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(54) Benævnelse: **SAMMENSÆTNING DER I DET VÆSENTLIGE ER VANDFRI ISÆR TIL ANVENDELSE SOM NÆRINGSUPPLEMENT**

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WO-A1-2016/135482
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GIGLIOTTI J C ET AL: "Extraction and characterisation of lipids from Antarctic krill (Euphausia superba)", FOOD CHEMISTRY, ELSEVIER LTD, NL, Bd. 125, Nr. 3, 1. April 2011 (2011-04-01) , Seiten 1028-1036, XP027477867, ISSN: 0308-8146, DOI: 10.1016/J.FOODCHEM.2010.10.013 [gefunden am 2010-11-04]
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The present invention concerns an essentially anhydrous composition, in particular foruse as a food supplement, and a process for its preparation.

Description

The absorption of fat-soluble and certain water-soluble food components from the human gut is limited. Thus, only a small percentage of fat-soluble food components are absorbed by the human intestine. In addition, the digestion of fat is very susceptible to malfunctions. Unlike other food components, it requires the entire length of the intestine and requires enzymes from the mouth, stomach and pancreas as well as sufficient bile flow. And the passage time of the food pulp through the intestine must be adjusted accordingly so that the enzymes have enough time to take effect. From this, a variety of reasons can be deduced for a less than optimal fat digestion and thus for a reduced absorption of fat-soluble food components.

The absorption of certain water-soluble components, such as iron, from the human intestine is also extremely susceptible to interference. Most of the iron is absorbed only in the first 30 cm of the small intestine.

In order to improve the absorption of fat-soluble or water-soluble active substances in the human intestine, it has been proposed to use micellar nanoparticles. DE 10 2010 021688 A1 describes the production of an active substance concentrate from micellar nanoparticles, whereby a liquid pre-emulsion comprising glycerol and phospholipids is first produced and this pre-emulsion is then stirred with water and an oil-active substance mixture. By stirring under high shear forces, particles with a size between 750 nm and 1250 nm are obtained. Subsequent high-pressure homogenization produces micelles in the nano range. The micellar active substance concentrate obtained can then be subjected to ultracentrifugation, whereby a first phase is obtained from glycerol and water and a second phase from an oily micelle paste.

The finished products described in DE 10 2010 021 688 A1 have a water activity (a_w value) of 0.78 to 0.84. This means that filling, e.g. in soft or hard gelatine capsules, cannot take place because of the resulting instability of the capsule material. It must

be taken in an aqueous emulsion as a paste. This makes permanent application hardly possible due to taste problems.

The present invention is therefore based on the technical object of improving the disadvantages known from the state of the art and of providing a product which enables effective and permanently problem-free absorption of fat-soluble and certain water-soluble active substances in high concentrations.

According to the invention, the object is solved by a composition with the features of claim 1.

Accordingly, an essentially anhydrous composition is provided, which comprises the following components:

- Krill oil pretreated by ultracentrifugation, wherein the krill oil is pretreated by ultracentrifugation at 200,000 to 250,000 g, preferably 210,000 to 240,000 g, for 20 to 30 minutes,
- optionally silica as emulsifier,
- at least one water-soluble active substance and/or at least one fat-soluble active substance, and
- at least one antioxidant substance.

"Essentially anhydrous" means, for the purposes of the present composition, that the water content is so low that the growth of micro-organisms, in particular of fungi and bacteria, is not supported and excluded. Thus, the present composition in one embodiment has a water activity a_w between 0.2 and 0.5, preferably between 0.25 and 0.4. Filling in soft or hard gelatine capsules is therefore possible.

The krill oil used in the preparation of the present composition is an oil extracted from Antarctic krill (*Euphausia superba*). The krill oil used consists on average of 44.7% neutral lipids and 44% polar lipids. Among the polar lipids, phosphatidylcholine dominates (> 86 %). This makes it one of the few oils with a high proportion of phospholipids. For comparison: soya oil contains 2% phospholipids.

Accordingly, the present composition comprises phospholipids, in particular phosphatidylcholine, which are contained in krill oil and, where appropriate, recovered from it.

