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(54) Title: NEW SUGAR-FREE FORMULATIONS, THEIR MANUFACTURE AND USE

(57) Abstract: The present invention is directed to a formulation with a self-heating temperature ≥ 120°C, whereby said formulation consists of a fat-soluble vitamin in an amount of at least 10 weight-%, whereby the fat-soluble vitamin is vitamin A or a derivative thereof and optionally vitamin D or a derivative thereof; gelatin in an amount of at least 60 weight-%; at least one antioxidant in an amount of ≤ 5 weight-%; an anti- caking agent; optionally an oil; optionally residual moisture; whereby the amounts a), b) and c) are based on the total weight of a) to e). The present invention is further directed to a container with a volume ranging from 450 l to 3000 l comprising such formulation, a process for the manufacture of such formulation, the use of such formulation as additive to feed or premixes, and feed additives, premixes or feed comprising such formulation.

New sugar-free formulations, their manufacture and use

Summary of the invention

The present invention is directed to a formulation with a self-heating temperature ≥ 120° C, whereby said formulation consists of a fat-soluble vitamin in an amount of at least 10 weight-%, whereby the fat-soluble vitamin is vitamin A or a derivative thereof and optionally vitamin D or a derivative thereof; gelatin in an amount of at least 60 weight-%; at least one antioxidant in an amount of ≤ 5 weight-%; an anti-caking agent; optionally an oil; optionally residual moisture; whereby the amounts a), b) and c) are based on the total weight of a) to e). The amount of the residual moisture is preferably at most 6 weight-%, more preferably at most 5 weight-%, even more preferably at most 3.5 weight-%, most preferably at most 2.5 weight-%, based on the total weight of the formulation.

The present invention is further directed to a container with a volume of up to 3000 l comprising such formulation, a process for the manufacture of such formulation, the use of such formulation as additive to feed or premixes, and feed additives, premixes or feed comprising such formulation.

When the formulation is prepared according to the process as disclosed below, it is also called “beadlets”. It was a surprise that such formulation/beadlets with the advantageous properties as laid down below could be prepared without the use of a sugar as cross-linker. It was further surprising that the self-heating temperature of such formulations/beadlets is increased though their antioxidant content is decreased compared to similar formulations of the prior art. So far it was expected that an amount of at least 10 weight-% of an antioxidant such as e. g. BHT is needed to ensure a self-heating temperature of at least 120° C.

Background of the invention

Formulations with oxidation sensitive compounds such as fat-soluble vitamins, especially vitamin A, vitamin D and any derivatives and mixtures thereof, have a potential for oxidation processes already at ambient conditions while storing or transporting such formulations. Depending on the reaction velocity of such

exothermic degradation processes, the storage or transport temperature and the volume of the stored or transported formulation, heat accumulation can result which may lead to self-heating and even auto-ignition of such formulations.

To minimize the degradation processes and thus decreasing also the self-heating effect, the oxidation sensitive compounds have to be protected in a suitable matrix and form.

Formulations of vitamin A, vitamin D and any derivatives and mixtures thereof having a self-heating temperature ≥ 100°C, but lower than 120°C have to be stored and transported in flexible intermediate containers with a volume of < 450 l. Furthermore, they have to be classified as "Dangerous goods class 4.2" and special equipment has to be used for their storage and transport which adds to the overall costs of such formulation.

Formulations of vitamin A, vitamin D and any derivatives and mixtures thereof having a self-heating temperature ≥ 120°C (as measured as described below) are allowed to be stored and transported in containers, especially in **f**lexible **i**ntermediate **b**ulk **c**ontainer**s** ("FIBCs"), of volumes up to 3000 l (= 3 m^3), preferably in containers, especially in FIBCs, of volumes ranging from 450 l to 3000 l. Furthermore, no classification as "dangerous goods" is needed. For reasons of sustainability it is highly desired to use such containers, especially such FIBCs, i.e. such bigger bags of volumes up to 3000 l compared to smaller bags of volumes < 450 l : First, because due to their larger size, less bags are needed to store and transport the same amount of formulation. Second, since the containers, especially the FIBCs, until now are not re-usable, less bags have to be discarded.

Thus, there is the need to provide a formulation of vitamin A, vitamin A derivatives and any mixtures thereof and any of their mixtures with vitamin D which has a self-heating temperature ≥ 120°C so that it can be stored and transported in containers, especially in FIBCs, of volumes up to 3000 l, preferably in FIBCs of volumes ranging from 450 to 3000 l, more preferably in FIBCs of volumes ranging from 480 to 2000 l,

even more preferably in FIBCs of volumes ranging from 500 to 1500 l and from 500 to 1000 l, most preferably in FIBCs of volumes ranging from 600 to 800 l.

