



(51) International Patent Classification:

A61K 31/202 (2006.01) **A61K 47/02** (2006.01)
A61K 47/10 (2017.01) **A61K 47/12** (2006.01)
A61K 47/54 (2017.01) **A61K 47/14** (2017.01)
A61P 3/06 (2006.01) **A61K 47/24** (2006.01)
A61P 9/10 (2006.01) **A61K 47/26** (2006.01)
A61P 29/00 (2006.01) **A61K 9/00** (2006.01)
A61K 9/10 (2006.01)

EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(21) International Application Number:

PCT/EP2020/078716

(22) International Filing Date:

13 October 2020 (13.10.2020)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

19203420.5 15 October 2019 (15.10.2019) EP

(71) Applicant: **HERMES ARZNEIMITTEL GMBH**
[DE/DE]; Georg-Kalb-Str. 5-8, 82049 Pullach (DE).

(72) Inventors: **WEISS, Gerd**; c/o GW PharmaConsult Schlotthauerstrasse 16, 81541 München (DE). **GARSUCH, Verena**; c/o Hermes Arzneimittel GmbH Georg-Kalb-Str. 5-8, 82049 Pullach (DE). **SCHIEMENZ, Wolfgang**; c/o Hermes Arzneimittel GmbH Georg-Kalb-Str. 5-8, 82049 Pullach (DE).

(74) Agent: **PHARMA PATENTS INTERNATIONAL AG**; Leonhardsgraben 52, 4051 Basel (CH).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,

(54) Title: LIQUID OMEGA-3 FATTY ACID COMPOSITIONS FOR DIRECT ORAL ADMINISTRATION

(57) Abstract: The invention provides a substantially water-free liquid composition for direct oral administration of omega 3 fatty acids which can be easily swallowed without e.g. added liquids, yet provides a pleasant smell, taste and mouthfeel; as well as good stability. The composition comprises a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids and an omega-3 fatty acid composition which comprises at least about 80 wt.-% omega-3 fatty acid esters in a weight ratio ranging between about 1 : 1 and about 10 : 1; a thickening agent, and at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers, aroma, and optionally a gel stabilizer.

TITLE: **LIQUID OMEGA-3 FATTY ACID COMPOSITIONS FOR DIRECT ORAL ADMINISTRATION**

Description

BACKGROUND OF THE INVENTION

5 Omega-3 fatty acids (also referred to as ω -3 fatty acids or *n*-3 fatty acids) are poly-unsaturated fatty acids exhibiting a plurality of C = C double bonds, at least one of them being positioned three atoms from the terminal methyl group of the fatty acid chemical structure. Examples of omega-3 fatty acids include α -linolenic acid (ALA), eicosapentaenoic acid (EPA; C₂₀, 5 double bonds) and docosahexaenoic acid (DHA; C₂₂,
10 6 double bonds); the latter two found mostly in fish oils krill oil, or algal oils. In nature, omega-3 fatty acids occur in two forms, triglycerides and phospholipids; however, semisynthetic products such as methyl esters or ethyl esters of the omega-3 fatty acids are commercially available, too; for instance, 'omega-3-acid ethyl esters 90' (K85EE) by BASF/Pronova Biocare. The latter is, inter alia, marketed in soft gelatin capsules under
15 the tradename Omacor® or Lovaza™ for the treatment of hypertriglyceridemia and/or post-myocardial infarction.

Omega-3 fatty acids play an important role in the human diet and are known to provide a number of health benefits; for instance, reducing blood triglyceride levels, lowering blood pressure; lowering inflammation levels, alleviating certain circulatory problems by
20 stimulating the blood circulation, and assumingly aiding in learning and cognitive development. Therefore, omega-3 fatty acids, and in particular fish oils containing these fatty acids, are commercially available in a variety of 'omega-3 enriched' food products; for instance, as parenteral nutrition formulations as well as other pharmaceutical or nutraceutical products.

25 The main disadvantage with omega-3 fatty acids is their sensitivity to oxidation and their rather characteristic, often disagreeable, 'fishy' odor and taste; the latter an issue which increases upon progressing oxidization. Poor taste and/or odor ultimately often lead to decreasing compliance of the consumer, or patient. One approach is to provide the omega-3 fatty acids in (soft) capsule form to a) prevent, or limit, oxidation, and
30 b) to mask the odor and/or taste. However, quite a number of consumers, or patients, experience difficulties with swallowing capsules or tablet formulations, including elderly people, children, or people suffering from xerostomia (dry mouth due to hyposalivation)

or general phobias around swallowing 'foreign' objects. The issue of swallowability is partially overcome by the provision of drinkable compositions, such as the water-beased, fish oil containing drinking liquids described in US2016/0316810A1 or US20130078362A1.

- 5 Another issue is that rather large amounts need to be taken, or ingested, for the omega-3 fatty acids to be effective; with studies suggesting a daily dose of about 4 g omega-3 fatty acids. While the semisynthetic products, such as the above-mentioned commercially available 'omega-3-acid ethyl esters 90' (K85EE), partially address this issue insofar as they are typically more concentrated and highly enriched with the
- 10 desirable omega-3 fatty acids, the high daily doses are still only achieved by ingesting a multitude of capsules per day (e.g. 2-4 Omacor® capsules). Such frequent dosing is not only challenging for consumers, or patients, struggling with the swallowing of solid dosage forms such as capsules; it is also highly inconvenient in that it requires access to, for instance, clean drinking water 2-4 times a day in order to swallow the capsules.
- 15 Alternatively, with products such as those described in US2016/0316810A1 or US20130078362A1, one would need to consume rather large volumes (>650 mL) in order to administer 2 g omega-3 fatty acids, double the volume for 4 g. This is neither safe for patients on a fluid restricted diet (e.g. due to kidney diseases), nor is it convenient for other patients, or consumers, looking for an easy-to-administer alternative, optionally for
- 20 'on-the-go' purposes, that should be both light-weight (i.e. small volume), and preferably compliant with airtravel safety regulations (e.g. max. 100 mL).

- Products such as 'NORSAN Omega-3 KIDS Jelly' address the swallowability issue for children by providing a chewable, gummi bear-like soft-gel composition comprising water, gelatin, 250 mg omega-3 fatty acids from natural cod fish oil, lecithin as an
- 25 emulsifier, strawberry-lemon aroma, xylitol and sorbitol as sucrose-free sweeteners, and malic acid as an antioxidant.

- Similarly, US9452150B2 suggests jelly compositions as an alternative to the conventional capsule products, the jelly compositions containing water, an organic gelling agent, an emulsifying agent, emulsified polyunsaturated fatty acids in an amount greater than
- 30 10 wt.-% in order to decrease the amount of a single dose unit of the composition. The jelly compositions of US9452150B2 are manufactured by adding an appropriate amount of a specific gelling agent (preferably, carrageenan and/or locust bean gum) to an oil-in-

water emulsion prepared by the addition of a suitable amount of a specific emulsifying agent to a polyunsaturated fatty acid, preferably, eicosapentaenoic acid ethyl esters (EPA-EE) and/or docosahexanoic acid ethyl esters (DHA-EE). However, the compositions proposed in US9452150B2 are rather complex; for instance, they require the addition of not only water and an emulsifier to ensure sufficiently rapid release of the fatty acids from the jelly, but also a syneresis inhibitor (e.g. carmellose sodium and pullulan) to ensure stability and prevent syneresis of water from the jelly during storage. Moreover, the use of water in the prior art emulsified compositions may be detrimental to their microbial stability.

In addition, unlike natural fishoils, which comprise the omega-3 fatty acids in their triglyceride form (i.e. tri-esters of the fatty acids with glycerol) at a content of only about 20 %, most of the semi-synthetic products, such as the above-mentioned 'omega-3-acid ethyl esters 90' (K85EE), are enriched to comprise the desirable omega-3 fatty acids at contents well above 60 wt.-% or more; and while this is desirable in terms of reducing the volume of a single dose to be administered, it also renders the higher concentrated products more sensitive to oxidation and more 'chemical' in taste and smell than natural fish-oils, making the development of compositions without a capsule shell-type tastemasking, yet palatable to humans, particularly challenging.

This illustrates that there is still a need for improved compositions for direct oral administration which can be easily swallowed without e.g. added liquids, yet providing a pleasant smell, taste and mouthfeel; as well as good stability. It is thus an object of the present invention to provide such compositions, in particular, liquid compositions for direct oral administration which are storage-stable, exhibit a high content of omega-3 fatty acids and a pleasant taste and smell. Further objects of the invention will be clear on the basis of the following description of the invention, examples and claims.

SUMMARY OF THE INVENTION

In a first aspect, the invention relates to a liquid composition for direct oral administration, the composition comprising:

- (a) a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids,
- (b) an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid esters, based on the weight of the

omega-3 fatty acid composition, and wherein the weight ratio of the C₂-C₄ polyol ester under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,

(c) a thickening agent, and

- 5 (d) at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

10 In a second aspect, the present invention relates to a process for the preparation of the liquid composition according to the first aspect of the invention, the process comprising the steps of:

- Providing a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids; a thickening agent; at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma; and an omega-3 fatty acid
15 composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition; and
- Combining the components provided, such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and
20 about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In a third aspect, the invention relates to the liquid composition according to the first aspect of the invention for use in the treatment and/or prevention of rheumatoid arthritis, hypertriglyceridemia, and/or post-myocardial infarction.

25 DEFINITIONS

The following terms or expressions as used herein should normally be interpreted as outlined in this section, unless explicitly defined otherwise by the description or unless the specific context clearly indicates or requires otherwise.

30 All technical terms as used herein shall be understood to have the same meaning as is commonly understood by a person skilled in the relevant technical field.

The words 'comprise', 'comprises' and 'comprising' and similar expressions are to be construed in an open and inclusive sense, as 'including, but not limited to' in this description and in the claims.

The singular forms 'a', 'an' and 'the' should be understood as to include plural referents.

5 In other words, all references to singular characteristics or limitations of the present disclosure shall include the corresponding plural characteristic or limitation, and vice versa. The terms 'a' 'an' and 'the' hence have the same meaning as 'at least one' or as 'one or more'. For example, reference to 'an ingredient' includes mixtures of ingredients, and the like.

10 The expressions, 'one embodiment', 'an embodiment', 'a specific embodiment' and the like mean that a particular feature, property or characteristic, or a particular group, or combination, of features, properties or characteristics, as referred to in combination with the respective expression, is present in at least one of the embodiments of the invention. These expressions, occurring in various places throughout this description, do not
15 necessarily refer to the same embodiment. Moreover, the particular features, properties or characteristics may be combined in any suitable manner in one or more embodiments.

The terms 'substantially consisting of' or 'essentially consisting of' mean that no further components are added to a composition or dosage form other than those listed.

Nevertheless, very small amounts of other materials may potentially be present, such as
20 material-inherent impurities. Furthermore, when referring to e.g. 'essentially consisting of A, B, C and optionally D' this means that no further components are added to a composition or dosage form other than A, B, C and D, with D being an optional component (i.e. not mandatory) in said composition or dosage form.

All percentages, parts and/or ratios in the context of numbers should be understood as
25 relative to the total number of the respective items. Furthermore, all percentages parts and/or ratios are intended to be by weight of the total weight; i.e. '%' should be read as 'wt.-%'.

The term 'substantially free of X' means that the respective material (e.g. a chemical compound or a composition) contains less than a functional amount of the optional
30 ingredient X, typically less than 5 wt.-%, or less than 1 wt.-%, preferably less than 0.1 wt.-% or even less than 0.01 wt.-%, and also including 0 wt.-% of the respective ingredient X. The expression refers, *inter alia*, to very small amounts of the respective

ingredient X, such as material-inherent impurities or residual moisture, which may potentially be present in (raw) materials despite the aim to render a material completely free of them. For example, 'substantially free of water' means that no water is deliberately included in a material but does not exclude the presence of residual moisture.

The term 'synthetic drug substance' shall be understood as referring to substances, namely active pharmaceutical ingredient (APIs) which are administered, e.g. ingested, so as to cause an intentional therapeutic effect (i.e. an intentional change in a subject's physiology or, in some cases, psychology), and which are commonly produced or obtained by chemical synthesis. In other words, 'synthetic drug substances', as understood herein, typically do not occur naturally. Furthermore, synthetic drug substances are commonly understood as being distinguished from, for instance, food, dietary supplements, and other substances that provide nutritional support; such as vitamins, minerals, or the omega-3 fatty acids of the present invention. Examples of synthetic drug substances which are not incorporated into the liquid compositions for direct oral administration according of the present invention include statins such as pravastatin, or other HMG-CoA reductase inhibitors (i.e. inhibitors of the cholesterol synthesizing enzyme CSE); cholesterol absorption inhibitors like ezetimibe; 'fibrates' such as fenofibrate or gemfibrozil; nicotinic acid and its derivatives; ion exchange resins such as colestyramine.

The term 'pharmaceutically acceptable' means that a material is useful in preparing a pharmaceutical or nutraceutical composition that is generally safe, non-toxic and exhibits neither biologically nor otherwise undesirable properties which would prevent, or exclude, it from pharmaceutical or nutraceutical use in humans.

Terms such as 'about', 'approximately', 'ca.', 'essentially', 'substantially' are meant to compensate for the variability allowed for in the pharmaceutical industry and inherent in pharmaceutical or nutraceutical products, such as differences in content due to manufacturing variation and/or time-induced product degradation. The terms in connection with an attribute or value include the exact attribute or the precise value, as well as any attribute or value typically considered to fall within a normal range or variability accepted in the technical field concerned.

The term 'room temperature' shall be understood as ranging from 15 °C to 25 °C, as is for instance defined by the European Pharmacopoeia or by the WHO guidance 'Guidelines for the Storage of Essential Medicines and Other Health Commodities' (2003).

5 The terms 'direct oral administration' or 'direct oral composition' refer to compositions that are intended to be administered directly from a container (e.g. a bottle, vial, sachet, ampoule, or the like) into the mouth and/or onto the tongue of the consumer, and swallowed easily – typically with no or at best moderate chewing – and with an agreeable taste and/or smell, without the need for further additions of, *inter alia*, further excipients or comestibles (e.g. fluids such as water, juice, semi-solids such as yoghurt or pudding, or
10 the 'spoonful of sugar'). In other words, the compositions are taken directly 'as is' and, thus, get in direct contact with the taste-buds of the tongue. It is not necessary – though, of course, allowable – to e.g. drink or eat something to 'wash' the composition down and 'cleanse' the tongue. Compositions for direct oral administration are often intended to be administrable when the consumer is 'on the go' and/or in areas of restricted access to
15 clean drinking water. For this purpose, direct oral compositions are often packaged and provided in single dose units. For the avoidance of doubt, while theoretically some consumers are capable of ingesting even conventional tablets or capsules without water (e.g. by simply chewing them and forcing them down just dispersed in saliva), this does not render conventional tablets 'direct oral compositions' in the sense of the present
20 invention. Likewise, the mere fact that most omega-3 oils derived from fish, krill, or algae, or prior art capsule-fills of omega-3 fatty acids (such as the above-mentioned K85EE) are inherently liquids, and hence could – in theory – be ingested 'as is', too, also does not render them 'direct oral compositions', or suitable for direct oral administration, in the sense of the present invention, since their taste and smell is experienced as being too
25 'fishy' or too 'smelly' for the majority of people, especially if, after swallowing the 'raw' oil or capsule fill, the mouth and palate cannot be rinsed or otherwise cleaned from the residual oil film.

The term 'sugar', as used herein, refers to water-soluble, sweet-tasting carbohydrates, in particular to monosaccharides, disaccharides, oligosaccharides and polysaccharides.