As mentioned above, the krill oil is pre-treated by ultracentrifugation before use. According to the invention, the pre-treatment comprises an ultracentrifugation at 200,000 to 250,000 g, preferably 210,000 to 240,000 g for 20 to 30 minutes at 30°C.

The krill oil pre-treated in this way (i.e. krill oil exposed to high shear stress) is, in contrast to native krill oil, very quickly and easily (in a few seconds) completely emulsifiable in water. This is a prerequisite for optimal availability in the stomach.

In an alternative embodiment, water (e.g. between 20 and 100 µl sterile water per ml krill oil) is added to the native krill oil prior to pretreatment by ultracentrifugation. As a result of ultracentrifugation, the phospholipids contained in krill oil settle as a solid sediment (solid) and can be recovered by draining the oily supernatant. The water content of the sediment can be regulated as required by the g number during ultracentrifugation and subsequent treatment with heat. The complete emulsification of the sediment in different thin-bodied oils (e.g. coconut oil) or water is given.

In an aqueous environment, krill oil, or more precisely the phospholipids contained in krill oil, forms liposomes with a diameter of between 50 and 100 nanometers. No other substances or components for stabilizing the formed liposomes are intended.

In the case of a fat-soluble active ingredient, it is absorbed into the formed membrane of the particle. The advantage is that such small particles have a high affinity to surfaces, i.e. they attach themselves to the mucous membrane of the stomach and intestines. Only through contact with the mucous membrane can fat-soluble substances enter the bloodstream. The formation of liposomes is left to the natural processes in the stomach and intestines. Normal human fat digestion requires "liposomes", which have an average diameter of 65 nm. To form it, the full function of enzymes from the mouth, stomach and pancreas, sufficient bile flow and functioning

stomach muscles (to break down the food) is needed. The products therefore perform these functions for the absorption of fat-soluble substances.

In addition, the triglycerides introduced by krill oil follow the normal fat degradation pathway, bringing fat-soluble substances such as coenzyme Q10 into the blood.

The following occurs only if medium-chain triglycerides are added to the product, e.g. from coconut oil. The isomerised diglycerides, which are formed in the stomach by the action of gastric lipase and gastric acid, are also absorbed from the intestine with a time delay, so that fat-soluble substances can then be absorbed from the intestine for hours if necessary.

In the case of certain water-soluble active substances, such as iron in the form of iron-II sulphate, these bind directly to the phospholipids. These then form liposomes through the aqueous environment in the stomach with a high affinity to the small intestinal mucosa. The iron thus attaches itself with the liposomes to the mucous membrane in the first area of the small intestine, where it is absorbed into the blood with high efficiency. Therefore a significantly lower dosage than in conventional products is possible, so that the dreaded subjective side effects in the stomach and intestinal area do not occur.

In a preferred embodiment, the present composition contains phospholipids, in particular phosphatidylcholine, in an amount of between 20 and 35% by weight, preferably between 23 and 33.5% by weight.

In a further version, the present composition contains silica (silicon dioxide) in an amount of between 5 and 15% by weight, preferably between 6 and 10% by weight in relation to the total amount. The amount of silíca used can accordingly be 30 - 36 mg (5.1-6.2 wt%). Preferably silica with an average diameter of 70 to 90 µm, especially 75 µm, and a minimum diameter of 5 to 15 µm, especially 10 µm, is used.

As mentioned above, silica or silica gel serves as an emulsifying agent and enables good mixing and distribution of the components of the composition; the mixing of the

components of the composition is improved. This applies in particular to aqueous preparations (e.g. water or orange juice). This is the situation when taking the product with liquid in the stomach. During in-vitro suspension in water, nanoparticles with an average size of typically 65 - 85 nm are formed. The resulting nanoparticles consist of phospholipids and form a physiological form of administration.

As mentioned above, the present composition contains fat-soluble or water-soluble active substances. Active substances are substances that have a specific effect in the human organism and cause a specific reaction. Active substances are used in the following meanings: food components or medically active substances.

The water-soluble active ingredient used in the present composition preferably comprises metal cations and/or organic cations. Iron cations or even selenium cations are preferably used as metal cations. In the case of iron, this is added in the form of ferrous sulphate.

For example, cations of chondroitin sulfate can be used as organic cations.