Detailed description

Thus, this need is fulfilled by the present invention, which is directed to a formulation with a self-heating temperature ≥ 120°C consisting of

a) a fat-soluble vitamin in an amount of at least 10 weight-%, whereby the fat-soluble vitamin is vitamin A or a derivative thereof and optionally vitamin D or a derivative thereof;
b) gelatin in an amount of at least 60 weight-%;
c) at least one antioxidant in an amount of ≤ 5 weight-%;
d) an anti-caking agent;
e) optionally an oil;
f) residual moisture;

whereby all amounts a) to e) sum up to 100 weight-% and are based on the total weight of a) to e).

The term "consisting of" means that the formulation does not comprise any further ingredients besides a) to f). It also means that the formulation does not comprise a lignosulfonate.

The amount of residual moisture is preferably at most 6 weight-%, more preferably at most 5 weight-%, even more preferably at most 3.5 weight-%, most preferably at most 2.5 weight-% and at most 2.0 weight-%, based on the total weight of the formulation, i.e. the total weight of a) to f).

Though the amount of antioxidant is low in these formulations, they show a self-heating temperature ≥ 120°C. Furthermore, they show a good stability and a good homogeneity in premixes. Since the formulations according to the present invention show a self-heating temperature ≥ 120°C and a $\Delta T < 60$ K, they can be transported in containers, especially in FIBCs ("**f**lexible **i**ntermediate **b**ulk **c**ontainer"), of volumes up to 3000 l, preferably in containers, especially in FIBCs, of volumes ranging from 450 l to 3000 l.

Determination of the self-heating temperature

The tests are performed according to Norm E-15188 and VDI 2263 Part 1.

The samples are placed in a cubic shaped wire basket (either 16 ml or 1000 ml) in the center of an oven. The temperature of the oven is measured at two spots and remains constant during the testing period (24 hours), i.e. so called "isoperibolic test".

The temperature probe for the sample is placed in the center of the sample. Then the sample temperature reaches a temperature being 2 K below the oven temperature the 24 hour testing period starts.

When the temperature difference "ΔT" between sample and oven is < 60 K, the test criteria according to UN Orange book "Manual of Tests and Criteria, 6th revised edition, chapter 33.3, Division 4.2 is passed, and the sample is considered as being self-heating stable according to the present invention.

When the temperature difference "ΔT" between sample and oven is > 60 K, the sample is considered as undergoing spontaneous ignition or dangerous self-heating.

As illustrated by the examples, the formulations of the present invention show a self-heating temperature ≥ 120°C and a ΔT < 60 K, especially on large scale production of several thousand tons.

Container

Any kind of container with a volume up to 3000 l, preferably with a volume ranging from 450 to 3000 l, more preferably with a volume ranging from 480 to 2000 l, even more preferably with a volume ranging from 500 to 1500 l and from 500 to 1000 l, most preferably with a volume ranging from 600 to 800 l, may be used.

A "**f**lexible **i**ntermediate **b**ulk **c**ontainer" ("FIBC"), "jumbo", "bulk bag", "super sack", "tote bag", or "big bag", is an industrial container made of flexible fabric that is designed for storing and transporting dry, flowable products, such as sand, fertilizer, and feed additives.

FIBCs are most often made of thick woven polyethylene or polypropylene, either coated or uncoated, and normally measure around 45–48 inches (114–122 cm) in diameter and varies in height from 100 to 200 cm (39 to 79 inches). Its capacity is normally around 1,000 kg or 2,200 lb, but the larger units can store even more. A bulk bag designed to transport one metric ton (0.98 long tons; 1.1 short tons) of material will itself only weigh 5–7 lb (2.3–5.0 kg).

Transporting and loading is done on either pallets or by lifting it from the loops. Bags are made with either one, two or four lifting loops. The single loop bag is suitable for one man operation as there is no need for a second man to put the loops on the loader hook. Emptying is made easy by a special opening in the bottom such as a discharge spout, of which there are several options, or by simply cutting it open.

In the present invention preferably a big bag with four lifting loops is used. Its volume preferably ranges from 480 to 2000 l, more preferably from 500 to 1500 l, even more preferably from 500 to 1000 l, most preferably from 600 to 800 l. A loading with 200 to 1500 kg of the formulation according to the present invention is preferred. More preferred is a loading with 300 to 1200 kg of the formulation according to the present invention. Most preferred is a loading with 500 to 900 kg of the formulation according to the present invention.

Thus, the present invention is also directed to a big bag, especially to a big bag with 3 or more lifting loops such as e. g. 4 lifting loops, having a volume ranging from 480 l to 2000 l and comprising a formulation according to the present invention with the preferences as given below.