30 Solubility provisions as used herein, such as 'slightly soluble', shall be understood as aqueous solubilities at room temperature (15-25 °C) as determined and ranked according to pharmacopoeial standards (e.g. European Pharmacopoeia, Ph.Eur.):

| | Approximate volume of solvent per 1 g of solute |
|-----------------------|---|
| Very soluble | < 1 mL |
| Freely soluble | 1-10 mL |
| Soluble | 10-30 mL |
| Sparingly soluble | 30-100 mL |
| Slightly soluble | 100-1000 mL |
| Very slightly soluble | 1000-10000 mL |
| Practically insoluble | > 10000 mL |

Any reference signs in claims should not be construed as a limitation to the embodiments represented in any of the drawings.

DETAILED DESCRIPTION OF THE INVENTION

- 5 In a first aspect, the invention relates to a liquid composition for direct oral administration, the composition comprising:
- (a) a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids,
 - (b) an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid esters, based on the weight of the
 - 10 omega-3 fatty acid composition, and wherein the weight ratio of the C₂-C₄ polyol ester under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, and
 - (d) at least one flavor additive selected from the group consisting of sugars, sugar
 - 15 alcohols, sweeteners, acidifiers and aroma;
- wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

For reasons of brevity and simplification, the expressions 'C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids' and 'the omega-3 fatty acid composition

20 comprising at least about 80 wt.-% omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition' will herein commonly be referred to shortly as 'the

C₂-C₄ polyol ester' and as 'the omega-3 fatty acid composition', respectively. According to the present invention, the two components, the C₂-C₄ polyol ester and the omega-3 fatty acid composition, are miscible with each other.

It should be understood that, given the low water content (and preferably being substantially free of water), the liquid composition according to the first aspect of the invention is clearly not an emulsion product, and thus is not comparable with, nor identical to, for instance, prior art emulsion products comprising omega-3 fatty acids and/or C₆-C₁₂ medium chain fatty acids for parenteral, intraperitoneal, or endotracheal administration. Such products would typically not be consumed orally and hence do not have to address palatability issues. And even though some emulsion products exist which may be intended for direct oral consumption (e.g. in the form a nutritional drinking liquid), the water content of said drinkable emulsions is usually pretty high (often 70 wt.-% or higher) so that the taste of the omega-3 fatty acid composition in the thus highly diluted system is far less noticeable, and less of a formulation challenge.

In addition, administering a daily recommended dose of 2-4 g omega-3 fatty acids is inconvenient and requires consumption of rather large volumes (typically over 500 mL) when using products with a water content over 60 wt.-% or higher.

Furthermore, unlike so-called 'pre-concentrates', or self(micro)emulsifying delivery systems, the liquid composition according to the first aspect of the invention predominantly represents an alternative delivery means to e.g. soft capsules filled with an omega-3 fatty acid composition (or similar solid, or semi-solid, dosage forms that require either to be swallowed 'as is', or the preparation of drinkable liquid therefrom after the addition of water or other comestibles); and more specifically, an alternative delivery means that allows for palatable, direct oral administration as defined herein, while not aiming to change the overall bioavailability of said omega-3 fatty acid composition.

In one embodiment, the C₂-C₄ polyol of said C₂-C₄ polyol ester, i.e. its 'backbone', is selected from propylene glycol, glycerol, and/or butylene glycol. In a further embodiment, the C₂-C₄ polyol ester is selected from mono- and/or di-esters of propylene glycol, mono-, di- and/or tri-esters of glycerol, and/or mono- and/or di-esters of butylene glycol.

In one embodiment, the one or more C₆-C₁₂ medium chain fatty acids of the C₂-C₄ polyol ester may be of plant origin. In one embodiment, the one or more C₆-C₁₂ medium chain fatty acids are aliphatic fatty acids. In one embodiment, the one or more C₆-C₁₂ medium chain fatty acids are saturated fatty acids. In one embodiment, the one or more

5 C₆-C₁₂ medium chain fatty acids are aliphatic, saturated fatty acids (including e.g. hexanoic acid (C₆), caprylic acid (C₈), capric acid (C₁₀) and lauric acid (C₁₂)). In a further embodiment, the C₂-C₄ polyol ester comprises aliphatic, saturated fatty acid chains with 8 to 12 carbon atoms, or it comprises aliphatic, saturated fatty acid chains with 8 to 10 carbon atoms. In a yet further embodiment, the C₂-C₄ polyol ester comprises
10 aliphatic, saturated fatty acid chains of plant origin with 8 to 12, or 8 to 10, carbon atoms.

In one embodiment, the C₂-C₄ polyol ester comprises not more than 2 wt.-% of either long chain fatty acids with more than 12 carbon atoms, or short chain fatty acids with less than 6 carbon atoms. In a further embodiment, the C₂-C₄ polyol ester comprises not more than 2 wt.-% of short chain fatty acids with less than 6 carbon atoms. In a yet further
15 embodiment, the C₂-C₄ polyol ester comprises not more than 2 wt.-% of long chain fatty acids with more than 12 carbon atoms, and not more than 2 wt.-% of short chain fatty acids with less than 6 carbon atoms.

In one embodiment, the liquid composition comprises a mixture of two or more C₂-C₄ polyol esters, preferably C₂-C₄ polyol esters which are miscible with each other.

20 In one embodiment, the C₂-C₄ polyol ester exhibits a mean viscosity of from about 2 mPas to about 50 mPas as measured by capillary viscosimetry at a temperature of 20 ± 0.1 °C; or from about 5 mPas to about 40 mPas; or from about 25 mPas to about 35 mPas. As used herein, the term capillary viscosimetry refers to the method as described in the European Pharmacopoeia (Ph.Eur.) monograph "2.2.9. Capillary Viscometer Method".

25 In a further embodiment, at least one, optionally all, of the C₂-C₄ polyol ester in a mixture of two or more C₂-C₄ polyol esters exhibits a mean viscosity of from about 2 mPas to about 50 mPas as measured by capillary viscosimetry at a temperature of 20 ± 0.1 °C; or from about 5 mPas to about 40 mPas; or from about 25 mPas to about 35 mPas.

In a yet further embodiment, the mixture of two or more C₂-C₄ polyol esters exhibits a
30 mean viscosity of from about 2 mPas to about 50 mPas as measured by capillary viscosimetry at a temperature of 20 ± 0.1 °C; or from about 5 mPas to about 40 mPas; or from about 25 mPas to about 35 mPas.

In a specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT), or in other words a triester of glycerol; for instance, a triglyceride with saturated C₈ to C₁₂ fatty acids, or a triglyceride with saturated C₈ to C₁₀ fatty acids; e.g. caprylic acid (C₈), capric acid (C₁₀) and lauric acid (C₁₂). Advantageously, these MCTs exhibit a neutral odor and taste, as well as a favourable mean viscosity of from about 25 mPas to about 35 mPas as measured by capillary viscosimetry at a temperature of 20 ± 0.1 °C. Due to the very low amounts of water in MCTs (typically ≤ 0.1 wt.-%), they also contain almost no microorganisms, and hence exhibit good microbial stability. Furthermore, most commercially available MCT-grades are free of additives such as catalyst residues or antioxidants. Examples of commercially available MCTs suitable for the present invention include Miglyol® 812 or Miglyol® 810, which are triglycerides comprising fractionated plant-derived C₈ and C₁₀ fatty acids, with Miglyol® 810 having a higher C₁₀-content compared to Miglyol® 812.

In an alternative embodiment - or in a mixture with the above-mentioned MCTs - the C₂-C₄ polyol ester is a monoglyceride, or in other words a monoester of glycerol; for instance, a monoglyceride with saturated C₈ to C₁₂ fatty acids, or a monoglyceride with saturated C₈ to C₁₀ fatty acids; e.g. caprylic acid (C₈), capric acid (C₁₀) and lauric acid (C₁₂). Examples of commercially available monoglycerides suitable for the present invention include Capmul® MCM (glyceryl monocaprylocaprate) and Capmul® MCM C8 (glyceryl monocaprylate).

In a further alternative embodiment - or in a mixture with the above-mentioned MCTs and/or monoglycerides - the C₂-C₄ polyol ester is a mono- and/or di-ester of propylene glycol or butylene glycol; for instance, a diester of propylene glycol or butylene glycol with saturated C₈ to C₁₀ fatty acids (e.g. caprylic acid (C₈) and capric acid (C₁₀)), or a monoester of propylene glycol with saturated C₈ to C₁₂ fatty acids (e.g. caprylic acid (C₈), capric acid (C₁₀) and lauric acid (C₁₂)). Examples of commercially available mono- and/or di-esters of propylene glycol or butylene glycol suitable for the present invention include Miglyol® 840 (propylene glycol dicaprylate/dicaprate), Miglyol® 8810 (butylene glycol dicaprylate/ dicaprate), Capmul® PG-8 (propylene glycol monocaprylate) and Capmul® PG-12 (propylene glycol monolaurate).

These above-mentioned, exemplary Miglyol® or Capmul®-grades, and in particular Miglyol® 810 or 812, are suitable for all embodiments of the liquid composition according to the first aspect described herein.

The Miglyol® grades 812, 810, 840 and/or 8810 are favoured over other commercially available Miglyol® grades (such as Miglyol® 818 or 829) for the present invention. Unlike the first-named grades, Miglyol® 818 and Miglyol® 829 comprise more than 2 wt.-% of long chain fatty acids with more than 12 carbon atoms and more than 2 wt.-% of short chain fatty acids with less than 6 carbon atoms, respectively; in particular, Miglyol® 818 comprises about 5 wt.-% of linoleic acid (C₁₈), and Miglyol® 829 is combined with succinic acid (C₄). The presence of unsaturated linoleic acid is less favoured in that it is particularly sensitive to oxidation, thus, requiring the addition of an antioxidant to the Miglyol® 818 grade. The addition of succinic acid is less favoured in that it increases the mean viscosity of the Miglyol® 829 grade to about 230 mPas at 20 °C, and would thus likely render the liquid composition too viscous to flow.

In one embodiment, the omega-3 fatty acid composition comprises at least about 90 wt.-% omega-3 fatty acid esters, based on the weight of the fatty acid composition. In a further embodiment, the omega-3 fatty acid composition comprises at least about 80 wt.-%, or at least about 90 wt.-%, esters of eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), based on the weight of the fatty acid composition. In a yet further embodiment, the omega-3 fatty acid composition comprises from about 40 wt.-% to about 60 wt.-% esters of eicosapentaenoic acid (EPA) and from about 25 wt.-% to about 50 wt.-% esters of docosahexanoic acid (DHA), based on the weight of the omega-3 fatty acid composition. In a specific embodiment, the omega-3 fatty acid composition comprises from about 43 wt.-% to about 50 wt.-% esters of eicosapentaenoic acid (EPA), and from about 34 wt.-% to about 41 wt.-% esters of docosahexanoic acid (DHA), based on the weight of the omega-3 fatty acid composition.

In one embodiment, the esters of the omega-3 fatty acid composition are selected from alkyl esters, preferably from ethyl esters or methyl esters; for instance, eicosapentaenoic acid ethyl esters (EPA-EE) and/or docosahexanoic acid ethyl esters (DHA-EE). In a specific embodiment, the omega-3 fatty acid composition comprises from about 43 wt.-% to about 50 wt.-% eicosapentaenoic acid ethyl ester (EPA-EE), and from about 34 wt.-%

to about 41 wt.-% docosahexanoic acid ethyl ester (DHA-EE), based on the weight of the omega-3 fatty acid composition.

In an alternative embodiment, or in addition to these weight-percentages, the weight ratio of the eicosapentaenoic acid ethyl ester (EPA-EE) and the docosahexanoic acid ethyl ester (DHA-EE) in the omega-3 fatty acid composition ranges between about 1 : 1 and about 1.5 : 1, or between about 1.1 : 1 and about 1.4 : 1, or between about 1.2 : 1 and about 1.3 : 1. One example of a commercially available omega-3 fatty acid composition suitable for the present invention according to the first aspect of the invention includes 'omega-3-acid ethyl esters 90', also called K85EE (BASF/Pronova Biocare), which is also available in soft gelatin capsules (e.g. marketed under the tradename Omacor® or Lovaza™). This exemplary omega-3 fatty acid composition (K85EE) is suitable for all embodiments described herein, and its EPA-EE to DHA-EE weight ratio is 1.26 : 1.

As mentioned above, unlike natural fishoils, which comprise the omega-3 fatty acids in their triglyceride form at a content of only about 20 %, the omega-3 fatty acid compositions according to the invention – and, in particular, compositions such as 'omega-3-acid ethyl esters 90' (K85EE) – are semi-synthetic products which are highly enriched with the desirable omega-3 fatty acids. While desirable in terms of e.g. reducing the volume of a single dose unit, this also renders these omega-3 fatty acid compositions more sensitive to oxidation and more 'chemical' in taste and smell than natural fish-oils. It is, thus, far harder to prepare them in the form of liquid compositions for direct oral administration which are taken without further additions, or dilutions and get in direct contact with the tongue and its taste buds.

In one embodiment, the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 5 : 1, or between about 1 : 1 and about 2 : 1, or between about 1.15 : 1 and about 1.85 : 1, or between about 1.3 : 1 and about 1.7 : 1. In a specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT), such as the above-mentioned Miglyol® 810/812; and the weight ratio of the medium chain triglyceride (MCT) and the omega-3 fatty acid composition ranges between about 1 : 1 and about 5 : 1, or between about 1 : 1 and about 2 : 1, or between about 1.15 : 1 and about 1.85 : 1, or between about 1.3 : 1 and about 1.7 : 1.

Blending the C₂-C₄ polyol ester - and in particular, a medium chain triglyceride such as Miglyol® 810 or 812 - and the omega-3 fatty acid composition in these ratios, yields

a liquid composition which offers excellent stability against oxidation, which is flowable enough to allow for easy and sufficient emptying, or discharging, of the liquid composition from its container into the mouth, or onto the tongue, of a consumer, or patient, and which provides a pleasant, favorable taste and mouthfeel (not too viscous, sticky or gooey). For instance, in one embodiment, the liquid composition exhibits a viscosity which allows to empty out at least 85 wt.-%, preferably at least 90 wt.-%, more preferably at least 93 wt.-% of the liquid composition from its primary packaging within about 5 to 10 seconds after

i) briefly shaking the closed primary packaging manually (about 2 to 10 times);

10 ii) removing the lid, or otherwise opening the primary packaging;

iii) placing, or holding, it at a pouring angle of about 45° for about 10 seconds; and

iv) lightly tapping the still upward-facing bottom end of the primary packaging with a fingertip after the about 10 seconds. In other words, the liquid composition exhibits a viscosity such that after this simple test - which resembles the steps and provisions a

15 user would typically undertake, or be instructed to undertake, in order to drink the liquid composition – less than 15 wt.-%, preferably less than 10 wt.-%, more preferably less than 7 wt.-% of the liquid composition remain in the primary packaging. The primary packaging in this test may, for instance, a vial or bottle made from glass or polyethylene terephthalate (PET), optionally equipped with a crimp neck or with a threaded neck.

20 Furthermore, the liquid composition provides stable suspensions of any of the suspended particles comprised therein (e.g. the at least one flavor additive or parts thereof) when blending the C₂-C₄ polyol ester - and in particular, a medium chain triglyceride such as Miglyol® 810 or 812 - and the omega-3 fatty acid composition in these ratios. This facilitates ease of application by the consumer or patient as well as during primary

25 packaging processes; for instance, by favourable redispersion characteristics: any suspended particles comprised in the liquid composition according to the first aspect of the invention were found to either not sediment at all, or to be redispersable quickly by simply shaking the bottle, vial or other primary packaging in which the liquid composition is provided.