The water-soluble active ingredient is contained in the present final composition in an amount of between 0.05 and 10% by weight, preferably between 0.2 and 8.6% by weight.

The fat-soluble active substance used in the present composition comprises preferably fat-soluble food components or medicinal substances. Thus, the fat-soluble active ingredient may be selected from the group containing coenzyme Q10, alpha-carotene, curcumin, naringin, olive oil flavonoids or lycopene.

The fat-soluble active ingredient is contained in the present final composition in an amount of between 5.0 and 25% by weight, preferably 10 to 23.0% by weight, e.g. 8.6 - 23% by weight. Thus, the present composition allows the administration of a relatively high amount of active ingredients.

As mentioned above, the present composition may contain at least one fat-soluble antioxidant substance. This fat-soluble antioxidant substance may be selected from a group comprising substances with vitamin E activity, in particular tocopherols and trienols, and carotenoids.

Tocopherols or derivatives thereof are in particular alpha-tocopherol, beta- and gamma-tocopherol, delta-tocopherol. Trienols are in particular alpha-trienol, beta-trienol, gamma-trienol and delta-trienol.

Carotenoids are a preferred group of antioxidants which can be used in the present invention. These antioxidants are a class of compounds that are divided into two main groups: Carotenes and xanthophylls. In contrast to carotenes, which are pure polyene hydrocarbons such as beta-carotene or lycopene, xanthophylls contain functional oxygen groups such as hydroxyl, epoxy and/or oxo groups. Typical examples of the xanthophyll group are astaxanthin, canthaxanthin, lutein, zeaxanthin and fucoxanthin. Natural sources of astaxanthin are krill, lobster, by-products of crustacean processing, bacteria, yeasts, algae and higher plants.

Possible carotenoids are alpha-carotene, beta-carotene, lutein, zeaxanthin, retinal, astaxanthin, cryptoxanthin, natural mixed carotenoids, lycopene and resveratrol.

Lutein and zeaxanthin are particularly preferred, which, in addition to their antioxidant properties, are said to counteract degeneration of the retina of the eye and thus vision.

Concentrations of carotenoids in formulations may vary, but correspond to amounts useful in food supplements or supplementary balanced diets.

In addition to the components already mentioned, the present composition may also contain other ingredients. Further components which may be present in the formulation according to the present invention are vitamins, such as vitamin A, vitamin A acetate, vitamin A palmitate, riboflavin, vitamin B, ascorbic acid, ascorbyl palmitate, nicotinic acid, nicotinamide, Pyridoxine hydrochloride, vitamin D3, vitamin K, thiamine, calcium pantothenate, biotin, alpha lipoic acid, compounds with vitamin or coenzyme properties

such as choline chloride, carnitine, taurine, creatine, ubiquinones, S-methyl and S-adenosylmethionine. These vitamins and substances may, where appropriate, be used either as antioxidants according to the present invention, or as other factors in support of one or more components of the formulation according to the present invention, or simply function as other beneficial ingredients.

Preferably vitamin D3 is added. If vitamin D3 is present, it is preferably present in a concentration of 0.000017 - 0.000034% by weight in the final composition.

Where appropriate, the formulation according to the invention may also include physiologically acceptable excipients such as lecithin, mono-, glycerol monostearate, coconut and soybean oil.

Coconut oil contains approx. 50 % so-called medium-chain fatty acids. These have the property that they only need one enzyme from the stomach to be absorbed into the bloodstream, so they are easier to digest. They can be absorbed in the stomach and the entire intestine. They are always found in triglyceride (the classic fat) at the peripheral positions (position 1 or 3). On the one hand, their cleavage can lead to an absorption of fat-soluble substances, on the other hand, the influence of gastric acid leads to an isomerisation (from 2-3 or 1-2 diglycerides to 1-3 diglycerides). This influences the further absorption of fat from the intestine.

Soybean oil serves as a solvent for the fat-soluble antioxidant substances such as tocopherols and trienols.

In a preferred variant, the present composition comprises phospholipids derived from krill oil, in particular phosphatidylcholine, silica, ferrous sulphate, tocopherols and soya oil. In a particularly preferred variant, the composition comprises phospholipids derived from krill oil, in particular phosphatidylcholine, silica, ferrous sulphate, soya oil, alpha-tocopherol, beta- and gamma-tocopherol and delta-tocopherol.