It is especially advantageous if the FIBC has an "inliner", which protects its content from light, oxygen and water, as well as if it is a Type C FIBC. Openings at the top for loading and at the bottom for unloading are convenient. Therefore, such openings are preferably present. Such openings will be tightly closed during storage and transport.

Formulation

The formulation is described in more detail below. The essential ingredients and their amounts, as well as the ingredients being absent in the formulations are further disclosed.

As already stated the formulation of the present invention does not comprise any further ingredients besides a) to f). For reasons of clarity, however, the non-present ingredients are further exemplified and listed below.

Not present ingredients

In contrast to the formulations disclosed in EP 494 417 A2 the matrix of the formulations of the present invention does **not** comprise any of the following salts: water-soluble salts of carboxylic acids, sodium carbonate, potassium carbonate, calcium sulfate, and calcium phosphate. Examples of such water-soluble salts of carboxylic acids not being present in the matrix of the formulations of the present invention are: aluminum subacetate, sodium tartrate, sodium glutarate, sodium acetate, calcium acetate, sodium propionate, calcium propionate and sodium benzoate. Some of these salts may, however, be used as anti-caking agents during drying of the formulation, especially during the powder-catch process step. Preferably none of these salts is used in the manufacture of the formulations of the present invention; thus, the formulations of the present invention do not comprise any of these salts; i.e. no water-soluble salts of carboxylic acids, no sodium carbonate, no potassium carbonate, no calcium sulfate, and no calcium phosphate.

In EP-A 494 417 these salts are used for the cross-linking of the gelatin with a reducing sugar at temperatures ranging from 55°C to 85°C for 2-24 hours which was

believed to be necessary for stable formulations. The present invention showed that cross-linking with a reducing sugar is not necessary at all to obtain stable formulations.

The process of the present invention has the advantage that no organic solvent except water is used, so that the formulation according to the present invention is substantially free of organic solvents. “substantially free” means that the amount thereof is ≤ 5 weight-%, preferably ≤ 3 weight-%, more preferably ≤ 1 weight-%, even more preferably ≤ 0.5 weight-%, most preferably ≤ 0.1 weight-%.

Furthermore, the formulations according to the present invention do neither comprise any reducing sugars nor any non-reducing sugars.

An example of a non-reducing sugar is sucrose (= saccharose).

Examples of reducing sugars are aldohexoses and ketohexoses with a hydroxy group in α-position such as e.g. glucose, fructose, galactose and any mixture thereof.

Reducing disaccharides such as e.g. lactose and maltose and reducing oligosaccharides, as well as aldopentoses and ketopentoses with a hydroxy group in α-position are also not part of the formulation according to the present invention.

In the formulations of the present invention neither invert sugar nor glucose syrup nor high fructose corn syrup are present.

Preferably the formulations according to the present invention do not comprise any oligo- and polysaccharides in their matrix. Polysaccharides such as starch may, however, be used as anti-caking agent during the drying of the formulation according to the present invention.

Further ingredients that are not present in the formulations according to the present invention are polyhydric alcohols. Examples of absent polyhydric alcohols are glycerol, monoesters of glycerol with C_{1-5} monocarboxylic acids, monoethers of glycerol, diglycerol, triglycerol, polyglycerol, propylene glycol, dipropylene glycol, 1,3-butylene glycol, ethylene glycol, polyethylene glycol, sorbitol, xylitol, maltitol, erythritol, mannitol, etc.

Furthermore, no cross-linking agent such as e.g. acetaldehyde, glutaraldehyde or glyoxal are present in the formulations of the present invention.

Phenols with bulky alkyl groups such as e.g. **b**utylated **h**ydroxy**a**nisoles ("BHA") and **b**utylated **h**ydroxy**t**oluenes ("BHT") are also not present in the formulations of the present invention.

The BHA is preferably a mixture of 2-*tert*-butyl-4-hydroxy-anisole and 3-*tert*-butyl-4-hydroxy-anisole. The BHT is preferably 2,6-di-*tert*-butyl-p-cresol (IUPAC name = 2,6-di-*tert*-butyl-4-methylphenol).

Ethoxyquin, also known as "EMQ" (IUPAC name: 6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline), is also not present in the formulations of the present invention; whereas according to EP-A 494 417 the presence of ethoxyquin is necessary to obtain stable formulations.

Furthermore, no lignosulfonate is present in the formulations of the present invention. Non-limiting examples of lignosulfonates that are not present in the formulations of the present invention are: sodium lignosulfonate, ammonium lignosulfonate, magnesium lignosulfonate, calcium lignosulfonate; as well as any of their mixtures. Suppliers of lignosulfonates are: Borregaard Industries Limited, Norway; Burgo Group, Rayonier Advanced Materials, Wuhan Xinyingda Chemicals, Shenyang Xingzhenghe Chemical, Abelin Polymers, GREENAGROCHEM, Harbin Fecino Chemical, Karjala Pulp, Nippon Paper Industries, Pacific Dust Control, Sappi, The Dallas Group of America, Venki Chem and Xinyi Feihuang Chemical.