30 In addition, blending in these ratios the poorly tasting and smelling omega-3 fatty acid composition with the more C₂-C₄ polyol ester – and, in particular, with a medium chain triglyceride such as Miglyol® 810 or 812 – of neutral taste and smell also yields an initial

reduction in the 'fishy' smell and/or taste of the resulting blend, though, not enough to render it palatable enough for most human consumers, yet.

In one embodiment, the liquid composition comprises at least about 40 wt.-% of the C₂-C₄ polyol ester based on the total weight of the liquid composition; or at least
5 about 45 wt.-%; or at least about 48 wt.-%. In a specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as the above-mentioned Miglyol® 810/812), and the liquid composition comprises at least about 40 wt.-% of the medium chain triglyceride (MCT), based on the total weight of the liquid composition; or at least about 45 wt.-%; or at least about 48 wt.-%.

10 In one embodiment, the liquid composition comprises at least about 20 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 25 wt.-%; or at least about 28 wt.-%. In a specific embodiment, the omega-3 fatty acid composition is one which comprises from about 43 wt.-% to about 50 wt.-% eicosapentaenoic acid ethyl ester (EPA-EE), and from about 34 wt.-% to about 41 wt.-%
15 docosahexanoic acid ethyl ester (DHA-EE), based on the weight of the omega-3 fatty acid composition (such as the above-mentioned 'omega-3-acid ethyl esters 90'; K85EE), and the liquid composition comprises at least about 20 wt.-% of said omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 25 wt.-%; or at least about 28 wt.-%.

20 In one embodiment, the liquid composition comprises at least about 40 wt.-% of the C₂-C₄ polyol ester and at least about 20 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 48 wt.-% of the C₂-C₄ polyol ester and at least about 28 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition.

25 In a specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as the above-mentioned Miglyol® 810/812), and the liquid composition comprises at least about 40 wt.-% of the medium chain triglyceride (MCT) and at least about 20 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 48 wt.-% of the medium chain triglyceride (MCT) and at
30 least about 28 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition. In a further specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as the above-mentioned Miglyol® 810/812) and

the omega-3 fatty acid composition is one which comprises from about 43 wt.-% to about 50 wt.-% eicosapentaenoic acid ethyl ester (EPA-EE), and from about 34 wt.-% to about 41 wt.-% docosahexanoic acid ethyl ester (DHA-EE), based on the weight of the omega-3 fatty acid composition (such as the above-mentioned 'omega-3-acid ethyl esters 90'; K85EE); and the liquid composition comprises at least about 40 wt.-% of the medium chain triglyceride (MCT) and at least about 20 wt.-% of said omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 48 wt.-% of the medium chain triglyceride (MCT) and at least about 28 wt.-% of said omega-3 fatty acid composition based on the total weight of the liquid composition.

- 10 In one embodiment, the thickening agent comprised in the liquid composition according to the first aspect of the invention is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with at least the C₂-C₄ polyol ester. In a further embodiment, the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with a mixture of the C₂-C₄ polyol ester and the omega-3 fatty acid composition. In a specific
- 15 embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as such as the above-mentioned Miglyol® 810/812), and the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with at least the medium chain triglyceride (MCT). In a further specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as such as the above-mentioned Miglyol® 810/812), and
- 20 the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with a mixture of the medium chain triglyceride (MCT) and the omega-3 fatty acid composition. In a yet further specific embodiment, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT; such as the above-mentioned Miglyol® 810/812) and the
- 25 omega-3 fatty acid composition is one which comprises from about 43 wt.-% to about 50 wt.-% eicosapentaenoic acid ethyl ester (EPA-EE), and from about 34 wt.-% to about 41 wt.-% docosahexanoic acid ethyl ester (DHA-EE), based on the weight of the omega-3 fatty acid composition (such as the above-mentioned 'omega-3-acid ethyl esters 90'; K85EE); and the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with the mixture of the medium chain triglyceride (MCT) and said
- 30 omega-3 fatty acid composition.

In one embodiment, the thickening agent comprised in the liquid composition is an anorganic oleo-gel forming component. In a specific embodiment, the thickening agent is an anorganic oleo-gel forming component selected from the group consisting of fumed

silica, precipitated silica, aluminum silicates, bentonite, and mixtures thereof. In a further specific embodiment, the thickening agent is fumed silica or precipitated silica. In a yet further specific embodiment, the thickening agent is a hydrophilic fumed silica exhibiting a specific surface area in the range of 50 - 500 m²/g, or in the range of 200 - 300 m²/g; or
5 a hydrophobic fumed silica treated with dimethyldichlorosilane (DDS). Examples of commercially available fumed silica grades suitable for the present invention include Aerosil® 200, Aerosil® 300, Aerosil® 380, and Aerosil® R972.

In one embodiment, the liquid composition comprises from about 0.1 wt.-% to about 5.0 wt.-% of the thickening agent, based on the total weight of the liquid composition;
10 or from about 0.4 wt.-% to about 4.0 wt.-%; or from about 0.7 wt.-% to about 4.0 wt.-%; or from about 0.9 wt.-% to about 3.5 wt.-%; or from about 0.9 wt.-% to about 3.0 wt.-%; for instance, about 0.9 wt.-% or about 1.8 wt.-% or about 2.7 wt.-%. In a specific embodiment, the liquid composition comprises from about 1.5 wt.-% to about 3.5 wt.-% of a hydrophilic fumed silica exhibiting a specific surface area in the range of 50 - 500 m²/g,
15 or in the range of 200 - 300 m²/g; or of a hydrophobic fumed silica treated with dimethyldichlorosilane (DDS) based on the total weight of the liquid composition. In a more specific embodiment, the liquid composition comprises from about 1.5 wt.-% to about 3.5 wt.-% of a hydrophilic fumed silica exhibiting a specific surface area in the range of 200 - 300 m²/g, based on the total weight of the liquid composition.

20 Anorganic oleo-gel forming components such as fumed or precipitated silicas, aluminum silicates or bentonite - in particular in the above-mentioned amounts - were found to be most suitable for the present invention, yielding an optimized increase in viscosity and thixotropic gel-formation in the liquid composition which comprises not more than 5 wt.-% of water; - in particular, when employing anorganic oleo gel forming components
25 in the above-mentioned amounts, and/or when blending the C₂-C₄ polyol ester (e.g. Miglyol® 810 or 812) and the omega-3 fatty acid composition in the above-mentioned ratios. This yields a liquid composition which offers excellent stability against oxidation, is flowable enough to allow for easy and sufficient emptying, or discharging, from a container into the mouth, or onto the tongue, of a consumer, or patient, while
30 avoiding spills or reducing the risks for spills; and which furthermore provides a pleasant, favorable taste and mouthfeel (not too viscous, sticky or goeey).

For instance, in one embodiment, the liquid composition exhibits a viscosity which allows to empty out at least 85 wt.-%, preferably at least 90 wt.-%, more preferably at least 93 wt.-% of the liquid composition from its primary packaging within about 5 to 10 seconds after

- 5 i) briefly shaking the close primary packaging manually (about 2 to 10 times);
ii) removing the lid, or otherwise opening the primary packaging;
iii) placing, or holding, it at a pouring angle of about 45° for about 10 seconds; and
iv) lightly tapping the still upward-facing bottom end of the primary packaging with a fingertip after the about 10 seconds. In other words, the liquid composition exhibits
10 a viscosity such that after this simple test - which resembles the steps and provisions a user would typically undertake, or be instructed to undertake, in order to drink the liquid composition - less than 15 wt.-%, preferably less than 10 wt.-%, more preferably less than 7 wt.-% of the liquid composition remain in the primary packaging. The primary packaging in this test may, for instance, a vial or bottle made from glass or polyethylene
15 terephthalate (PET), optionally equipped with a crimp neck or with a threaded neck.

The thixotropic properties are in particular useful in that they allow for a shear-thinning (i.e. a reduced viscosity) of the liquid composition during manufacturing steps, primary packaging processes and/or during application by the consumer, while at the same time stabilizing any suspended particles comprised therein, such as the at least one flavor
20 additive, or parts thereof, during storage. Like this, an optimum balance is obtained for the flow properties of the liquid composition, which facilitates mixing and filling steps during manufacture, as well as easy emptying from the container during consumption, while at the same time keeping the composition viscous enough to prevent undesirable
25 spilling during minor mishaps upon opening the container (e.g. holding a vial at a slightly 'off' angle, squeezing a stickpack at a wrong position, etc.), as well as providing favourable redispersion characteristics. For instance, any suspended particles comprised in the liquid composition were found to either not sediment at all, or to be quickly redispersible by simply shaking the bottle or vial in which the liquid composition is provided manually a few times prior to open the lid.

30 Furthermore, the viscosity- and thixotropy properties obtained using these anorganic oleo-gel forming components, and in particular using fumed silica or precipitated silica, were found to be favourable compared to those achieved with other common gel forming polymers, commonly organic gel forming polymers, which have been used in prior art

omega-3 containing liquid formulations, such as cellulose ethers, pectins, alginates, caseinates, chitosan, psyllium, gum arabic, or other natural gums like guar, konjac/glucomanuan, gellan, tragacanth, karaya, acacia, xanthan, carrageenan or locust bean gum. It is believed that the latter gel-forming polymers are too hydrophilic to get sufficiently solubilized in the lipophilic liquid composition of the first aspect of the invention with not more than 5 wt.-% of water; and thus would not be capable to establish a gel network in the lipophilic composition and/or would require long, inefficient incorporation times for sufficient solubilisation and swelling of the more hydrophilic gel forming components; thereby increasing processing times. Hence, in one embodiment, the liquid composition is substantially free of organic gel forming components.

According to the invention, the liquid composition comprises at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma. It should be understood, that as used herein, the term flavor additive is used broadly and encompasses both taste- and/or smell optimizing additives; in other words, the liquid composition comprises at least one taste- and/or smell optimizing additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma. The addition of one or more flavor additives is deemed necessary to provide an acceptable, preferably even a good, taste and/or smell to the liquid composition. While preferences vary, it is believed, that without such additives, the pure omega-3 fatty acid composition, or even the diluted mixture of said omega-3 fatty acid composition with the C₂-C₄ polyol ester, would taste and/or smell rather poorly; this may lead to compliance issues, with subjects not taking their supplements, or medication, as advised.

In case, a plurality of such additives is selected from said group, the expression 'flavor additive' refers to the entirety of the selected additives, especially where referring to their content in the liquid composition. Hence, unless a content is explicitly provided for a specific flavor additive, any contents provided refer to the total of all flavor additives. In one embodiment, the liquid composition comprises at least about 10 wt.-% of the flavor additive based on the total weight of the liquid composition; or at least about 15 wt.-%; or at least about 16 wt.-%; or at least about 17 wt.-%. In a specific embodiment, the liquid composition comprises about 17 wt.-%, or about 18 wt.-%, of the flavor additive based on the total weight of the liquid composition.

In one embodiment, at least parts of the flavor additive is present in solid, particulate form and suspended in the liquid composition according to the first aspect of the invention. In this regard, the expression 'at least parts of' refers both to quantitative fractions of a single component that may be present in solid, particulate form, and to the qualitative components (e.g. a sugar comprised in the flavor additive being suspended while the aroma component gets solubilized in the liquid composition).

As mentioned above, flavor additives are deemed necessary in order to provide an acceptable, preferably even a good, palatable taste and/or smell to the liquid composition; and especially additives for improved taste typically need to be water-soluble in order to dissolve in the mouth and/or on the tongue and, thus, allow for proper taste perception. However, since the liquid composition according to the first aspect of the invention comprises not more than 5 wt.-% of water, preferably less, most of these water-soluble flavor additives are considered poorly soluble in the liquid composition (i.e. sparingly soluble or even less soluble), and are thus, at least in parts, present in solid, particulate form. This renders the liquid composition according to the first aspect of the invention a suspension. In a specific embodiment, at least about 50 wt.-% of the flavor additive is present in solid, particulate form and suspended in the liquid composition; or at least about 60 wt.-%; or at least about 70 wt.-%; or at least about 80 wt.-%.

During storage, the suspended parts of the at least one flavor additive are either held in suspended state within the "resting" gel structure; or – depending on their particle size and particle density - they may sediment to the bottom of the container. In the latter case, and due to the thixotropic gel structure formed throughout the liquid composition, they can easily be re-dispersed by agitation of the container (e.g. shaking of a vial, or squeezing of a foil-lined sachet, or stickpack) right before consumption, leading to a temporary shear-thinning of the liquid composition. However, agitation of the container right before consumption is considered useful irrespective of whether or not a sediment of the at least one flavor additive forms in the container during storage, since the shear-thinning of the liquid composition allows for a more complete emptying of the container, and thus more accurate dosing.

In one embodiment, the flavor additive comprised in the liquid composition according to the first aspect of the invention comprises a sugar or sugar alcohol. In a specific embodiment, the flavor additive comprises a sugar or sugar alcohol selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof. In a more specific embodiment, the flavor additive comprises sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof; preferably xylitol. The inventors found, that xylitol, sorbitol and isomaltitol are particularly suited because they do not only provide a sweet taste to the liquid composition but also offer a cooling effect which is perceived as fresh and more pleasant in taste, and thus is advantageous for addition to the omega-3 fatty acid composition, or the liquid composition comprising it, because it counteracts the somewhat 'fishy', or 'chemical', taste notes of the omega-3 fatty acid composition. In one the preferred embodiments, the flavor additive comprises xylitol. To the best of the inventors' knowledge, this focus on flavor additives with a cooling effect, such as xylitol, has not been reported before for pharmaceutical or nutraceutical liquid compositions of omega-3 fatty acids, let alone discussed as a means to provide a composition of omega-3 fatty acids that allows for direct oral administration as defined herein.

In one embodiment, the flavor additive comprises a sweetener. In a specific embodiment, the flavor additive comprises a sweetener selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof. In a more specific embodiment, the flavor additive comprises aspartame.

In one embodiment, the flavor additive comprises an aroma; for instance, natural, semi-synthetic and synthetic aromas, such as cherry, orange, citrus, mandarin, lime, strawberry, tropic, or mint aroma etc.. Aroma is mostly added to provide a specific taste and/or smell to the liquid composition beyond the mere 'sweet'/'sour' achieved by the addition of sugars, sugar alcohols, sweeteners and acidifiers; typically, a smell and/or taste of a component which is not actually present in the liquid composition. For instance, the aroma may be one with a taste and/or smell resembling cherries (i.e. a cherry aroma) without actual cherry pulp or cherry juice being present in the liquid composition. The aroma may be used alone or in combination; e.g. as a combination of cherry and spearmint aroma, orange and mandarin, or a combination of cherry aroma, peppermint menthol and limonen (preferably (R)-(+)-limonen for its citrusy taste and flavor.

In a specific embodiment, the flavor additive comprises an aroma that is volatile; e.g. a liquid peppermint aroma comprising menthol, a liquid orange aroma, or the like. The term volatile aroma, as used herein, predominantly refers to liquid aroma because liquid aroma typically contain a higher fraction of volatile compounds than solid aroma (the latter often employed more for their taste than their smell). Therefore liquid aroma are more easily perceptible by the nose of a consumer, e.g. upon opening a vial filled with the liquid composition according to the first aspect. The inventors have found that using volatile aromas, and more specifically liquid, volatile aromas, is advantageous for the present invention, in particular for containers which comprise the liquid composition and a gas-filled headspace (e.g. air, or inert gases such as nitrogen or argon). In such containers, the volatile aroma diffuses into the headspace with the highly beneficial effect that the liquid composition according to the first aspect of the invention does not smell poorly, e.g. 'fishy', to the consumer upon opening the container and upon pouring its contents into the mouth. And even while moving the liquid composition around in the mouth, the volatile aroma continues to diffuse into the gas-filled headspace withing the consumer's mouth, so that any air moved towards the nasal cavities by breathing does not smell 'fishy', or otherwise disagreeable, while the consumer has the liquid compositions, or residues thereof, in the mouth and on the tongue. Further advantageously, some of the volatile aroma, such as the above mentioned peppermint menthol even have a beneficial cooling effect of their own, and may thus intensify, or as the case may be replace, the cooling effect of flavor additives such as xylitol.