In another preferred variant, the present composition comprises phospholipids derived from krill oil, in particular phosphatidylcholine, silica, coenzyme Q10, tocopherols,

trienols, soybean oil and carotenoids. In a particularly preferred variant, the composition comprises phospholipids derived from krill oil, in particular phosphatidylcholine, silica, coenzyme Q10, soya oil, alpha-tocopherol, beta- and gamma-tocopherol, delta-tocopherol, alpha-trienol, beta-trienol, gamma-trienol and delta-trienol, lutein, zeaxanthin and vitamin D3.

After mixing the ingredients together, the composition may be subjected to ultracentrifugation (at 225 000 g) to produce an oily paste which may be ingested with water or another liquid. Alternatively, it can also be incorporated into other products.

Even more preferably, however, the composition is subjected to differential temperature centrifugation and the resulting fluid suspension is filled into capsules.

Accordingly, according to the present invention, a capsule is provided which contains the composition according to the invention. The capsule shell can be made of hard or soft gelatine. A capsule may contain between 500 and 1000 mg, preferably between 550 and 750 mg, in particular 580 mg of the composition according to the invention.

The task of the present invention is also solved by a process for producing the composition according to the invention, which comprises the following steps:

- Pre-treating krill oil by ultracentrifugation at 200,000 to 250,000 g, preferably 210,000 to 240,000 g for 20 to 30 minutes;
- Mixing the pre-treated krill oil with at least one water-soluble active substance and/or at least one fat-soluble active substance;
- Addition of silica and at least one antioxidant substance,
- Stirring the mixture of pre-treated krill oil, water soluble active substance and/or fat-soluble active ingredient, silica and antioxidant substance over a predetermined period of time, and
- Centrifugation of the mixture at 14.000 to 16.000 g with simultaneous reduction of the temperature of the mixture to a value between 3°C and 10°C, preferably between 5°C and 8°C

As described above, the pre-treatment of krill oil involves ultracentrifugation at 200,000 to 250,000 g, preferably 210,000 to 240,000 g for 20 to 30 minutes at 30°C. Either the krill oil as such is subjected to ultracentrifugation or some water is added to the krill oil before ultracentrifugation to cause separation of the phospholipids contained in the krill oil.

The specific centrifugation conditions result in a fluid suspension (of essentially solid composition prior to centrifugation) which can be filled into capsules. Accordingly, the viscosity of the preparation can be reduced by the specific centrifugation technique.

According to one variant of the process, the krill oil is heated to a temperature between 40°C and 90°C, preferably between 50°C and 80°C, preferably in an inert gas atmosphere, before mixing with at least one active ingredient.

The temperature during centrifugation (differential temperature centrifugation) is preferably lowered from an initial temperature of 80°C to 5°C.

The following starting formulations (prior to centrifugation) are preferred (each based on the pre-treated krill oil):

- 5 to 15 % by weight, preferably 6 to 10 % by weight of silica
- 5 to 25 % by weight, preferably 10 to 23 % by weight of fat-soluble active substances and/or

0,05 to 20 % by weight, preferably 0,1 to 10 % by weight, especially preferably 0,2 to 8,6

% by weight of water-soluble active substances; and

- Remainder of antioxidant substances and other components.

In one embodiment, the starting formulation comprises, for example, 18% by weight of ferrous sulphate heptahydrate, 6% by weight of silica, 4% by weight of soya oil and 4% by weight of tocopherols, based on the total amount of krill oil.

In a further embodiment, the starting formulation comprises e.g. 20 wt% coenzyme Q10, 10 wt% silica, 6 wt% soya oil, 3 wt% tocopherols, 1.5 wt% trienols based on the total amount of krill oil.

The invention is explained in more detail below by means of the examples.

Example 1: Pre-treatment of krill oil

(a) Ultracentrifugation of the krill oil at 235 000 g at 30°C for 20-30 minutes (Beckman Coulter Optima L-90K Ultracentrifuge - Rotor 45 Ti)

(b) Between 20 and 100 µl of sterile water per ml are added to the native krill oil, mixed intensively and then subjected to ultracentrifugation at 210 000 g at 30 °C for 25-30 minutes (Beckman Coulter Optima L-90K ultracentrifuge - Rotor 45 Ti).