Essential ingredients

Fat-soluble vitamin

The term "fat-soluble vitamins" comprises for the purpose of the present invention vitamins A and/or D, and the corresponding derivatives such as esters, especially C_1-C_{20} alkyl esters, as well as any mixture thereof.

"Vitamin D" means either Vitamin D_3 (cholecalciferol) or Vitamin D_2 (ergocalciferol) or both.

"Vitamin D derivative" means any derivative of Vitamin D as for example 25-hydroxy vitamin D_3 (so-called "HyD"), 1,25-dihydroxy vitamin D_3 or 24,25-dihydroxy vitamin D_3.

Especially preferred examples of fat-soluble vitamins are vitamin A, vitamin A acetate, vitamin A propionate, vitamin A butanoate, vitamin A palmitate, vitamin D_3 and 25-hydroxy-vitamin D, as well as any mixture thereof. More preferred are vitamin A acetate, vitamin D_3 and any mixture thereof. Most preferred the fat-soluble vitamin is vitamin A acetate or a mixture of vitamin A acetate and vitamin D_3, preferably in a weight ratio of vitamin A acetate to vitamin D_3 ranging from 1:1 to 100:1, more preferably ranging from 10:1 to 85:1.

The amount of the vitamin A or its derivative thereof is chosen in such a way so that its final amount in the formulation is preferably in the range of from 10 to 29 weight-%, more preferably its final amount is in the range of from 12 to 24 weight-%, even more preferably its final amount is in the range of from 15 to 23 weight-% most preferably its final amount is in the range of from 17 to 22 weight-%, based on the total weight of a) to e). By disclosing these ranges any combination of any lower value with any other value to a range is also disclosed, i.e. 10-22 weight-%, 12-29 weight-%, 15-24 weight-% etc.

If a mixture of Vitamin A acetate and vitamin D_3 is used, the amount of vitamin A acetate is as given above for the vitamin A derivative and the amount of vitamin D3 is chosen in such a way so that its final amount in the formulation is preferably in the range of from 0.01 to 10 weight-%, more preferably its final amount is in the range of from 0.05 to 5 weight-%, even more preferably its final amount is in the range of from 0.1 to 3.5 weight-%, most preferably its final amount is in the range of from 0.3 to 2.5 weight-%, based on the total weight of a) to e). By disclosing these ranges any combination of any lower value with any higher value to a range is also disclosed, i.e. 0.01-5 weight-%, 0.05-10 weight-%, 0.1-5 weight-% etc.

When vitamin D, preferably vitamin D_3, is present in the formulation of the present invention advantageously also an oil is present.

Oil

The oils can be from any origin. They can be natural, modified or synthetic. If the oils are natural they can be plant or animal oils. Thus, the term "oil" encompasses any vegetable oil or fat like corn oil, sunflower oil, soybean oil, safflower oil, rapeseed oil, peanut oil, palm oil, palm kernel oil, cotton seed oil, olive oil, coconut oil, canola oil, sesame oil, hazelnut oil, almond oil, cashew oil, macadamia oil, mongongo nut oil, pracaxi oil, pecan oil, pine nut oil, pistachio oil, sacha Inchi (Plukenetia volubilis) oil, walnut oil, as well as **m**iddle **c**hain **t**riglycerides ("MCT") and any mixture thereof. Preferably corn oil, peanut oil, safflower oil or sunflower oil are used.

The weight ratio of vitamin D to the oil is preferably ranging from 1:1 to 1:10, more preferably from 1:2 to 1:5.

Gelatin

Suitable gelatins are poultry gelatin, porcine gelatin, bovine gelatin and any mixture thereof, as well as fish gelatin and any mixture with the other gelatins. The gelatin is generally classified according to its Bloom value.

There are two types of gelatins: Type A gelatin is obtained from acid processing of collagen. Type B gelatin is obtained from alkaline processing of collagen.

Bloom is a test to measure the strength of a gel of gelatin. The test determines the weight (in grams) needed by a probe (normally with a diameter of 0.5 inch) to deflect the surface of the gel 4 mm without breaking it. The result is expressed in bloom (grades). In general gelatins with a Bloom ranging from 0 to 300 may be used.

Low bloom, medium bloom and high bloom gelatin are gelatins having a strength of less than about 120 Bloom (low Bloom), between about 120 and up to 200 Bloom (medium Bloom) or a strength of more than about 200 Bloom (high Bloom).