Liquid compositions according to the first aspect of the invention comprising a volatile aroma were found to significantly improve taste and smell, and in consequence consumer acceptance. In addition, also the volatile aroma as such is believed to function much alike an inert gas in the gas-filled headspace of e.g. vials or bottles filled with the liquid composition; thereby acting as yet a further means to prevent, or at least limit, oxidation. To the best of the inventors' knowledge, this preference of volatile flavor additives in particular has not been reported before for pharmaceutical or nutraceutical liquid compositions of omega-3 fatty acids, let alone discussed as a means to provide a composition of omega-3 fatty acids that allows for direct oral administration as defined herein.

In one embodiment, the flavor additive in the liquid composition comprises an acidifier. In a specific embodiment, the flavor additive comprises an acidifier selected from the group of organic acids, the respective salts thereof, and mixtures thereof. In a more specific embodiment, the flavor additive comprises an acidifier in the form of an organic acid selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof. In a further specific embodiment, the flavor additive comprises citric acid and/or salts thereof. In a yet further specific embodiment, the flavor additive comprises monosodium citrate. In a yet further specific embodiment, the flavor additive comprises a mixture of citric acid and monosodium citrate, a mixture which is believed to achieve an appropriate acidity both quickly (by the citric acid) and maintaining it for some period of time (by the more slowly dissolving monosodium salt). Again, to the best of the inventors' knowledge, this favorable effect of selecting both slow and fast dissolving acidifiers has not been reported before for pharmaceutical or nutraceutical liquid compositions of omega-3 fatty acids, let alone discussed as a means to provide a composition of omega-3 fatty acids that allows for direct oral administration as defined herein.

In one specific embodiment, the flavor additive in the liquid composition comprises a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, and aspartame; preferably xylitol and aspartame. In a further embodiment, the flavor additive in the liquid composition comprises a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, and citric acid and/or salts thereof; preferably xylitol and citric acid and/or salts thereof. According to one of the preferred embodiments, the flavor additive in the liquid composition comprises a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, and aspartame, and citric acid and/or salts thereof; preferably xylitol, aspartame, and citric acid and/or salts thereof, and optionally at a content of at least about 15 wt.-% (e.g. 17 wt.-%, or about 18 wt.-%) of the flavor additive based on the total weight of the liquid composition. This combination has been described as one of the most pleasantly and least 'fishy' tasting ones amongst those tested by the panelists. In a yet further specific embodiment, the flavor additive in the liquid composition comprises a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, and aspartame, citric acid and/or salts thereof, and a volatile aroma; preferably xylitol, aspartame, citric acid and/or salts thereof, and a volatile aroma, and optionally at a content of at least about 15 wt.-% (e.g. 17 wt.-%, or about 18 wt.-%) of the

flavor additive based on the total weight of the liquid composition. As described above, the addition of a volatile aroma is perceived as particularly agreeable because not only does the liquid composition taste good, it also smells good, upon opening the primary packaging, and emptying its contents into the mouth. Exemplary embodiments

5 comprising the above-described flavor additives are provided in the examples below.

In one embodiment, the liquid composition according to the first aspect of the invention further comprises at least one antioxidant; for instance, an antioxidant selected from lecithin, ascorbic acid or derivatives thereof (e.g. fatty acid esters of ascorbic acid, or sodium erythorbate), tocopherol or derivatives thereof, tertiary butylhydroquinone
10 (TBHQ), carotenoid derivatives, hydroxytoluene, propyl gallate, glycine, rosmarinic acid, or mixtures thereof. In a further embodiment, the liquid composition according to the first aspect of the invention comprises at least two antioxidants; for instance, two antioxidants selected from the exemplified group. In a yet further embodiment, the at least one antioxidant in the liquid composition is provided in the form of an antioxidant
15 complex comprising lecithin and a fatty acid ester of ascorbic acid. In a yet further embodiment, the fatty acid ester of ascorbic acid in said antioxidant complex is selected from ascorbyl stearate, ascorbyl palmitate, or mixtures thereof. According to one of the preferred embodiments, the weight ratio of lecithin and ascorbyl palmitate in the antioxidant complex ranges between about 3 : 1 and about 1 : 1, or between about 2.8 : 1
20 and about 1.2 : 1, or between about 2.7 : 1 and about 1.3 : 1. Both soy lecithin (such as Lipoid® P45 or P20) and sunflower lecithin (such as Lipoid® H20) were found to be suitable for the present invention; yet, lecithin from further sources may also be used.

The addition of lecithin to the antioxidant complex comprising a fatty acid ester of ascorbic acid, e.g. ascorbyl palmitate, was found to be advantageous to sufficiently
25 disperse the oily, viscous fatty acid ester within the liquid composition and thus ensure most efficient stabilization with low amounts of the antioxidant complex. Furthermore, the lecithin serves as a 'wetting agent' of the solid, suspended components of the flavor additive, or parts thereof. In other words, the addition of lecithin to the liquid composition according to the first aspect of the invention does not serve the purpose of
30 rendering the whole liquid composition as such water-dispersible, or enabling its homogeneous emulsification into water or other aqueous media, such as the gastric fluid upon oral administration. In fact, when attempting to disperse the liquid composition described herein into water at room temperature, and stirring briefly with a spoon

(as a consumer may inadvertently do, for instance, when not realizing that the liquid composition is intended for direct oral administration; i.e. without addition of water, or other comestibles), the liquid composition does not form an emulsion, or micro-emulsion, but instead separates into at least two different phases visible to the naked eye, either
5 floating on the water surface, sedimenting to the beaker bottom, and/or forming large oil-droplets, or 'oil puddles', depending on intensely the system is stirred. The inventors believe that the oils (omega-3 and e.g. MCT) partially sediment due their thickened texture in which the heavier flavor additive particles, such as xylitol, get enclosed and thus cause a fraction of the oils to get 'weighed down' in water.

10 This 'non-emulsifying' effect of the liquid composition according to the first aspect of the invention is intentional in so far as said liquid composition predominantly represents a delivery means which is an alternative to e.g. soft capsules filled with an omega-3 fatty acid composition, that allows for palatable, direct oral administration while not aiming to change the overall bioavailability of the omega-3 fatty acid composition.

15 In at least one of these aspects (water-dispersability, or emulsifiability, and bioavailability improvements), if not both, the liquid composition according to the first aspect of the invention clearly differs from various prior art compositions in the form of so-called pre-concentrates or self-(micro)emulsifying delivery systems which often exhibit a considerable amount of surfactants and optionally co-surfactants; typically at least
20 about 5 wt.-% or more (and e.g. up to 35 wt.-% or even 50 wt.-%) of (co)surfactants based on the total weight of the pre-concentrate composition. In contrast, the liquid composition according to the first aspect of the invention contains far less emulsifiers, or surface-active substances, such as the lecithin which may form part of the antioxidant complex.

25 For instance, in one embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% lecithin, or up to about 0.8 wt.-% lecithin, or up to about 0.5 wt.-% lecithin. In a specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% lecithin based on the total weight of the liquid composition, from about 0.05 wt.-% to about 0.80 wt.-%, or from
30 about 0.10 wt.-% to about 0.50 wt.-%; for instance, about 0.32 wt.-% lecithin, or about 0.20 wt.-% lecithin.

In one embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% ascorbylpalmitate, or up to about 0.6 wt.-% ascorbylpalmitate, or up to about 0.3 wt.-% ascorbylpalmitate. In a specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-%

5 ascorbylpalmitate based on the total weight of the liquid composition, from about 0.03 wt.-% to about 0.60 wt.-%, from about 0.06 wt.-% to about 0.30 wt.-%; for instance, about 0.24 wt.-% ascorbylpalmitate, or about 0.08 wt.-% ascorbylpalmitate.

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% lecithin and up to about 1 wt.-%

10 ascorbylpalmitate, based on the total weight of the liquid composition; or up to about 0.80 wt.-% lecithin and up to about 0.60 wt.-% ascorbylpalmitate; or up to about 0.50 wt.-% lecithin and up to about 0.30 wt.-% ascorbylpalmitate.

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises from about 0.01 wt.-% to about 1 wt.-% lecithin and from

15 about 0.01 wt.-% to about 1 wt.-% ascorbylpalmitate, based on the total weight of the liquid composition; or from about 0.05 wt.-% to about 0.80 wt.-% lecithin and from about 0.03 wt.-% to about 0.60 wt.-% ascorbylpalmitate; or from about 0.10 wt.-% to about 0.50 wt.-% lecithin and from about 0.06 wt.-% to about 0.30 wt.-% ascorbylpalmitate.

20 In one of the further preferred embodiments, the liquid composition according to the first aspect of the invention comprises about 0.32 wt.-% lecithin and about 0.24 wt.-% ascorbylpalmitate, based on the total weight of the liquid composition. In a specific embodiment, this equals about 0.40 wt.-% lecithin and about 0.30 wt.-% ascorbylpalmitate, based on the weight of the flavor additive-free liquid composition
25 (i.e. without the flavor additive(s)).

In another further preferred embodiment, the liquid composition comprises about 0.20 wt.-% lecithin and about 0.08 wt.-% ascorbylpalmitate, based on the total weight of the liquid composition. In a specific embodiment, this equals about 0.25 wt.-% lecithin and about 0.10 wt.-% ascorbylpalmitate, based on the weight of the

30 flavor additive-free liquid composition (i.e. without the flavor additive(s)).

In one embodiment, the antioxidant complex in the liquid composition according to the first aspect of the invention further comprises a tocopherol selected from alpha tocopherol, beta tocopherol, gamma tocopherol, or delta tocopherol. In a specific embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% tocopherol, or up to about 0.3 wt.-% tocopherol, or up to about 0.2 wt.-% tocopherol. In a more specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% tocopherol based on the total weight of the liquid composition, from about 0.01 wt.-% to about 0.30 wt.-%, from about 0.08 wt.-% to about 0.20 wt.-%; for instance, about 0.12 wt.-% tocopherol, or about 0.13 wt.-% tocopherol.

In a yet more specific embodiment, the tocopherol is comprised in, or an integral part of, the omega-3 fatty acid composition under item (b) of the liquid composition according to the first aspect of the invention; for instance, a commercially available omega-3 fatty acid composition. In other words, the tocopherol is then added to the liquid composition upon addition of said tocopherol-containing omega-3 fatty acid composition, rather than being a separately added antioxidant. One example of a commercially available omega-3 fatty acid composition comprising such an inherent tocopherol addition, which is suitable for the present invention, includes 'omega-3-acid ethyl esters 90', also called K85EE (BASF/Pronova Biocare).

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% lecithin, up to about 1 wt.-% ascorbylpalmitate, and up to about 1 wt.-% tocopherol, based on the total weight of the liquid composition; or up to about 0.80 wt.-% lecithin, up to about 0.60 wt.-% ascorbylpalmitate, and up to about 0.30 wt.-% tocopherol; or up to about 0.50 wt.-% lecithin, up to about 0.30 wt.-% ascorbylpalmitate and up to about 0.20 wt.-% tocopherol.

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises from about 0.01 wt.-% to about 1 wt.-% lecithin, from about 0.01 wt.-% to about 1 wt.-% ascorbylpalmitate and from about 0.01 wt.-% to about 1 wt.-% tocopherol, based on the total weight of the liquid composition; or from about 0.05 wt.-% to about 0.80 wt.-% lecithin, from about 0.03 wt.-% to about 0.60 wt.-% ascorbylpalmitate and from about 0.01 wt.-% to about 0.30 wt.-% tocopherol; or from

about 0.10 wt.-% to about 0.50 wt.-% lecithin, from about 0.06 wt.-% to about 0.30 wt.-% ascorbylpalmitate and from about 0.08 wt.-% to about 0.20 wt.-% tocopherol.

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises about 0.32 wt.-% lecithin, about 0.24 wt.-% ascorbylpalmitate and about 0.12 wt.-% tocopherol, based on the total weight of the liquid composition.

In one of the further preferred embodiments, the liquid composition according to the first aspect of the invention comprises about 0.20 wt.-% lecithin, about 0.08 wt.-% ascorbylpalmitate, and about 0.12 wt.-% tocopherol, based on the total weight of the liquid composition.

The triple combination of fatty acid esters of ascorbic acid (e.g. ascorbylpalmitate), lecithin and tocopherol has been found to be particularly advantageous for the present invention in terms of stabilizing the liquid composition against oxidation. This is, of course, advantageous in terms of shelf-life, and in so far as it is known that the taste and/or smell of omega-3 fatty acid containing compositions typically deteriorates, or worsens, as a result of oxidation. However, this is not to say that the inventive task of providing an alternative delivery means to e.g. soft capsules filled with an omega-3 fatty acid composition as described herein (more specifically, the task of providing an alternative delivery means that allows for palatable, direct oral administration as defined herein, while not aiming to change the overall bioavailability of said omega-3 fatty acid composition) can only be solved in the presence of antioxidants, or only in the presence of the specifically combination(s) of lecithin, ascorbylpalmitate and/or tocopherol.

The adjustment of consistency, taste and/or smell of the omega-3 fatty acid composition, or the liquid composition comprising it, so as to render it palatable and pleasant for consumers or patients, is mainly the result of the careful selection of the thickening agent(s), the flavor additive(s), and of the carriers such as the C₂-C₄ polyol ester(s), as well as their respective amounts and ratios to each other and to the omega-3 fatty acid composition. Antioxidants, or the antioxidant complex, mainly help to maintain this taste/smell adjusting effect upon storage, so that excipients such as said thickening agent(s), flavor additive(s), and carriers can be employed in the smallest amounts required, and thereby keeping the volume of a single-dose unit to a minimum.

In one embodiment, the liquid composition according to the first aspect of the invention further comprises a gel stabilizer selected from the group of polyhydroxylated compounds, said polyhydroxylated compounds serving as hydrogen bond donors. In a specific embodiment, the gel stabilizer comprises a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof. In a further specific embodiment, the gel stabilizer comprises the gel stabilizer comprises a polysorbate. In a yet further specific embodiment the gel stabilizer is polysorbate 80.

Some of these substances, used herein as gel stabilizer, are also known or used as emulsifiers or surfactants in other applications. However, as mentioned before for lecithin, the addition of these gel stabilizers (e.g. polysorbates) to the liquid composition according to the first aspect of the invention also does not serve the purpose of rendering the whole liquid composition as such water-dispersible, or enabling its homogeneous emulsification into water or other aqueous media. The liquid composition according to the first aspect of the invention contains far less emulsifiers, or surface-active substances (e.g. lecithin, and optional gel stabilizers such as polysorbates) than commonly used in prior art pre-concentrates, and in particular self-(micro)emulsifying pre-concentrates.

For instance, in one embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-%, or up to about 0.3 wt.-%, of the gel stabilizer, e.g. polysorbate 80, based on the total weight of the liquid composition.

In a specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% of the gel stabilizer, or from about 0.05 wt.-% to about 0.3 wt.-% of the gel stabilizer, based on the total weight of the liquid composition. In a specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% polysorbate 80, or from about 0.05 wt.-% to about 0.3 wt.-% polysorbate 80, based on the total weight of the liquid composition.