Example 2: First composition with coenzyme Q10

This composition aims to support the functions of brain performance, muscle and vision that are particularly important in old age. The ingredients are fat-soluble substances that are usually only absorbed to a small percentage from the human intestine.

Pre-treated krill oil is mixed with 99,9 % nitrogen at 80 °C for 20 minutes at 6,3 Ncm by means of a three-bladed nozzle stirrer under light shielding and gassing with 99,9 % nitrogen at 80 °C. Then 119 mg of coenzyme Q10 per g of krill oil are added in powder form while stirring continuously. After coenzyme Q10 has been completely stirred in, 47 mg silica, 29 mg soya oil, 1,6 mg alpha-tocopherol, 13,5 mg beta- and gamma-tocopherol and 5,8 mg delta-tocopherol are added. After complete mixing, 47 mg silica, 29 mg soya oil, 5.8 mg alpha-tocopherol, 5 mg alpha-trienol, 0.6 mg beta-trienol, 7.2 mg gamma-trienol and 2.0 mg delta-trienol follow. Then 12 mg lutein, 24 mg zeaxanthin and 46 µg vitamin D3 are added in this order.

After stirring for 20 minutes under the above conditions, a differential temperature centrifugation is carried out, during which the temperature is continuously reduced from

80 °C to 5 °C for 30 minutes at 15 970 g. The resulting fluid suspension can be filled into hard gelatine capsules. The a_w-value is 0.283. Germs growth is therefore not possible.

Alternatively, a paste containing the ingredients can be obtained by ultracentrifugation at 235 000 g and further processed as required.

When suspended in water (corresponding to the stomach) particles with an average size of 59 nm are found.

Resorption studies were performed in 8 subjects by consensus. Blood was taken before taking the composition and after 15 minutes, 1 hour, 2 hours, 4 hours and 6 hours. By analyzing coenzyme Q10 with high-pressure liquid chromatography or ELISA, the absorption could be detected after only 15 minutes and over the entire period. This was not possible with a conventional product in the form of a coenzyme Q10 powder.

For analysis, the blood serum was separated by ultracentrifugation into very-low-density lipoproteins, high-density and low-density lipoproteins and lipoprotein-free serum. The increase in coenyzm-Q-10 concentration was found in the fraction with a density of < 1.006 g/ml. Phospholipids, on the other hand, have a density of > 1.006 g/ml at 18°C. From this it can be concluded that the present product uses the usual regulated uptake pathways for coenzyme Q10 and a non-specific uptake via nanoparticles that penetrate the intestinal wall does not take place. As expected, the phospholipids are cleaved before absorption in the intestine, thereby destroying the nanoparticle structure.

Coenzyme Q10 does not have its own transport system in the human body, but uses the fat metabolism. There is therefore a close correlation between the level of blood lipid parameters and coenzyme Q10 blood concentrations. However, this also means that the level of coenzyme Q10 changes with lipid metabolism disorders without this having anything to do with absorption. For example, people who release many triglycerides from the liver after eating have very high concentrations. On the other

hand, those who completely burn the fatty acids in the liver from food have very low concentrations. Without exact knowledge of fat metabolism, for which the determination of cholesterol, triglycerides, HDL- and LDL-cholesterol is insufficient, the bioavailability of coenzyme Q10 cannot be assessed.

Example 3: Second composition with coenzyme Q10

Pre-treated krill oil is mixed with 99,9 % nitrogen at 80 °C for 20 minutes at 6,3 Ncm by means of a three-bladed nozzle stirrer under light shielding and gassing with 99,9 % nitrogen. Then 119 mg of coenzyme Q10 per g of krill oil are added in powder form while stirring continuously. After coenzyme Q10 has been completely stirred in, 47 mg silica, 29 mg soya oil, 1,6 mg alpha-tocopherol, 13,5 mg beta- and gamma-tocopherol and 5,8 mg delta-tocopherol are added.

After stirring for 20 minutes under the above conditions, a differential temperature centrifugation is carried out, during which the temperature is continuously reduced from 80 °C to 5 °C for 30 minutes centrifuging at 15 970 g.