Low bloom gelatin, preferably gelatin with Bloom ranging from 0 to <120, more preferably gelatin with 60-110 Bloom, even more preferably gelatin with 70-90 Bloom, most preferably gelatin with 80 Bloom, can be used as well as medium bloom gelatin,-preferably-gelatin with 120-160 Bloom, more preferably gelatin with 140 Bloom, and high Bloom gelatin, preferably gelatin with 200-300 Bloom, more preferably gelatin with 200-270 Bloom, even more preferably gelatin with 200-250 Bloom, most preferably gelatin with 200 Bloom.

The amount of gelatin in the formulations of the present invention is chosen in such a way so that its final amount in the formulation is preferably at least 62 weight-%, more preferably at least 65 weight-%, even more preferably at least 68 weight-%, most preferably at least 70 weight-%, based on the total weight of a) to e). The maximum amount of gelatin in the formulation may preferably be 88 weight-%, more preferably 85 weight-%, even more preferably 82 weight, and most preferably 80 weight-%, based on the total weight of a) to e).

By disclosing these lower and higher values any combination of any lower value with any higher value to a range is also disclosed, i.e. 62-80 weight-%, 68-80 weight-%, 65-85 weight-% etc.

Antioxidant

The antioxidant may be a water-soluble antioxidant or a fat-soluble antioxidant or any mixture thereof. Thus, mixtures of water-soluble antioxidants, mixtures of fat-soluble antioxidants and mixtures of one or more water-soluble antioxidants and one or more fat-soluble antioxidants are also included in the term "antioxidant". Preferred are fat-soluble antioxidants as well as mixtures thereof and mixtures of water- and fat-soluble antioxidants. Inorganic antioxidants may also be present.

Examples of inorganic antioxidants are $NaBH_4$, Na_2SO_3 and/or $Na_2S_2O_3$.

Examples of fat-soluble antioxidants are ascorbyl palmitate, polyphenols, flavones being substituted with one or more hydroxy groups, isoflavones being substituted with one or more hydroxy groups, tocotrienols and analogues thereof, tocopherols and analogues thereof, or any mixture thereof. Preferred examples of fat-soluble antioxidants are ascorbyl palmitate, tocotrienols and analogues thereof, tocopherols and analogues thereof, or any mixture thereof.

Analogues of tocopherols and tocotrienols are especially compounds with a shorter side chain in position 2 compared to tocopherols and tocotrienols.

Examples of flavones substituted with one or more hydroxy groups are: 6-hydroxyflavone, 5,7-dihydroxyflavone (= chrysin), 4',5,7-trihydroxyflavone (= apigenin), 3',4',5,7-tetrahydroxyflavone (luteolin) and 4',5,6,7,8-pentamethoxy-flavone (tangeritin).

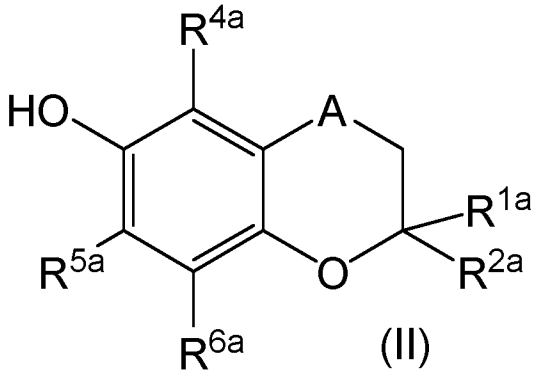
Examples of isoflavones substituted with one or more hydroxy groups and optionally methoxy groups are daidzein (= 4',7-dihydroxyisoflavone), genistein (= 4',5,7-trihydroxyisoflavone), prunetin (= 4',5-dihydroxy-7-methoxyisoflavone), biochanin A (= 5,7-dihydroxy-4'-methoxy-soflavone), orobol (= 3',4',5,7-tetrahydroxyisoflavone), santal (= 3',4',5-trihydroxy-7-methoxy-isoflavone) and pratensein (= 3',5,7-trihydroxy-4'-methoxyisoflavone).

Examples of water-soluble antioxidants are ascorbic acid and its salts such as e.g. sodium ascorbate, citric acid and its salts such as e.g. sodium citrate, as well as any mixture thereof.

Examples of mixtures of water- and fat-soluble antioxidants are tocopherol and sodium ascorbate, tocopherol and ascorbic acid, whereby the tocopherol may be alpha-, beta-, gamma- or delta-tocopherol, preferably whereby the tocopherol is alpha- or delta-tocopherol, more preferably whereby the tocopherol is alpha-tocopherol, most preferably whereby the tocopherol is DL-alpha-tocopherol.