In a further embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-%, or up to about 0.3 wt.-%, of the gel stabilizer, e.g. polysorbate 80, based on the weight of the mixture of the C₂-C₄ polyol ester and the omega-3 fatty acid composition (e.g. a mixture of an MCT such as Miglyol® 812 and K85EE). In a specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% of the gel stabilizer, or from about 0.05 wt.-% to about

0.3 wt.-% of the gel stabilizer, based on the weight of the mixture of the C₂-C₄ polyol ester and the omega-3 fatty acid composition (e.g. a mixture of an MCT such as Miglyol® 812 and K85EE). In a further specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% polysorbate 80, or from about 0.05 wt.-% to about 0.3 wt.-% polysorbate 80 based on the weight of the mixture of the C₂-C₄ polyol ester and the omega-3 fatty acid composition.

It was found by the inventors that small additions of such gel stabilizers promote the gel stability, presumably via interactions with functional groups of the thickening agent (e.g. the silanol groups of the fumed or precipitated silica), and hence yield more stable gels at lower concentrations of the thickening agent than would otherwise be required.

Furthermore, where the liquid composition according to the first aspect of the invention comprises multiple surface-active substances, such as the gel stabilizer in combination with the lecithin of the antioxidant complex, their total amount shall not exceed 3.0 wt.-% based on the total weight of the liquid composition. In one of the preferred embodiments, the content of surface-active substances is not more than 2.0 wt.-%, or not more than 1.5 wt.-%, or not more than 1.0 wt.-%, or not more than 0.5 wt.-%; e.g. about 0.3 wt.-%, or about 0.4 wt.-%.

In one embodiment, the liquid composition according to the first aspect of the invention comprises up to about 1 wt.-% of the gel stabilizer (e.g. polysorbate 80), and up to about 1 wt.-% lecithin, based on the total weight of the liquid composition. In a specific embodiment, the liquid composition comprises up to about 0.3 wt.-% of the gel stabilizer (e.g. polysorbate 80), and up to about 0.8 wt.-%, lecithin based, on the total weight of the liquid composition. In a more specific embodiment, the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% of the gel stabilizer (e.g. polysorbate 80), and from about 0.01 wt.-% to about 1 wt.-% lecithin, based on the total weight of the liquid composition. In a yet more specific embodiment, the liquid composition comprises from about 0.05 wt.-% to about 0.3 wt.-% of the gel stabilizer (e.g. polysorbate 80), and from about 0.05 wt.-% to about 0.80 wt.-% lecithin, based on the total weight of the liquid composition. For instance, in one embodiment, the liquid composition comprises about 0.08 wt.-% of the gel stabilizer (e.g. polysorbate 80), and about 0.32 wt.-% lecithin, based on the total weight of the liquid composition; or about 0.08 wt.-% of the gel

stabilizer (e.g. polysorbate 80), and about 0.20 wt.-% lecithin, based on the total weight of the liquid composition.

In one of the preferred embodiments, the liquid composition according to the first aspect of the invention comprises:

- 5 (a) a medium chain triglyceride (MCT),
- (b) an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between
 - 10 about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,
 - (d) a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - 15 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and
 - 20 mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and
 - (e) optionally a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures
 - 25 thereof;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In one of the further preferred embodiments, the liquid composition according to the first aspect of the invention, based on its total weight, comprises:

- 30 (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
- (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid

composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,

(c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,

5 (d) from about 10 wt.-% to about 39 wt.-% of a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,

- wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,

10 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,

- wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and

15 (e) optionally from about 0.01 wt.-% to about 1.0 wt.-% of a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

20 In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention, based on its total weight, comprises:

(a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),

(b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 90 wt.-%

25 omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,

(c) from about 0.1 wt.-% to about 5.0 wt.-% of fumed silica,

(d) from about 10 wt.-% to about 39 wt.-% of flavor additives, said flavor additives

30 comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma, and

(e) optionally from about 0.01 wt.-% to about 1.0 wt.-% of polysorbate 80;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention essentially consists of:

- 5 (a) a medium chain triglyceride (MCT),
- (b) an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between
 - 10 about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,
 - (d) a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - 15 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and
 - 20 mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and
 - (e) optionally, a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures
 - 25 thereof;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention, based on its total weight, essentially consists of:

- 30 (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
- (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid

composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,

(c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,

5 (d) from about 10 wt.-% to about 39.9 wt.-% a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,

- wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,

10 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,

- wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof;

15 wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention, based on its total weight, essentially consists of:

(a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),

20 (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%

omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,

25 (c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,

(d) from about 10 wt.-% to about 39.89 wt.-% a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,

30 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,

- wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and

mixtures thereof,

- wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and

- (e) from about 0.01 wt.-% to about 1.0 wt.-% a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention, based on its total weight, essentially consists of:

- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
(b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 90 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
(c) from about 0.1 wt.-% to about 5.0 wt.-% of fumed silica, and
(d) from about 10 wt.-% to about 39.9 wt.-% of flavor additives, said flavor additives comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma; wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In yet a further preferred embodiment, the liquid composition according to the first aspect of the invention, based on its total weight, essentially consists of:

- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
(b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 90 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
(c) from about 0.1 wt.-% to about 5.0 wt.-% of fumed silica,
(d) from about 10 wt.-% to about 39.89 wt.-% of flavor additives, said flavor additives comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof,

and aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma, and

(e) from about 0.01 wt.-% to about 1.0 wt.-% of polysorbate 80;

wherein the liquid composition comprises not more than 5 wt.-% of water as

5 detetermined by Karl Fischer titration.

In one of the further preferred embodiments, the liquid composition according to the first aspect of the invention comprises not more than 4 wt.-% of water as detetermined by Karl Fischer titration; or not more than 3 wt.-%; or not more than 2 wt.-%; not more than 1 wt.-% of water. In a particularly preferred embodiment, the liquid composition is

10 substantially free of water; i.e. no water deliberately included while not excluding the presence of potential residual moisture.

In one embodiment, the liquid composition according to the first aspect of the invention is a suspension. As mentioned above, it is mainly the at least one flavor additive, or a part thereof, that is present in solid, particulate form and suspended in the liquid composition.

15 In one embodiment, the liquid composition according to the first aspect of the invention is a pharmaceutical, nutraceutical and/or dietary composition.

In one embodiment, a single dose unit comprises from about 4 g to about 32 g; or from about 8 g to about 24 g; or from about 10 g to about 20 g; or about 16 g, or about 13.6 g, or about 13.2 g of the liquid composition according to the first aspect of the invention; for

20 instance a liquid composition as detailed in the Examples as H01, H02, J01, J02, K01 or K02. In a further embodiment, a single dose unit essentially consists of from about 4 g to about 32 g; or from about 8 g to about 24 g; or from about 10 g to about 20 g; or about 16 g, or about 13.6 g, or about 13.2 g of said liquid composition; for instance a liquid composition as detailed in the Examples as H01, H02, J01, J02, K01 or K02.

25 In a yet further embodiment, a single dose unit of, for instance, from about 10 g to about 20 g of the liquid composition comprises from about 3240 mg to about 5400 mg; e.g. about 4320 mg, or about 3680 mg, or about 3560 mg omega-3 fatty acids in total. Of these total omega-3 fatty acids preferably from about 2560 mg to about 4320 mg are eicosapentaenoic acid ethyl esters (EPA-EE) and/or docosahexanoic acid ethyl

30 esters (DHA-EE); e.g. about 3440 mg, or about 2960 mg or about 2840 mg. More preferably about 2920 mg to about 4840 mg of these total omega-3 fatty acids are

eicosapentaenoic acid ethyl esters (EPA-EE) and/or docosahexanoic acid ethyl esters (DHA-EE); e.g. about 3880 mg, or about 3320 mg, or about 3200 mg.

An exemplary single dose unit of from about 13 g to about 14 g of the liquid composition typically has a volume of about 15 mL and thus fits in a regular screw-cap or snap-fit cap vial with a volume of about 17 to 20 mL, preferably a vial made of glass or PET. Such volumes are both easily ingested in one gulp, and easy to transport, if needed.

In a yet further embodiment, the daily dose of the liquid composition according to the first aspect of the invention for adults comprises, or is administered as, 1 to 4, preferably 1 to 3, further preferably 1 to 2, and most further preferably 1 single dose unit(s) as described above per day.

In one embodiment, a single dose unit of the liquid composition according to the first aspect of the invention is provided in bottles, vials, sachets or stickpacks. The packages may be formed from any suitable material; for instance, glass, plastic (e.g. polyethylene terephthalate (PET)), or composite materials such as multi-layered packaging foils.

As mentioned above, the weight ratio of the medium chain triglyceride (MCT) and the omega-3 fatty acid composition is chosen such as to range between about 1 : 1 and about 5 : 1, and/or such that the liquid composition exhibits thixotrop viscosity characteristics, and a viscosity which allows to empty out at least 85 wt.-%, preferably at least 90 wt.-%, more preferably at least 93 wt.-% of the liquid composition from its primary packaging (e.g. a crimp neck glass vial or PET bottle) within about 5 to 10 seconds after i) briefly shaking the closed primary packaging manually (about 2 to 10 times); ii) removing the lid, or otherwise opening the primary packaging; iii) placing, or holding, it at a pouring angle of about 45° for about 10 seconds; and iv) lightly tapping the still upward-facing bottom end of the primary packaging with a fingertip after the about 10 seconds. Like this, the liquid composition offers both excellent stability against oxidation and compositions which are flowable enough to allow for easy emptying, or discharging, of the liquid composition from its container into the mouth, or onto the tongue, of a subject.

Compositions provided in side-sealed bags, such as sachets or stickpacks, can typically be formulated a bit 'thicker', i.e. more viscous, since the sachet or stickpack can be squeezed empty with the help of the fingers. This thicker consistency is beneficial in terms of preventing the at least one flavor additive from sedimentation and 'caking' during

storage. At the same time, a slightly thicker consistency of the liquid composition provided in sachets or stickpacks helps to prevent, or at least reduce, spilling over the fingers, especially when squeezing closer to the opening of the sachet or stickpack.

The latter is advantageous, in particular, for the liquid composition for direct oral

5 administration (i.e. intended to be administrable directly from a container and easily swallowed without the need for added fluids) since spilled composition often causes the finger to smell disagreeably 'fishy', which in turn would require consumers to find water or other means to clean their hands, and thus at least partially defeat the purpose of these types of liquid compositions.

10 In one of the preferred embodiments, a single dose unit of the liquid composition according to the first aspect of the invention is provided in bottles or vials; for instance, glass bottles, glass vials, or polyethylene terephthalate (PET) bottles. Further preferably, the bottles or vials are overlayered, or flushed, with an inert gas (e.g. nitrogen or argon), closed and hermetically sealed with a cap; optionally with a screw-cap, hinged cap, snap-
15 fit cap, crown cap or a plug made from suited materials such as plastic, metal or rubber.

It should be understood, that as used herein, the omega-3 fatty acids are considered the active principle to be administered, or the active pharmaceutical/nutraceutical ingredient of the composition. In other words, the omega-3 fatty acid composition is not used in the liquid composition according to the first aspect as merely an excipient,

20 or vehicle, for another active principle. For instance, the omega-3 fatty acid composition is not added to improve the solubility and/or bioavailability of another active principle, such as active principles of natural, semisynthetic or synthetic origin with lipid regulating properties. For instance, in one of the preferred embodiments, the liquid composition for direct oral administration is free of a synthetic drug substance; for instance, free of other
25 antihyperlipidemic (i.e. lipid-lowering) drug substances like 'statins' such as pravastatin, or other HMG-CoA reductase inhibitors (i.e. inhibitors of the cholesterol synthesizing enzyme CSE); cholesterol absorption inhibitors like ezetimibe; 'fibrates' such as fenofibrate or gemfibrozil; nicotinic acid and its derivatives; ion exchange resins such as colestyramine. Similarly, in a further embodiment, the liquid composition for direct oral
30 administration is free of plant extracts which are known to, or at least reported to, exhibit antihyperlipidemic properties; for instance, plant extracts such as amla, moringa, green tea, coffee, cinnamon, garlic, turmeric, artichoke, psyllium, fenugreek, or the like.

In a second aspect, the present invention relates to a process for the preparation of the liquid composition according to the first aspect of the invention as described above, the process comprising the steps of:

- (i) Providing a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids; a thickening agent; at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma; and an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition; and
- (ii) Combining the components provided, such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

In one embodiment of said process, the at least one flavor additive is added to the liquid composition after combining the C₂-C₄ polyol ester and the thickening agent.

In an alternative embodiment of said process, the at least one flavor additive and the thickening agent are combined simultaneously with the C₂-C₄ polyol ester. In a specific embodiment, the thickening agent is first mixed with the flavor additives, or at least a fraction thereof, prior to combining this pre-mix with the other components.

- In one embodiment, the process according to the second aspect of the invention further comprises the steps of providing and adding an antioxidant. In a specific embodiment, said antioxidant is provided in the form of an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid to the liquid composition. In a further specific embodiment, the lecithin and the fatty acid ester of ascorbic acid are dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, prior to combining the resulting antioxidant-pre-mix with the other components. In a yet further specific embodiment, the lecithin and the fatty acid ester of ascorbic acid are dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, at elevated temperatures of from about 80 °C to about 120 °C, prior to combining the resulting antioxidant-pre-mix with the other components.
- When dissolving the lecithin and the fatty acid ester of ascorbic acid in the C₂-C₄ polyol ester, optionally, first the fatty acid ester of ascorbic acid is dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof; and subsequently the lecithin is added and dissolved

to form the antioxidant-pre-mix. Further optionally, first the fatty acid ester of ascorbic acid is dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, at a temperature of from about 90 °C to about 120 °C, or from about 100 °C to about 110 °C; and subsequently the lecithin is added and dissolved at a reduced temperature of from about 80 °C to about 100 °C, or from about 90 °C to about 95 °C, to form the antioxidant-pre-mix.

In one embodiment of the process according to the second aspect of the invention, the omega-3 fatty acid composition is added to the liquid composition

- after combining the C₂-C₄ polyol ester, the thickening agent, and the at least one flavor additive; or
- after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.

In one embodiment of the process according to the second aspect of the invention,

the flavor additive comprises an aroma that is volatile. In a specific embodiment, the volatile aroma is added to the liquid composition

- after combining the C₂-C₄ polyol ester, the thickening agent, and the at least one flavor additive; or
- after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.

In one embodiment, the process according to the second aspect of the invention further comprises the steps of providing and adding a gel stabilizer selected from the group of polyhydroxylated compounds to the liquid composition, optionally a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof. In a specific embodiment, the gel stabilizer is added to the liquid composition

- after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the omega-3 fatty acid composition; or
- after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid, and the omega-3 fatty acid composition;

- by adding the gel stabilizer to the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid, or to a pre-mix of said the antioxidant complex with at least parts of the C₂-C₄ polyol ester; or

5 - by adding the gel stabilizer to any liquid flavor additive (if present), e.g. to the liquid aroma(s), and adding the resulting combined blend to the liquid composition as a final preparation step.

In one embodiment of the process according to the second aspect of the invention, the components provided (e.g. the raw materials), and/or the intermediate or final combinations of said components are degassed. This step, or these steps, are useful in
10 avoiding oxidation of the omega-3 fatty acid composition, with the aim to exclude oxygen as much as possible during processing. In a specific embodiment, the components provided, and/or the intermediate or final combinations of said components are degassed by means of reduced pressure or vacuum. In a further specific embodiment, when degassing by reduced pressure, the pressure is reduced to values not higher than
15 100 mbar; or not not higher than 50 mbar; or not higher than 20 mbar. In a further specific embodiment, at least parts of the components provided, and/or at least parts of the intermediate or final combinations of said components are degassed by means of reduced pressure or vacuum; for instance, some components, or blends thereof, may not be degassed or may be degassed by means other than reduced pressure or vacuum, such
20 as by using ultrasound.