The resulting fluid suspension can be filled into hard gelatine capsules. The a_w-value is 0.460. Bacterial or fungal growth is therefore not possible.

Alternatively, a paste containing the ingredients can be obtained by ultracentrifugation at 235 000 g and further processed as required, e.g. by adding coconut oil.

Dilution in water results in a particle distribution with an average size of approx. 60 nm.

Example 4: Composition with iron

Krill oil is stirred in darkness in a nitrogen atmosphere at a temperature of 48 °C for 20 minutes at 6,3 Ncm. Then 104 mg of ferrous sulphate heptahydrate (processed with a homogeniser) per 393 mg of krill oil is slowly stirred in.

Five minutes later they are added, also to the original 393 mg of krill oil:
33 mg silica (average diameter 75 µm, minimum diameter 10 µm)
24 mg soya oil
2 mg alpha-tocopherol
17 mg beta- and gamma-tocopherol
7 mg delta-tocopherol

Iron II sulphate heptahydrate binds to phospholipids and can be enriched by centrifugation at 14 500 g. By ultracentrifugation at 235 000 g, an anhydrous mass can be prepared from phospholipids and iron II sulphate heptahydrate. This is suitable for further processing into various products, e.g. in food products.

Silica is added to facilitate the emulsification of krill oil in an aqueous solution (taking the product with a glass of water or orange juice (vitamin C)). During the in-vitro suspension in water, nanoparticles with an average size of 65 nm are formed. The tocopherols are dissolved in soybean oil and serve as additional oxidation protection for the various fatty acids contained.

The a_w-value of the product is 0.420. Bacterial or fungal growth can be excluded with this water activity. Filling in soft or hard gelatine capsules is possible.

By binding to phosphatidylcholine and the physiological formation of nanoparticles in aqueous solution, the absorption of iron can be increased. In the course of healing trials by a physician, 10 people were evaluated who could not be treated effectively with other iron products.

The 10 volunteers in the healing experiment were given a hard gelatine capsule with 20 mg of bivalent iron at 9.00 a.m. on an empty stomach. Blood was taken from an arm vein immediately before taking the capsule and after 1 hour, 2 hours and 4 hours.

The following table shows in µg/dl the basal concentration and the maximum concentration in the context of iron exposure. The iron concentrations were measured with an AU 400 Beckman Coulter Analyzer.

Person	Basal concentration [µg/dl]	Maximum concentration [µg/dl]
1	67	192
2	40	185
3	64	183
4	83	194
5	34	137
6	27	209
7	50	143
8	77	185
9	79	207
10	56	154
Mean value	*57,7*	*178,9*
Standard deviation	*19,6*	*25,4*

The elimination of the iron deficiency could be proven by determining the storage form of the iron, ferritin. Side effects in the form of nausea, upper abdominal pain, flatulence, constipation, diarrhoea or black stools have not been observed. All patients reported an improvement of the clinical symptoms due to the iron deficiency within a few days. Compared to the preparation described above as a paste (DE 10 2010 021688 A1), the absorption of iron in the iron resorption test was significantly higher. The maximum increase with the paste (10 mg) was 43 µg/dl on average (patients with iron deficiency).

In addition, 12 persons without iron deficiency (ferritin > 30 ng/ml) were subjected to an iron resorption test to determine whether the uptake of inorganic iron from the intestine, which is regulated by hepcidin, is maintained. Thus it could be determined that the intake is significantly lower in the absence of iron deficiency. The higher the storage iron (ferritin), the lower the absorption. It is therefore not possible for the product to overload the body with iron.

The following table shows the results of iron resorption tests from the literature compared to the present product:

Type of iron	***Iron quantity***	***Increase in blood serum concentration***	***n***
Iron sulphate	105 mg	158 µg/dl	20
Iron fumarate	65 mg	100 µg/dl (F)/ 67 µg/dl (M)	49
Iron sulphate	100 mg	93 µg/dl	10
Iron sulphate	80 mg	86 µg/dl°/164 µg/dl°	69
Iron sulphate	200 mg	114 µg/dl	111
Iron sulphate	10 mg	28 µg/dl /F)/17 µg/dl (M)	122
Iron sulphate	**20 mg**	**121 µg/dl*/65 µg/dl****	**22**