Tocopherols, tocotrienols and analogues thereof

Examples of suitable tocopherols and analogues thereof are e.g. compounds of formula (II)



(II)

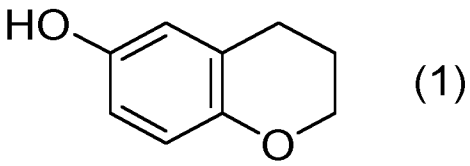
wherein R^{1a} and R^{2a} are independently from each other H or C_{1-11}-alkyl or $(CH_2)_n$—OH with n being an integer from 1 to 4, or R^{1a} and R^{2a} represent together a keto group, A is CHR^{3a} or C(=O), and wherein R^{3a}, R^{4a} and R^{6a} are independently from each other H or C_{1-4}-alkyl, and wherein R^{5a} is H or OH or C_{1-4}-alkyl or C_{1-4}-alkoxy, as disclosed in WO 2019/185894.

Further suitable tocopherols are compounds of formula (II), wherein one of the two substituents R^{1a} and R^{2a} is C_{12-21}-alkyl and the other of the two substituents R^{1a} and R^{2a} is either hydrogen or C_{1-5}-alkyl or $(CH_2)_n$-OH with n being an integer from 1 to 5, and wherein A is $CH(R^{3a})$, and wherein R^{3a}, R^{4a} and R^{6a} are independently from each

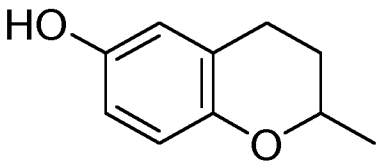
other H or C_{1-4}-alkyl, and wherein R^{5a} is H or OH or C_{1-4}-alkyl or C_{1-4}-alkoxy, as disclosed in WO 2019/185938.

Compounds of formula (II), wherein A is CH_2, R^{1a} is C_{1-5}-alkyl, R^{2a} is either H or C_{1-2}-alkyl, R^{5a} is either H or C_{1-4}-alkoxy or C_{1-4}-alkyl, and R^{4a} and R^{6a} are independently from each other either H or C_{1-4}-alkyl, with the preferences as disclosed in WO 2019/185900 are also suitable antioxidants in the formulations of the present invention.

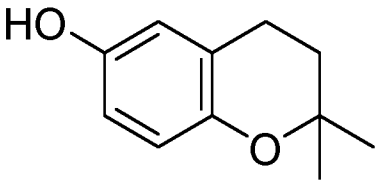
Preferred examples of the antioxidants of formula (II) as disclosed in WO 2019/185894 are the following compounds of formula (1)-(11) with "Me" being methyl:



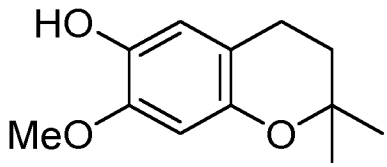
(1)



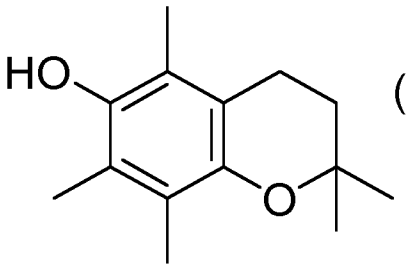
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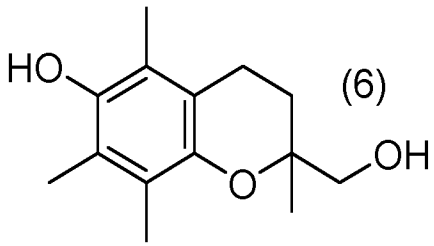
(3)



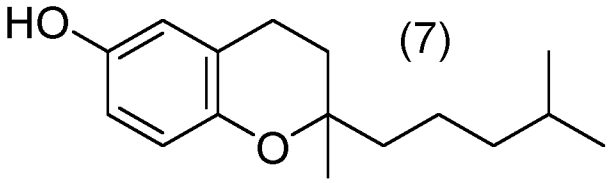
(4)



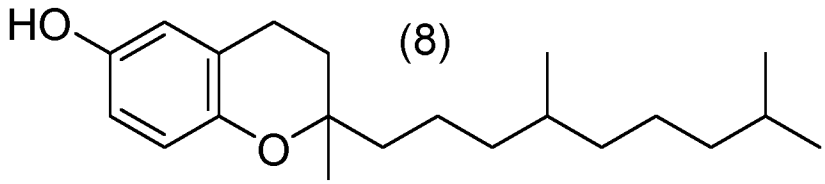
(5)