In one of the preferred embodiments of the process according to second aspect of the invention, degassing is performed at least after combining the C₂-C₄ polyol ester, the thickening agent, and at least one flavor additive.

In one embodiment of the process according to second aspect of the invention,
25 the components provided and/or the combined components are overlayed, or flushed, with an inert-gas atmosphere. In a specific embodiment, at least parts of the components provided, and/or at least parts of the intermediate or final combinations of said components are overlayed, or flushed, with an inert-gas atmosphere. This step, or these steps, are also useful in avoiding oxidation of the omega-3 fatty acid composition, with
30 the aim to exclude oxygen as much as possible during processing. In one of the preferred embodiments, the components provided, and/or the intermediate or final combinations of said components are both degassed and overlayed, or flushed, with an inert-gas

atmosphere. Optionally, the inert-gas is selected from nitrogen or argon. In case, degassing is achieved by reduced pressure or vacuum, the respective pump providing the reduced pressure or vacuum needs to be interrupted at times throughout the process, of course, to allow for the introduction of the inert-gas atmosphere.

- 5 In one of the preferred embodiments, the process according to second aspect of the invention comprises the steps of:
- (i) Dissolving the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid in the C₂-C₄ polyol ester at elevated temperatures of from about 80 °C to about 120 °C under stirring to form an antioxidant-pre-mix;
 - 10 (ii) Degassing the resulting antioxidant-pre-mix of step (i) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - (iii) Adding the thickening agent to the degassed antioxidant-pre-mix of step (ii) under stirring;
 - (iv) Degassing the resulting thickened antioxidant-pre-mix of step (iii) by means of
15 reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - (v) Adding at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma to the degassed, thickened antioxidant-pre-mix of step (iv) under stirring;
 - 20 (vi) Degassing the resulting mixture of step (v) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - (vii) Adding the omega-3 fatty acid composition to the degassed resulting mixture of step (vi) under stirring;
 - (viii) Degassing the resulting mixture of step (vii) by means of reduced pressure or
25 vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
- wherein steps (i) to (viii) are performed such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
- 30 In a further preferred embodiment, the process according to second aspect of the invention comprises the steps of:
- (i) Degassing a first fraction of about 80-95 wt.-% of the amount of the C₂-C₄ polyol ester by means of reduced pressure or vacuum, and overlaying with an inert-gas

atmosphere of nitrogen or argon;

(ii) Adding the thickening agent to the degassed C₂-C₄ polyol ester of step (i) under stirring;

(iii) Degassing the resulting thickened C₂-C₄ polyol ester of step (ii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

(iv) In a separate vessel, dissolving the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid in a second fraction of about 5-20 wt.-% of the amount of the C₂-C₄ polyol ester at elevated temperatures of from about 80 °C to about 120 °C under stirring to form an antioxidant-pre-mix;

(v) Degassing the resulting antioxidant-pre-mix of step (iv) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

(vi) Adding the degassed antioxidant-pre-mix of step (v) to the degassed, thickened C₂-C₄ polyol ester of step (iii) under stirring;

(vii) Degassing the resulting thickened antioxidant-pre-mix of step (vi) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

(viii) Adding at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma to the degassed, thickened

antioxidant-pre-mix of step (vii) under stirring;

(ix) Degassing the resulting mixture of step (viii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

(x) Adding the omega-3 fatty acid composition to the degassed resulting mixture of step (ix) under stirring;

(xi) Degassing the resulting mixture of step (x) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

wherein steps (i) to (xi) are performed such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by

Karl Fischer titration.

In one embodiment, the flavor additive employed in the process according to the second aspect of the invention - and in particular the process according to the two embodiments described above comprising steps (i)-(viii) and (i)-(xi), respectively - comprises an aroma

that is volatile; and the volatile aroma is added under stirring after the addition of the omega-3 fatty acid composition. In a further embodiment, the process according to the second aspect of the invention - and in particular the process according to the two embodiments described above comprising steps (i)-(viii) and (i)-(xi) -further comprises

5 the steps of subjecting the mixture comprising the at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma (either an intermediate mixture, or the ultimately resulting liquid composition) to a high shear mixing step, preferably under vacuum, for reducing the mean particle size of any solid, suspended parts of the at least one flavor additive; optionally using a high shear

10 mixer of the rotor/stator-type (e.g. an UltraTurrax®) or other suitable means such as a colloid mill with defined slit size. Small particle sizes of the at least one flavor additive, preferably not more than 150 µm, or not more than 100 µm, or not more than 75 µm, or not more than 50 µm, support a pleasant mouth feel and, at the same time, improve the suspension stability. Alternatively, or in addition, to such high-shear mixing, the at least

15 one flavor additive can be purchased in the desirable particle size range; for instance, xylitol is provided in a quality with a mean particle size of about 90 µm (e.g. Xivia CM90 as available from Dupont Nutrition & Health).

In a yet further embodiment, the process according to the second aspect of the invention - and in particular the process according to the two embodiments described

20 above comprising steps (i)-(viii) and (i)-(xi) -further comprises the steps of providing and adding a gel stabilizer selected from the group of polyhydroxylated compounds to the liquid composition, optionally a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof; wherein the gel stabilizer is either added to the liquid

25 composition under stirring after the addition of the omega-3 fatty acid composition, or added to the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid first (e.g. the antioxidant-pre-mix of steps (i) or (iv) as described above), and then further processed together with said antioxidant complex.

In one of the preferred embodiments of the process according to second aspect of the

30 invention, the C₂-C₄ polyol ester is a medium chain triglyceride (MCT).

In a further preferred embodiment of the process according to second aspect of the invention, the thickening agent is fumed silica or precipitated silica.

In a yet further preferred embodiment of the process according to second aspect of the invention, the esters of the omega-3 fatty acid composition are selected from alkyl esters, preferably from ethyl esters or methyl esters.

5 In all embodiments of the process in which an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid is added, the fatty acid ester of ascorbic acid may be selected from ascorbylstearate, ascorbylpalmitate, or mixtures thereof.

In one embodiment, the process according to second aspect of the invention, comprises a further step of packaging a single dose unit of the liquid composition into bottles, vials, sachets or stickpacks. Optionally, the liquid composition is degassed under reduced
10 pressure prior to packaging; and/or the packaging step is performed in an inert-gas atmosphere.

Technical feasibility provided, all embodiments, including all specific or preferred embodiments, as described above in connection with the liquid composition of the first aspect of the invention also apply to the process for the preparation of said liquid
15 composition according to the second aspect of the invention.

In a third aspect, the invention relates to the liquid composition according to the first aspect of the invention as described above for use in the treatment and/or prevention of rheumatoid arthritis, hypertriglyceridemia, and/or post-myocardial infarction.

Again, all embodiments, including all specific or preferred embodiments, as described
20 above in connection with the liquid composition of the first aspect of the invention also apply to the use thereof in the treatment and/or prevention of rheumatoid arthritis, hypertriglyceridemia, and/or post-myocardial infarction according to the third aspect of the invention.

EXAMPLES

25 The following examples serve to illustrate the invention, however should not to be understood as restricting the scope of the invention.

Example 1 - Liquid compositions H01 and H02

Compositions H01 and H02 as listed below in Tables 1 and 2, respectively, are examples of the components and respective amounts provided per single dose of exemplary liquid
30 compositions according to the first aspect of the invention.

The compositions differ mainly in the amount of the antioxidant complex added, with H01 comprising about 0.32 wt.-% lecithin (L) and about 0.24 wt.-% ascorbylpalmitate (AP), and H02 comprising about 0.20 wt.-% lecithin (L) and about 0.08 wt.-% ascorbylpalmitate (AP), based on the total weight of the liquid composition. This equals about 0.40 wt.-% + 0.30 wt.-% and about 0.25 wt.-% + 0.10 wt.-% L + AP, based on the weight of the flavor additive-free liquid composition (i.e. without the flavor additive(s)), for H01 and H02, respectively.

Both compositions were prepared, using a process exemplary to the process according to the second aspect of the invention, by dissolving the ascorbylpalmitate in about 10 wt.-% of the MCT at elevated temperatures of about 100-110 °C under stirring, and subsequently adding and dissolving the lecithin under stirring, at elevated temperatures of about 90-95 °C, such as to form an L + AP antioxidant-pre-mix. In a separate vessel, the thickening agent Aerosil® 200 was blended with the other about 80 wt.-% of the MCT at a temperature of 20± 10 °C, prior to adding the L + AP antioxidant-pre-mix to the MCT-Aerosil® 200 blend. Approximately half of the remaining 10 wt.-% of the MCT were used for rinsing the antioxidant-pre-mix vessel and other parts used for manufacturing, and transferring the resulting 'rinsing fluid' with the residuals of the antioxidant complex into the vessel comprising the MCT-Aerosil® 200 mixture. To this mixture, the flavor additives xylitol, aspartame, citric acid and cherry aroma (all in powder form) were added under stirring, followed by adding the omega-3 fatty acid composition (K85EE) under stirring. The container from which the omega-3 fatty acid composition (K85EE) was added to the mixture was then also rinsed with the other remaining half of the MCT. In a final step, the resulting liquid composition was filled into capped glass bottles or polyethylene terephthalate (PET) bottles, under inert gas atmosphere (argon).

All liquid components provided, as well as their respective intermediate or final blends were degassed by means of reduced pressure (≤ 100 mbar), and overlaid, or flushed, with a nitrogen inert-gas atmosphere (argon).

A distinct positive anti-oxidant effect was found for the liquid compositions (as indicated by significantly elongated induction times, in comparison to omega-3 fatty acid composition (K85EE) / MCT blends without the described anti-oxidant mixture, in aggravated oxidation tests at 80 °C using a Methrom 678 Rancimat-tester); and the liquid compositions exhibited a pleasant, agreeable taste upon direct oral administration (see e.g. Example 3).

| Composition H01 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6724.40 | 49.44 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.41 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.12</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.65</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>10.82</i> |
| Xylitol (powder) | 2000.00 | 14.71 |
| Lecithin | 43.20 | 0.32 |
| Ascorbylpalmitate | 32.40 | 0.24 |
| Fumed silica (Aerosil® 200) | 360.00 | 2.65 |
| Citric acid (powder) | 300.00 | 2.21 |
| Aroma Cherry (powder) | 100.00 | 0.74 |
| Aspartame (powder) | 40.00 | 0.29 |
| | 13600.00 | 100.00 |

Table 1

| Composition H02 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6762.20 | 49.72 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.41 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.12</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.65</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>10.82</i> |
| Xylitol (powder) | 2000.00 | 14.71 |
| Lecithin | 27.00 | 0.20 |
| Ascorbylpalmitate | 10.80 | 0.08 |
| Fumed silica (Aerosil® 200) | 360.00 | 2.65 |
| Citric acid (powder) | 300.00 | 2.21 |
| Aroma Cherry (powder) | 100.00 | 0.74 |
| Aspartame (powder) | 40.00 | 0.29 |
| | 13600.00 | 100.00 |

Table 2

Example 2 – Liquid compositions with J01, J02, K01 and K02 with added gel stabilizer

Compositions J01 and J02 as well as K01 and K02 (with aroma combinations cherry / limonen / peppermint-menthol and orange / mandarin), all listed below in Tables 3-4 as well as 5-6, respectively, are further examples of the components and
5 respective amounts provided per single dose of exemplary liquid compositions according to the first aspect of the invention. These compositions comprise polysorbate 80 as a gel stabilizer and thus reduced amounts of fumed silica (Aerosil® 200) compared to H01 and H02 of Example 1 above. They also comprise liquid aroma (namely, (R)-(+)-limonen, peppermint-menthol, orange, and mandarin), optionally in addition to solid aroma. This
10 offers the benefit of more pronounced volatility, and hence a more pleasant taste and/or smell experience.

The compositions were prepared in a similar manner as described in Example 1 above, with the minor differences that

- the gel stabilizer polysorbate 80 was added to the L + AP antioxidant-pre-mix,
- 15 - the flavor additives comprised not only xylitol, aspartame, citric acid, and the aroma combination cherry /limonen / peppermint menthol (all in powder form), but also monosodium citrate,
- in case of compositions K01 and K02, the liquid orange / mandarin aroma combination was not added along with the powderous flavor additives, but instead subsequent to
20 adding the omega-3 fatty acid composition (K85EE) in a final mixing step; and
- the liquid compositions were subjected to a high-shear mixing step using a rotor/stator-type mixer (UltraTurrax®).

The resulting liquid compositions of J01, J02, K01 and K02 were filled into capped glass bottles, or polyethylene terephthalate (PET) bottles, under inert gas atmosphere (argon).

25 Instead of adding the gel stabilizer polysorbate 80 to the L + AP antioxidant-pre-mix, it was also successfully tested that the gel stabilizer can instead be dispersed in a further small aliquot of the total MCT (approx. 3-5 % of the total MCT) at a temperature of about 50 °C to 70 °C, before being adding this polysorbate/MCT-mix to the final liquid composition in a final step.

A distinct positive anti-oxidant effect was found for the liquid compositions (as indicated by significantly elongated induction times, in comparison to omega-3 fatty acid composition (K85EE) / MCT blends without the described anti-oxidant mixture, in aggravated oxidation tests at 80 °C using a Methrom 678 Rancimat-tester); and the liquid compositions exhibited a pleasant, agreeable taste upon direct oral administration (see e.g. Example 3).

| Composition J01 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6713.60 | 49.84 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.70 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.12</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.78</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>10.93</i> |
| Xylitol (powder) | 2000.00 | 14.85 |
| Lecithin | 43.20 | 0.32 |
| Ascorbylpalmitate | 32.40 | 0.24 |
| Fumed silica (Aerosil® 200) | 360.00 | 2.67 |
| Polysorbate 80 | 10.80 | 0.08 |
| Citric acid (powder) | 40.00 | 0.30 |
| Monosodium citrate (powder) | 120.00 | 0.89 |
| Aroma Cherry (powder) | 80.00 | 0.59 |
| Aroma Limonen ((R)-(+)-Limonen; liquid) | 40.00 | 0.30 |
| Aroma Peppermint-Menthol (liquid) | 6.00 | 0.04 |
| Aspartame (powder) | 24.00 | 0.18 |
| | 13470.00 | 100.00 |

Table 3

| Composition J02 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6751.40 | 50.57 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.96 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.12</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.90</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>11.03</i> |
| Xylitol (powder) | 2000.00 | 14.71 |
| Lecithin | 27.00 | 0.20 |
| Ascorbylpalmitate | 10.80 | 0.08 |
| Fumed silica (Aerosil® 200) | 240.00 | 1.80 |
| Polysorbate 80 | 10.80 | 0.08 |
| Citric acid (powder) | 40.00 | 0.30 |
| Monosodium citrate (powder) | 120.00 | 0.90 |
| Aroma Cherry (powder) | 80.00 | 0.60 |
| Aroma Limonen ((R)-(+)-Limonen; liquid) | 40.00 | 0.30 |
| Aroma Peppermint-Menthol (liquid) | 6.00 | 0.04 |
| Aspartame (powder) | 24.00 | 0.18 |
| | 13350.00 | 100.00 |