F = women, M = men

* People with iron deficiency (n = 10 - 8 women, 2 men, 29 - 83 years old)

** Persons without iron deficiency (n = 12)

° Persons older than 65 years with iron deficiency anaemia

°° Persons younger than 65 years with iron deficiency anaemia

Patentkrav

1. Sammensætning der i det væsentlig er vandfri, hvilken sammensætning omfatter

- krillolie der er forbehandlet ved ultracentrifugering, hvilken krillolie forbehandles ved ultracentrifugering ved 200.000 til 250.000 g i 20 til 30 minutter.
- eventuelt silica som emulgator,
- mindst et vandopløseligt aktivt stof og/eller mindst et fedtopløseligt aktivt stof, og
- mindst et antioxiderende stof.

2. Sammensætningen ifølge krav 1, **kendetegnet ved, at** den har en vandaktivitet a_w på mellem 0,2 og 0,5, fortrinsvis mellem 0,25 og 0,4.

3. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** phospholipider fra krillolien er til stede i en mængde på mellem 20 og 35 vægt-%, fortrinsvis 23 og 33,5 vægt-%.

4. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** silica er til stede i en mængde på mellem 5 og 15 vægt-%, fortrinsvis mellem 6 og 10 vægt-%.

5. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** krillolien forbehandles ved ultracentrifugering ved 210.000 til 240.000 g i 20 til 30 minutter.

6. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** det mindst ene vandopløselige aktive stof omfatter metalkationer, især jernkationer eller organiske kationer.

7. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** det vandopløselige aktive stof er til stede i en mængde på mellem 0,05 og 20 vægt-

%, fortrinsvis mellem 0,1 og 10 vægt-%, især fortrinsvis mellem 0,2 og 8,6 vægt-%.

8. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** det mindst ene fedtopløselige aktive stof omfatter fedtopløselige fødevarekomponenter eller lægemidler.

9. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** det fedtopløselige aktive stof er valgt fra gruppen, der omfatter coenzym Q10.

10. Sammensætning ifølge et af de foregående krav, **kendetegnet ved, at** det fedtopløselige aktive stof er indeholdt i en mængde på mellem 5 og 25 vægt-%, fortrinsvis mellem 10 og 23 vægt-%.

11. Sammensætning ifølge et af de foregående krav, k**endetegnet ved, at** mindst et fedtopløseligt antioxiderende stof er valgt fra en gruppe, der omfatter stoffer med vitamin E-aktivitet, især tocopheroler og trienoler, og carotenoider.

12. Sammensætning ifølge et af de foregående krav, der omfatter phospholipider som er afledt af krillolie, især phosphatidylcholin, silica, jern(II)sulfat, tocopheroler og sojabønneolie.

13. Sammensætning ifølge et hvilket som helst af kravene 1 til 11, der omfatter phospholipider som er afledt af krillolie, især phosphatidylcholin, silica, coenzym Q10, tocopheroler, trienoler, sojabønneolie og carotenoider.

14. Fremgangsmåde til fremstilling af en sammensætning ifølge et hvilket som helst af kravene 1 til 13, hvilken fremgangsmåde omfatter trinnene:

- at forbehandle krillolie ved ultracentrifugering ved 200.000 til 250.000 g i 20 til 30 minutter;
- at blande den forbehandlede krillolie med mindst et vandopløseligt aktivt stof og/eller mindst et fedtopløseligt aktivt stof;
- at tilsætte silica og mindst et antioxiderende stof,

- at omrøre blandingen af forbehandlet krillolie, vandopløseligt aktivt stof og/eller fedtopløseligt aktivt stof, silica og antioxidant stof over et forudbestemt tidsrum, og
- at centrifugere blandingen ved 14.000 til 16.000 g med samtidig reduktion af blandingens temperatur til en værdi på mellem 3 °C og 10 °C, fortrinsvis mellem 5 °C og 8 °C.

15. Fremgangsmåden ifølge krav 14, **kendetegnet ved, at** den forbehandlede krillolie opvarmes til en temperatur på mellem 40 °C og 90 °C, fortrinsvis mellem 60 °C og 80 °C, før blanding med den mindst ene aktive bestanddel, fortrinsvis i en inert gasatmosfære.