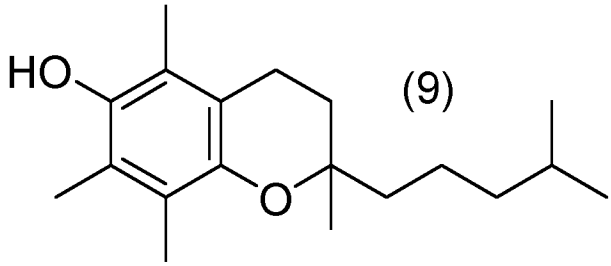
(6)



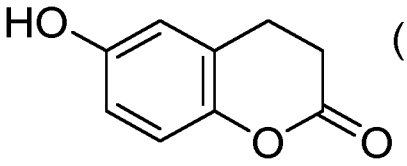
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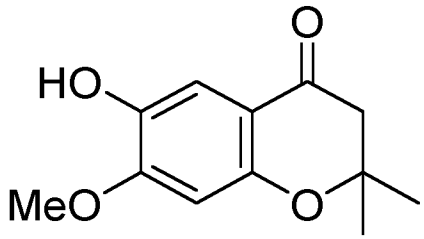
(8)



(9)

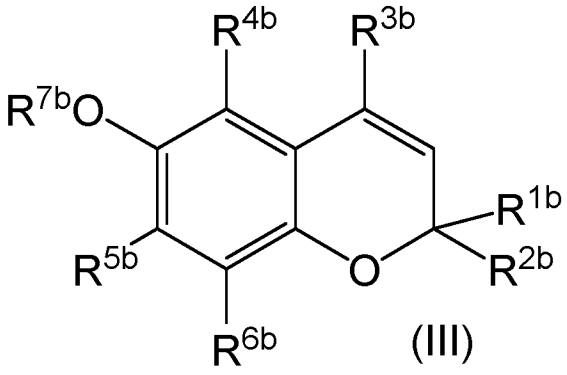


(10)

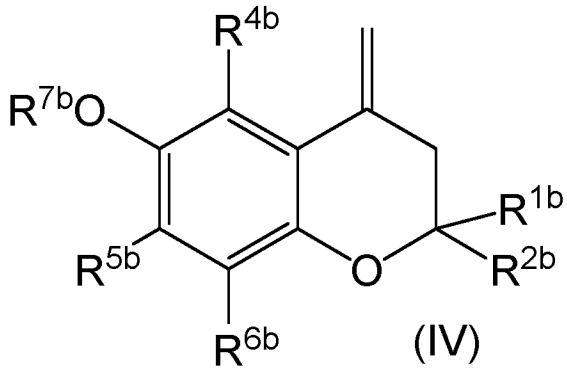


(11)

Further examples of suitable antioxidants that can be used in the formulations of the present invention are compounds of formula (III) and (IV),



(III)

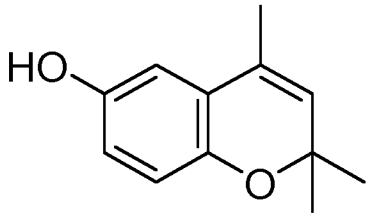


(IV)

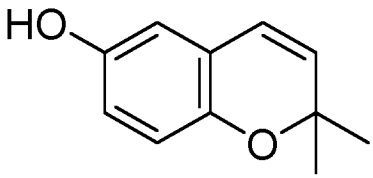
wherein R^{1b} and R^{2b} are independently from each other H or C_{1-11}-alkyl or $(CH_2)_n$—OH with n being an integer from 1 to 6 or R^{1b} and R^{2b} together represent a keto group, and wherein R^{3b}, R^{4b}, R^{5b}, and R^{6b} are independently from each other H or C_{1-6}-alkyl or C_{1-6}-alkoxy, and R^{7b} is H or C_{1-6}-alkyl, as disclosed in WO 2019/185898.

"alkyl" and "alkoxy" hereby encompass linear alkyl and branched alkyl, and linear alkoxy and branched alkoxy, respectively.

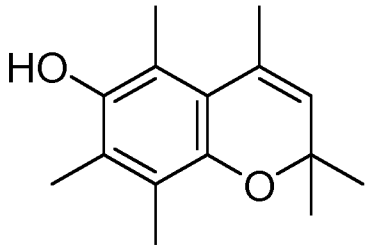
Preferred examples of compounds of formula (III) and (IV) are the following compounds (12)-(19):



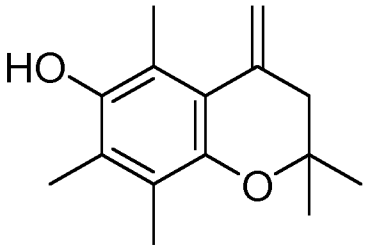
(12)



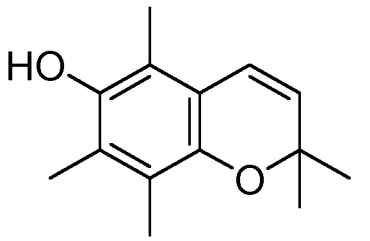
(13)