Table 4

| Composition K01 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6713.60 | 49.72 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.62 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.12</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.74</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>10.90</i> |
| Xylitol (powder) | 2000.00 | 14.81 |
| Lecithin | 43.20 | 0.32 |
| Ascorbylpalmitate | 32.40 | 0.24 |
| Fumed silica (Aerosil® 200) | 360.00 | 2.67 |
| Polysorbate 80 | 10.80 | 0.08 |
| Citric acid (powder) | 40.00 | 0.30 |
| Monosodium citrate (powder) | 120.00 | 0.89 |
| Aroma Orange (liquid) | 88.00 | 0.65 |
| Aroma Mandarin (liquid) | 72.00 | 0.53 |
| Aspartame (powder) | 24.00 | 0.18 |
| | 13504.00 | 100.00 |

Table 5

| Composition K02 | Amount [mg] | Amount [wt.-%] |
|---|------------------------|---------------------------|
| Medium chain triglycerides (Miglyol® 812) | 6751.40 | 50.44 |
| Omega-3-acid ethyl esters 90 (K85EE) | 4000.00 | 29.89 |
| <i>Tocopherol (in K85EE)</i> | <i>16.80</i> | <i>0.13</i> |
| <i>EPA ethyl ester (in K85EE)</i> | <i>1856.00</i> | <i>13.84</i> |
| <i>DHA ethyl ester (in K85EE)</i> | <i>1472.00</i> | <i>11.00</i> |
| Xylitol (powder) | 2000.00 | 14.94 |
| Lecithin | 27.00 | 0.20 |
| Ascorbylpalmitate | 10.80 | 0.08 |
| Fumed silica (Aerosil® 200) | 240.00 | 1.79 |
| Polysorbate 80 | 10.80 | 0.08 |
| Citric acid (powder) | 40.00 | 0.30 |
| Monosodium citrate (powder) | 120.00 | 0.90 |
| Aroma Orange (liquid) | 88.00 | 0.66 |
| Aroma Mandarin (liquid) | 72.00 | 0.54 |
| Aspartame (powder) | 24.00 | 0.18 |
| | 13350.00 | 100.00 |

Table 6Example 3 – Acceptance test (taste and smell)

Vials comprising about 15 mL of the liquid compositions of Examples 1 and 2 (equating to about 4 g of the omega-3 fatty acid composition; i.e. daily dose in just 1 vial) were subjected to the acceptance test for taste and smell with a panel of trained volunteers (n=13). Prior to ingestion of the tested compositions, the vials were briefly shaken to redisperse any potentially sedimented flavor additives. Then the full volume was ingested orally directly from the vial without any further added fluids (e.g. no drinking of water along with the ingestion of the vial contents). The panelists evaluated the criteria mouthfeel, taste, smell, acceptability of the volume and overall impression; and rated them with grades from 1 to 5 (1 = very good to 5 = very bad).

The results are shown in Table 7 below. All compositions were well received by the panelists, and achieved 'good' to 'very good' ratings. The panelists awarded slightly better ratings to J01 compared to H01 (indicating a preference of the more volatile cherry/limonen/mint-combination aroma over just cherry alone (i.e. powder + liquid
 5 aroma over powder alone)); and slightly better ratings for the high-shear treated compositions (indicating that solids, such as the flavor additive, and in particular xylitol, is at least partially comminuted and thus offers an intensified sweetness and cooling effect due to the increased surface area per weight).

| Composition | Criterion | | | | |
|------------------|-----------|-------|-------|--------|---------|
| | Mouthfeel | Taste | Smell | Volume | Overall |
| H01 | 2.2 | 2.2 | 2,5 | 1.9 | 2.5 |
| J01 (high-shear) | 1.7 | 2.0 | 1.7 | 1.8 | 1.9 |
| K01 (high-shear) | 1.7 | 1.6 | 1.2 | 1.7 | 1.7 |

10

Example 4 – Viscosity test and product recovery from primary packaging

Crimp neck glass vials were weighed empty and then filled with about 10 g of the liquid compositions of Examples 1 and 2. Thereafter, the filled vials were weighed again and then subjected to the following steps:

- 15 i) briefly shaking the closed vial manually (about 2 to 10 times);
 ii) removing the lid, or otherwise opening the primary packaging;
 iii) placing, or holding, it at a pouring angle of about 45° for 10 seconds; and
 iv) lightly tapping the still upward-facing bottom end of the primary packaging with a fingertip after these 10 seconds. The weight remaining in the vials after steps was
 20 determined gravimetrically.

All tested compositions allowed to empty out at least 90 wt.-% of the liquid composition from the vials; or in other words, less than 10 wt.-% remained inside the vials, for most compositions even less than 7 wt.-%. Further advantageously, it was also noticed, when monitoring the sedimentation behavior of the liquid compositions
 25 of Example 2, that no visible sedimentation of the suspended and/or redispersed particles occurred for at least 30 minutes, often for more than 1 hour or even longer.

The following list of numbered items are embodiments comprised by the present invention:

1. A liquid composition for direct oral administration, the composition comprising:
 - (a) a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids,
 - (b) an omega-3 fatty acid composition,
wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition,
wherein the weight ratio of the C₂-C₄ polyol ester under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, and
 - (d) at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma;wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
2. The liquid composition according to item 1, wherein the C₂-C₄ polyol ester is selected from mono- and/or di-esters of propylene glycol; mono-, di- and/or tri-esters of glycerol; and/or mono- and/or di-esters of butylene glycol; and/or wherein the C₂-C₄ polyol ester comprises aliphatic, saturated fatty acid chains with 8 to 12 carbon atoms, or 8 to 10 carbon atoms.
3. The liquid composition according to any one of items 1 to 2, wherein the C₂-C₄ polyol ester exhibits a mean viscosity of from about 2-50 mPas as measured by capillary viscosimetry; or from about 5-35 mPas; or from about 25-32 mPas.
4. The liquid composition according to any one of items 1 to 3, wherein the C₂-C₄ polyol ester comprises not more than 2 wt.-% of either
 - long chain fatty acids with more than 12 carbon atoms, or
 - short chain fatty acids with less than 6 carbon atoms.
5. The liquid composition according to any one of items 1 to 4, wherein the C₂-C₄ polyol ester is a medium chain triglyceride (MCT).
6. The liquid composition according to any one of items 1 to 5, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, or at least about 90 wt.-%,

esters of eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), based on the weight of the fatty acid composition; and/or
wherein the omega-3 fatty acid composition comprises from about 40-60 wt.-% (e.g. from about 43-50 wt.-%) esters of eicosapentaenoic acid (EPA); and from about 25-50 wt.-% (e.g. from about 34-41 wt.-%) esters of docosahexanoic acid (DHA), based on the weight of the omega-3 fatty acid composition; and
wherein optionally said esters are selected from alkyl esters, preferably from ethyl esters or methyl esters.

7. The liquid composition according to any one of items 1 to 6, wherein the weight ratio of the eicosapentaenoic acid ethyl ester (EPA-EE) and the docosahexanoic acid ethyl ester (DHA-EE) ranges between about 1 : 1 and about 1.5 : 1, or between about 1.1 : 1 and about 1.4 : 1, or between about 1.2 : 1 and about 1.3 : 1.
8. The liquid composition according to any one of items 1 to 7, wherein the weight ratio of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), and the omega-3 fatty acid composition ranges between about 1 : 1 and about 5 : 1, or between about 1 : 1 and about 2 : 1, or between about 1.15 : 1 and about 1.85 : 1, or between about 1.3 : 1 and about 1.7 : 1.
9. The liquid composition according to any one of items 1 to 8, wherein the composition comprises at least about 40 wt.-% of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), based on the total weight of the liquid composition; or at least about 45 wt.-%; or at least about 48 wt.-%; and/or wherein the composition comprises at least about 20 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition; or at least about 25 wt.-%; or at least about 28 wt.-%.
10. The liquid composition according to any one of items 1 to 9, wherein the composition comprises at least about 40 wt.-% of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), and at least about 20 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition; for instance, at least about 48 wt.-% of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), and at least about 28 wt.-% of the omega-3 fatty acid composition based on the total weight of the liquid composition.

11. The liquid composition according to any one of items 1 to 10, wherein the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with at least the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT).
12. The liquid composition according to any one of items 1 to 11, wherein the thickening agent is an anorganic oleo-gel forming component, optionally selected from the group consisting of fumed silica, precipitated silica, aluminum silicates, bentonite, and mixtures thereof; preferably a fumed silica or precipitated silica; for instance, a hydrophilic fumed silica exhibiting a specific surface area in the range of 50 - 500 m²/g, or in the range of 200 - 300 m²/g; or a hydrophobic fumed silica treated with dimethyldichlorosilane (DDS).
13. The liquid composition according to any one of items 1 to 12, wherein the composition comprises at least about 10 wt.-% of the flavor additive based on the total weight of the liquid composition, or at least about 15 wt.-%, or at least about 17 wt.-%; and/or wherein at least parts of the flavor additive is present in solid, particulate form and suspended in the liquid composition; for instance about 50 wt.-%, or at least about 60 wt.-%, or at least about 70 wt.-%, or at least about 80 wt.-%.
14. The liquid composition according to any one of items 1 to 13, wherein the flavor additive comprises a sugar or sugar alcohol, optionally a sugar or sugar alcohol selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof; preferably xylitol, sorbitol, isomaltitol, or mixtures thereof; and further preferably xylitol.
15. The liquid composition according to any one of items 1 to 14, wherein the flavor additive comprises a sweetener selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof; preferably aspartame.
16. The liquid composition according to any one of items 1 to 15, wherein the flavor additive comprises an aroma that is volatile.
17. The liquid composition according to any one of items 1 to 16, wherein the flavor additive comprises an acidifier selected from the group of organic acids, the

respective salts thereof, and mixtures thereof; optionally, an organic acid selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof; preferably at least citric acid and/or salts thereof.

18. The liquid composition according to any one of items 1 to 17, wherein the flavor additive comprises
 - xylitol and aspartame;
 - xylitol and citric acid and/or salts thereof; or
 - xylitol, aspartame, and citric acid and/or salts thereof;and wherein the flavor additive optionally further comprises a volatile aroma.
19. The liquid composition according to any one of items 1 to 18, wherein the composition further comprises at least one antioxidant; for instance, an antioxidant provided in the form of an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.
20. The liquid composition according to item 19, wherein the fatty acid ester of ascorbic acid is selected from ascorbylstearate, ascorbylpalmitate, or mixtures thereof; wherein optionally the weight ratio of lecithin and ascorbylpalmitate in the antioxidant complex ranges between about 3 : 1 and about 1 : 1, or between about 2.8 : 1 and about 1.2 : 1, or between about 2.7 : 1 and about 1.3 : 1.
21. The liquid composition according to any one of items 19 to 20, wherein the antioxidant complex further comprises a tocopherol selected from alpha tocopherol, beta tocopherol, gamma tocopherol, or delta tocopherol; wherein optionally the tocopherol is comprised in the omega-3 fatty acid composition under item 1(b).
22. The liquid composition according to any one of items 1 to 21, further comprising a gel stabilizer selected from the group of polyhydroxylated compounds; for instance, a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof; preferably a polysorbate; optionally a polysorbate 80.

23. The liquid composition according to item 22, wherein the liquid composition comprises from about 0.01 wt.-% to about 1 wt.-% of the gel stabilizer; or from about 0.05 wt.-% to about 0.3 wt.-%; for instance, from about 0.01 wt.-% to about 1 wt.-% polysorbate 80; or from about 0.05 wt.-% to about 0.3 wt.-% polysorbate 80.
24. The liquid composition according to any one of items 1 to 23, wherein the composition comprises, or essentially consists of:
- (a) a medium chain triglyceride (MCT),
 - (b) an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, wherein the thickening agent is fumed silica or precipitated silica,
 - (d) a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and
 - (e) optionally a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

25. The liquid composition according to any one of items 1 to 24, wherein the composition, based on its total weight, comprises:
- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
 - (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica, preferably fumed silica,
 - (d) from about 10 wt.-% to about 39 wt.-% of a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof,preferably from about 10 wt.-% to about 39 wt.-% of a flavor additive comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma, and
 - (e) optionally from about 0.01 wt.-% to about 1.0 wt.-% of a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof, preferably polysorbate 80;
- wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

26. The liquid composition according to any one of items 1 to 25, the composition essentially consisting of:

- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
- (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
- (c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica, preferably fumed silica, and
- (d) from about 10 wt.-% to about 39.9 wt.-% a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, preferably from about 10 wt.-% to about 39.5 wt.-% of a flavor additive comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma;

wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

27. The liquid composition according to any one of items 1 to 25, the composition, based on its total weight, essentially consisting of:
- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
 - (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-% omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica, preferably fumed silica,
 - (d) from about 10 wt.-% to about 39.89 wt.-% a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, preferably from about 10 wt.-% to about 39.49 wt.-% of a flavor additive comprising a sugar alcohol selected from xylitol, sorbitol, isomaltitol, or mixtures thereof, aspartame, citric acid, and aroma; preferably xylitol, aspartame, citric acid, and aroma, and
 - (e) from about 0.01 wt.-% to about 1.0 wt.-% a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof, preferably polysorbate 80; wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.

28. The liquid composition according to any one of items 1 to 27, wherein the liquid composition comprises not more than 4 wt.-% of water as determined by Karl Fischer titration; or not more than 3 wt.-%; or not more than 2 wt.-%; not more than 1 wt.-% of water; or wherein the liquid composition is substantially free of water.
29. The liquid composition according to any one of items 1 to 28, wherein said liquid composition is a suspension.
30. The liquid composition according to any one of items 1 to 29, wherein said liquid composition is a pharmaceutical, nutraceutical and/or dietary composition.
31. The liquid composition according to any one of items 1 to 30, wherein said liquid composition exhibits a viscosity which allows to empty out at least 85 wt.-%, preferably at least 90 wt.-%, more preferably at least 93 wt.-% of the liquid composition from its primary packaging within about 5 to 10 seconds after
 - i) briefly shaking the closed primary packaging manually (about 2 to 10 times);
 - ii) removing the lid, or otherwise opening the primary packaging;
 - iii) placing, or holding, it at a pouring angle of about 45° for about 10 seconds; and
 - iv) lightly tapping the still upward-facing bottom end of the primary packaging with a fingertip after the about 10 seconds.
32. The liquid composition according to any one of items 1 to 31, wherein a single dose unit comprises, or essentially consists of, from about 4 g to about 32 g; or from about 8 g to about 24 g; or from about 10 g to about 20 g; or about 16 g; or about 13.6 g; or about 13.2 g of said liquid composition; and wherein optionally a single dose unit of said liquid composition is provided in bottles, vials, sachets or stickpacks.
33. A process for the preparation of the liquid composition according to any one of items 1 to 32, the process comprising the steps of:
 - Providing a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids; a thickening agent; at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma; and an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition; and

- Combining the components provided, such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
34. The process according to item 33, wherein the at least one flavor additive is added to the liquid composition after combining the C₂-C₄ polyol ester and the thickening agent; or wherein the at least one flavor additive and the thickening agent are combined simultaneously with the C₂-C₄ polyol ester; wherein optionally the thickening agent is first mixed with at least one flavor additive, or at least a fraction thereof, prior to combining this pre-mix with the C₂-C₄ polyol ester.
35. The process according to any one of items 33 to 34, wherein the omega-3 fatty acid composition is added to the liquid composition after combining the C₂-C₄ polyol ester, the thickening agent, and the at least one flavor additive.
36. The process according to any one of items 33 to 35, wherein the process further comprises the steps of providing and adding an antioxidant; said antioxidant optionally being provided in the form of an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid to the liquid composition.
37. The process according to item 36, wherein the lecithin and the fatty acid ester of ascorbic acid are dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, prior to combining the resulting antioxidant-pre-mix with the other components; wherein optionally the lecithin and the fatty acid ester of ascorbic acid are dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, at elevated temperatures of from about 80 °C to about 120 °C.
38. The process according to any one of items 36 to 37, wherein first the fatty acid ester of ascorbic acid is dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof; and wherein subsequently the lecithin is added and dissolved to form the antioxidant-pre-mix.
39. The process according to any one of items 36 to 38, wherein first the fatty acid ester of ascorbic acid is dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, at a temperature of from about 90 °C to about 120 °C, or from about 100 °C to

about 110 °C; and

wherein subsequently the lecithin is added and dissolved at a reduced temperature of from about 80 °C to about 100 °C, or from about 90 °C to about 95 °C, to form the antioxidant-pre-mix.

