 % of the total energy content of the composition;

c) carbohydrate providing about 49 % of the total energy content of the composition, said composition having an energy density of about 2.4 kcal/ml.
EXAMPLES

The following composition according to the invention has been prepared (Table 1). The composition is produced in a manner known per se, e.g. by mixing the ingredients, without difficulties, is shelf-stable, has desirable organoleptic properties, has a very high nutrient density and is effective for a person in need thereof.

Table 1

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount per 100 ml of product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>240 kcal</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>16.0 En%</td>
</tr>
<tr>
<td>MCI : Na-caseinate (wt/wt)</td>
<td>9.6 g (about 6.3 g MCI)</td>
</tr>
<tr>
<td></td>
<td>65:35</td>
</tr>
<tr>
<td>Fat</td>
<td>35 En%</td>
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<tr>
<td>Fat mainly comprising canola oil</td>
<td>9.3 g</td>
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<td>Carbohydrates</td>
<td>49 En%</td>
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<tr>
<td>maltodextrase (DE47)</td>
<td>29.4 g</td>
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<tr>
<td>Minerals</td>
<td>16 % of RDI</td>
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<tr>
<td>Vitamins</td>
<td>16 % of RDI</td>
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<tr>
<td>Viscosity</td>
<td>40 to 45 (mPa.s at 20 °C at 100 s⁻¹)</td>
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<tr>
<td>Density</td>
<td>1.16 g/ml</td>
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<tr>
<td>Unit dosage</td>
<td>125 ml</td>
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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 may be made without departing from the spirit and scope of the invention and without diminishing its advantages. It is therefore intended that such changes and modifications are covered by the appended claims.
Claims

1. Liquid enteral nutritional composition comprising 6 to 14 g of protein per 100 ml of the composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml.

2. Liquid enteral nutritional composition comprising protein, said protein providing 10 % to 30 % of the total energy content of the composition, said protein including micellar casein and caseinate, the composition having an energy density of at least 2.0 kcal/ml.

3. Liquid enteral nutritional composition according to any one of claims 1 to 2, wherein the composition has an energy density of at least 2.4 kcal/ml.

4. Liquid enteral nutritional composition according to any one of claims 1 to 3, wherein the combined amount of micellar casein and caseinate is at least 95 weight% of the total protein.

5. Liquid enteral nutritional composition according to any one of claims 1 to 4, further comprising whey.

6. Liquid enteral nutritional composition according to any one of claims 1 to 5, wherein the caseinate is Na-caseinate, Mg-caseinate, K-caseinate or any mixture or combination thereof.

7. Liquid enteral nutritional composition according to any one of claims 1 to 6, wherein the weight ratio of micellar casein to caseinate ranges from 90:10 to 55:45.

8. Liquid enteral nutritional composition according to any one of claims 1 to 7, further comprising fat, said fat providing between 20 to 40 % of the total energy content of the composition.

9. Liquid enteral nutritional composition according to any one of claims 1 to 8, wherein the fat comprises long chain triglycerides.

10. Liquid enteral nutritional composition according to any one of claims 1 to 9, further comprising carbohydrate, said carbohydrate providing between 30 to 60 % of the total energy content of the composition.
11. Liquid enteral nutritional composition according to any one of claims 1 to 10, wherein the carbohydrate includes maltodextrine with a high DE of > 30, preferably with a high DE of about 47.

12. Liquid enteral nutritional composition according to any one of claims 1 to 11, wherein the carbohydrate includes maltodextrine with a low DE of 2 to 10, preferably with a low DE of about 2.

13. Liquid enteral nutritional composition according to any one of claims 1 to 10, wherein the carbohydrate includes trehalose.

14. Liquid enteral nutritional composition according to any one of claims 1 to 13, wherein the viscosity of the composition is lower than 50 mPa.s.

15. Liquid enteral nutritional composition according to any one of claims 1 to 14, wherein the viscosity of the composition is lower than 800 mOsm/1.

16. Liquid enteral nutritional composition according to any one of claims 1 to 15, wherein the unit dosage is about 125 ml.

17. Liquid enteral nutritional composition according to any one of claims 1 to 16, obtained by dissolving or reconstituting a powder.

18. Liquid enteral nutritional composition comprising:

   a) about 9.6 g of protein per 100 ml of the composition of a mixture of micellar casein and caseinate with a weight ratio of about 65:35, said protein providing about 16% of the total energy content of the composition;

   b) fat providing about 35% of the total energy content of the composition;

   c) carbohydrate providing about 49% of the total energy content of the composition, said composition having an energy density of about 2.4 kcal/ml.

19. A method of providing nutrition to a person in need thereof, comprising the steps of administering to said person the nutritional composition according to any one of claims 1 to 18.

20. The method according to claim 19, wherein the person is an elderly person, a person that is in a disease state, a person that is recovering from a disease state, or a person that is malnourished.
21. Simultaneous or sequential use of micellar casein and caseinate in the manufacture of a
liquid nutritional composition according to any one of claims 1 to 18.

* * * * *
**INTERNATIONAL SEARCH REPORT**

**International application No**
PCT/NL2007/050626

**A. CLASSIFICATION OF SUBJECT MATTER**

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According to International Patent Classification (IPC) or to both national classification and IPC.

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched.

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, FSTA, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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**Date of the actual completion of the international search**

26 September 2008

**Date of mailing of the international search report**

29/10/2008

**Name and mailing address of the ISA/ European Patent Office P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040 Fax (+31-70) 340-3016**

Stiegler, Petra

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## INTERNATIONAL SEARCH REPORT

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