40. The process according to any one of items 33 to 39, wherein the omega-3 fatty acid composition is added to the liquid composition
 - after combining the C₂-C₄ polyol ester, the thickening agent, and the at least one flavor additive; or
 - after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.
41. The process according to any one of items 33 to 40, wherein the flavor additive comprises an aroma that is volatile; and wherein optionally the volatile aroma is added to the liquid composition
 - after combining the C₂-C₄ polyol ester, the thickening agent, and the at least one flavor additive; or
 - after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.
42. The process according to any one of items 33 to 41, wherein the process further comprises the steps of providing and adding a gel stabilizer selected from the group of polyhydroxylated compounds to the liquid composition, optionally a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof.
43. The process according to item 42, wherein the gel stabilizer is added to the liquid composition
 - after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, and the omega-3 fatty acid composition; or
 - after combining the C₂-C₄ polyol ester, the thickening agent, the at least one flavor additive, the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid, and the omega-3 fatty acid composition;

- by adding the gel stabilizer to the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid, or to a pre-mix of said the antioxidant complex with at least parts of the C₂-C₄ polyol ester; or
 - by adding the gel stabilizer to any liquid flavor additive (if present), e.g. to the liquid aroma(s), and adding the resulting combined blend to the liquid composition as a final preparation step.
44. The process according to any one of items 33 to 43, wherein the components provided, and/or the intermediate or final combinations of said components are degassed; optionally degassed by means of reduced pressure or vacuum; wherein further optionally the pressure is reduced to values not higher than 100 mbar; or not higher than 50 mbar; or not higher than 20 mbar.
45. The process according to any one of items 33 to 44, wherein at least parts of the components provided, and/or at least parts of the intermediate or final combinations of said components are degassed by means of reduced pressure or vacuum; for instance, wherein degassing is performed at least after combining the C₂-C₄ polyol ester; the thickening agent; and the at least one flavor additive.
46. The process according to any one of items 33 to 45, wherein the components provided and/or the combined components are overlayed with an inert-gas atmosphere; optionally degassed and overlayed with an inert-gas atmosphere; wherein further optionally the inert-gas is selected from nitrogen or argon.
47. The process according to items 36 to 46, the process comprising the steps of:
- i. Dissolving the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid in the C₂-C₄ polyol ester at elevated temperatures of from about 80 °C to about 120 °C under stirring to form an antioxidant-pre-mix;
 - ii. Degassing the resulting antioxidant-pre-mix of step (i) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - iii. Adding the thickening agent to the degassed antioxidant-pre-mix of step (ii) under stirring;

- iv. Degassing the resulting thickened antioxidant-pre-mix of step (iii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - v. Adding at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma to the degassed, thickened antioxidant-pre-mix of step (iv) under stirring;
 - vi. Degassing the resulting mixture of step (v) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - vii. Adding the omega-3 fatty acid composition to the degassed resulting mixture of step (vi) under stirring;
 - viii. Degassing the resulting mixture of step (vii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
- wherein steps (i) to (viii) are performed such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
48. The process according to items 36 to 46, the process comprising the steps of:
- i. Degassing a first fraction of about 80-95 wt.-% of the amount of the C₂-C₄ polyol ester by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - ii. Adding the thickening agent to the degassed C₂-C₄ polyol ester of step (i) under stirring;
 - iii. Degassing the resulting thickened C₂-C₄ polyol ester of step (ii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - iv. In a separate vessel, dissolving the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid in a second fraction of about 5-20 wt.-% of the amount of the C₂-C₄ polyol ester at elevated temperatures of from about 80 °C to about 120 °C under stirring to form an antioxidant-pre-mix;
 - v. Degassing the resulting antioxidant-pre-mix of step (iv) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;

- vi. Adding the degassed antioxidant-pre-mix of step (v) to the degassed, thickened C₂-C₄ polyol ester of step (iii) under stirring;
 - vii. Degassing the resulting thickened antioxidant-pre-mix of step (vi) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - viii. Adding at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma to the degassed, thickened antioxidant-pre-mix of step (vii) under stirring;
 - ix. Degassing the resulting mixture of step (viii) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
 - x. Adding the omega-3 fatty acid composition to the degassed resulting mixture of step (ix) under stirring;
 - xi. Degassing the resulting mixture of step (x) by means of reduced pressure or vacuum, and overlaying with an inert-gas atmosphere of nitrogen or argon;
- wherein steps (i) to (xi) are performed such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration
49. The process according to any one of items 47 to 48, wherein the flavor additive comprises an aroma that is volatile; and wherein the volatile aroma is added under stirring after the addition of the omega-3 fatty acid composition.
50. The process according to any one of items 47 to 49, wherein the process further comprises the steps of providing and adding a gel stabilizer selected from the group of polyhydroxylated compounds to the liquid composition, optionally a polyhydroxylated compound selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof; and
- wherein the gel stabilizer is added under stirring either after the addition of the omega-3 fatty acid composition; or added to the antioxidant-pre-mix. complex comprising lecithin and a fatty acid ester of ascorbic acid, or to a pre-mix of said the antioxidant complex with at least parts of the C₂-C₄ polyol ester.

51. The process according to any one of items 33 to 50, wherein the C₂-C₄ polyol ester is a medium chain triglyceride (MCT);
wherein the thickening agent is fumed silica or precipitated silica; and/or
wherein the esters of the omega-3 fatty acid composition are selected from alkyl esters, preferably from ethyl esters or methyl esters.
52. The process according to any one of items 36 to 51, wherein the antioxidant complex comprises lecithin and a fatty acid ester of ascorbic acid selected from ascorbylstearate, ascorbylpalmitate, or mixtures thereof.
53. The process according to any one of items 33 to 52, wherein the process comprises a further step of packaging a single dose unit of the liquid composition into bottles, vials, sachets or stickpacks; and wherein optionally
 - the liquid composition is degassed under reduced pressure prior to packaging; and/or
 - the packaging step is performed in an inert-gas atmosphere.
54. The liquid composition according to any one of items 1 to 32 for use in the treatment and/or prevention of rheumatoid arthritis, hypertriglyceridemia, and/or post-myocardial infarction.

CLAIMS

1. A liquid composition for direct oral administration, the composition comprising:
 - (a) a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids,
 - (b) an omega-3 fatty acid composition,
wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition,
wherein the weight ratio of the C₂-C₄ polyol ester under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) a thickening agent, and
 - (d) at least one flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma;wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
2. The liquid composition according to claim 1, wherein the C₂-C₄ polyol ester is selected from mono- and/or di-esters of propylene glycol; mono-, di- and/or tri-esters of glycerol; and/or mono- and/or di-esters of butylene glycol; and/or wherein the C₂-C₄ polyol ester comprises aliphatic, saturated fatty acid chains with 8 to 12 carbon atoms, or 8 to 10 carbon atoms.
3. The liquid composition according to any one of claims 1 to 2, wherein the C₂-C₄ polyol ester is a medium chain triglyceride (MCT).
4. The liquid composition according to any one of claims 1 to 3, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, or at least about 90 wt.-%, esters of eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), based on the weight of the fatty acid composition; and/or wherein the omega-3 fatty acid composition comprises from about 40-60 wt.-% esters of eicosapentaenoic acid (EPA); and from about 25-50 wt.-% esters of docosahexanoic acid (DHA), based on the weight of the omega-3 fatty acid composition.

5. The liquid composition according to any one of claims 1 to 4, wherein the weight ratio of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), and the omega-3 fatty acid composition ranges between about 1 : 1 and about 5 : 1.
6. The liquid composition according to any one of claims 1 to 5, wherein the composition comprises at least about 40 wt.-%, preferably at least about 45 wt.-%, of the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT), and at least about 20 wt.-%, preferably at least about 25 wt.-%, of the omega-3 fatty acid composition based on the total weight of the liquid composition.
7. The liquid composition according to any one of claims 1 to 6, wherein the thickening agent is capable of forming an oleo-gel, preferably a thixotropic oleo-gel, with at least the C₂-C₄ polyol ester, optionally a medium chain triglyceride (MCT); wherein the thickening agent is an anorganic oleo-gel forming component, optionally selected from the group consisting of fumed silica, precipitated silica, aluminum silicates, bentonite, and mixtures thereof.
8. The liquid composition according to any one of claims 1 to 7, wherein the composition comprises at least about 10 wt.-% of the flavor additive based on the total weight of the liquid composition; and/or wherein at least parts of the flavor additive is present in solid, particulate form and suspended in the liquid composition.
9. The liquid composition according to any one of claims 1 to 8, wherein the flavor additive comprises a sugar or sugar alcohol selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof, preferably, xylitol, sorbitol, isomaltitol, or mixtures thereof, and further preferably xylitol; and/or wherein the flavor additive comprises an aroma that is volatile.
10. The liquid composition according to any one of claims 1 to 9, wherein the composition further comprises at least one antioxidant; optionally, an antioxidant provided in the form of an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.

11. The liquid composition according to any one of claims 1 to 10, wherein the composition, based on its total weight, comprises:
- (a) from about 40 wt.-% to about 60 wt.-% of a medium chain triglyceride (MCT),
 - (b) from about 20 wt.-% to about 40 wt.-% of an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid ethyl esters, based on the weight of the omega-3 fatty acid composition, wherein the weight ratio of the medium chain triglyceride under (a) and the omega-3 fatty acid composition under (b) ranges between about 1 : 1 and about 10 : 1,
 - (c) from about 0.1 wt.-% to about 5.0 wt.-% of a thickening agent, wherein the thickening agent is fumed silica or precipitated silica, preferably fumed silica,
 - (d) from about 10 wt.-% to about 39 wt.-% of a flavor additive selected from the group consisting of sugars, sugar alcohols, sweeteners, acidifiers and aroma,
 - wherein the sugar or sugar alcohol is selected from the group consisting of xylitol, sorbitol, isomaltitol, erythritol, trehalose, maltitol, sucrose, fructose, glucose, and inulin, and mixtures thereof,
 - wherein the sweetener is selected from the group consisting of aspartame, acesulfame potassium, cyclamate, saccharin, stevia, sucralose, neohesperidin, and thaumatin, and mixtures thereof,
 - wherein the acidifier selected from the group consisting of citric acid, malic acid, ascorbic acid, tartaric acid, the respective salts thereof, and mixtures thereof, and
 - (e) optionally from about 0.01 wt.-% to about 1.0 wt.-% of a gel stabilizer selected from the group of polysorbates, poloxamers, polyethyleneglycols, polyoxyethylen fatty acid glycerides, polidocanol, or mixtures thereof, preferably polysorbate 80;
- wherein the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration.
12. A process for the preparation of the liquid composition according to any one of claims 1 to 11, the process comprising the steps of:
- Providing a C₂-C₄ polyol ester with one or more C₆-C₁₂ medium chain fatty acids;
 - a thickening agent; at least one flavor additive selected from the group consisting

- of sugars, sugar alcohols, sweeteners, acidifiers and aroma; and an omega-3 fatty acid composition, wherein the omega-3 fatty acid composition comprises at least about 80 wt.-%, optionally at least about 90 wt.-%, omega-3 fatty acid esters, based on the weight of the omega-3 fatty acid composition; and
- Combining the components provided, such that the weight ratio of the C₂-C₄ polyol ester and the omega-3 fatty acid composition ranges between about 1 : 1 and about 10 : 1, and the liquid composition comprises not more than 5 wt.-% of water as determined by Karl Fischer titration, wherein optionally the components provided and/or the combined components are degassed by means of reduced pressure or vacuum, and overlaid with an inert gas atmosphere.
13. The process according to claim 12, wherein the process further comprises the steps of providing and adding an antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid to the liquid composition; wherein first the fatty acid ester of ascorbic acid is dissolved in the C₂-C₄ polyol ester, or at least a fraction thereof, at a temperature of from about 90 °C to about 120 °C; and wherein subsequently the lecithin is added and dissolved at a reduced temperature of from about 80 °C to about 100 °C to form the antioxidant-pre-mix.
14. The process according to any one of claims 12 to 13, wherein the omega-3 fatty acid composition is added to the liquid composition
- after combining the C₂-C₄ polyol ester; the thickening agent; and the at least one flavor additive; or
 - after combining the C₂-C₄ polyol ester; the thickening agent; the at least one flavor additive; and the antioxidant complex comprising lecithin and a fatty acid ester of ascorbic acid.
15. The liquid composition according to any one of claims 1 to 11 for use in the treatment and/or prevention of rheumatoid arthritis, hypertriglyceridemia, and/or post-myocardial infarction.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/078716

| A. CLASSIFICATION OF SUBJECT MATTER | | | | |
|---|--|-----------|--|-----------------------|
| INV. | A61K31/202 | A61K47/10 | A61K47/54 | A61P3/06 |
| | A61P29/00 | A61K9/10 | A61K47/02 | A61P9/10 |
| | A61K47/24 | A61K47/26 | A61K9/00 | A61K47/14 |
| 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) A61K A61P | | | | |
| 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 practicable, search terms used) EPO-Internal, WPI Data | | | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | | | Relevant to claim No. |
| Y | US 2006/034815 A1 (GUZMAN HECTOR [US] ET AL) 16 February 2006 (2006-02-16) paragraphs [0015], [0018], [0075], [0088], [0091], [0100], [0101], [0107], [0134], [0148] | | | 1-15 |
| Y | US 2016/316810 A1 (TERP MEGAN [US] ET AL) 3 November 2016 (2016-11-03) paragraphs [0056], [0057]; table 4 | | | 1-15 |
| Y | US 2013/078362 A1 (DEWILLE NORMANELLA T [US] ET AL) 28 March 2013 (2013-03-28) paragraphs [0004], [0008], [0030], [0068]; example 3 | | | 1-15 |
| Y | WO 2016/152054 A1 (BIZEN CHEMICAL CO LTD [JP]) 29 September 2016 (2016-09-29) the whole document | | | 1-15 |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex. | | | | |
| * Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family | | | | |
| Date of the actual completion of the international search 11 January 2021 | | | Date of mailing of the international search report 20/01/2021 | |
| 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 | | | Authorized officer Estañol, Inma | |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2020/078716

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|-----------------------------|
| US 2006034815 | A1 | 16-02-2006 | AU 2005271413 A1 16-02-2006 |
| | | | BR PI0514189 A 03-06-2008 |
| | | | CA 2576196 A1 16-02-2006 |
| | | | EP 1786414 A2 23-05-2007 |
| | | | JP 2008509154 A 27-03-2008 |
| | | | KR 20070038553 A 10-04-2007 |
| | | | NZ 552389 A 31-05-2009 |
| | | | US 2006034815 A1 16-02-2006 |
| | | | WO 2006017698 A2 16-02-2006 |
| US 2016316810 | A1 | 03-11-2016 | CN 105960173 A 21-09-2016 |
| | | | EP 3091851 A1 16-11-2016 |
| | | | US 2016316810 A1 03-11-2016 |
| | | | WO 2015095545 A1 25-06-2015 |
| US 2013078362 | A1 | 28-03-2013 | US 2007048405 A1 01-03-2007 |
| | | | US 2013078362 A1 28-03-2013 |
| WO 2016152054 | A1 | 29-09-2016 | NONE |