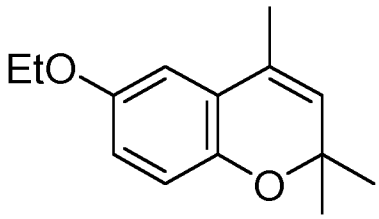
(14)



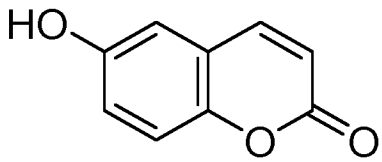
(15)



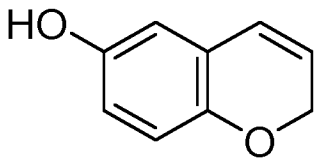
(16)



(17)

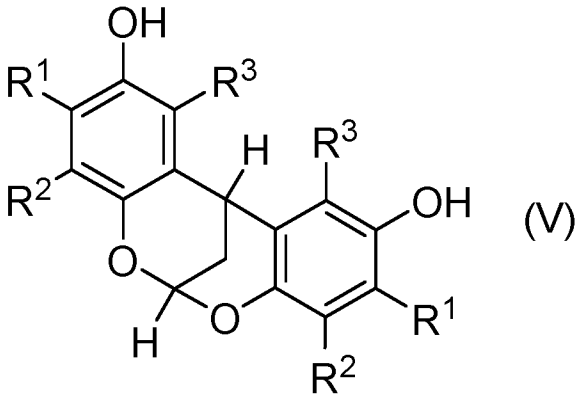


(18)



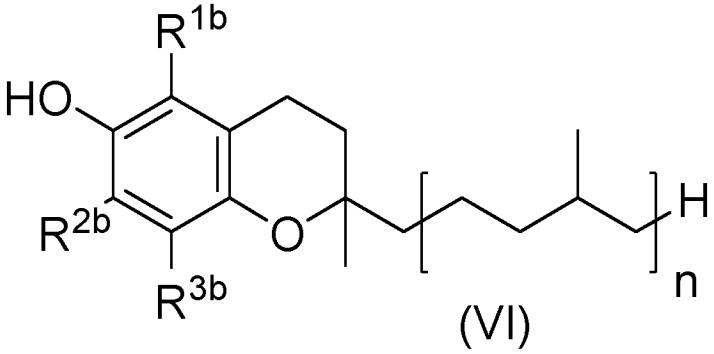
(19)

Further suitable antioxidants are compounds of formula (V), whereby R^1, R^2 and R^3 are independently from each other H or linear C_{1-6}-alkyl or branched C_{3-8}-alkyl, whereby preferably R^1 is H or methyl or ethyl or *n*-propyl or *iso*-propyl or *tert*-butyl and R^2 and R^3 are independently from each other H or methyl or ethyl, with the further preferences as disclosed in WO 2019/185940.



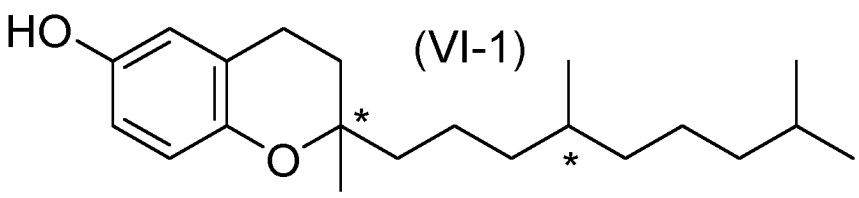
(V)

Also, the compounds of formula (VI) with n being 1 or 2, R^{1b} and R^{3b} being independently from each other H or C_{1-5}-alkyl, and R^{2b} being either H or C_{1-5}-alkyl or C_{1-5}-alkyloxy, preferably with the proviso at least one of R^{1b}, R^{2b} and R^{3b} being H, as disclosed in WO 2019/185904 can be used as antioxidants in the formulations of the present invention.

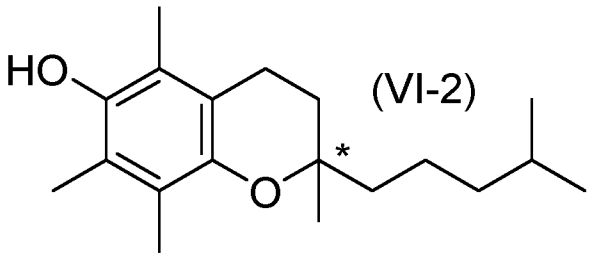


(VI)

Hereby the following compounds of formulae (VI-1) and (VI-2) are especially preferred:

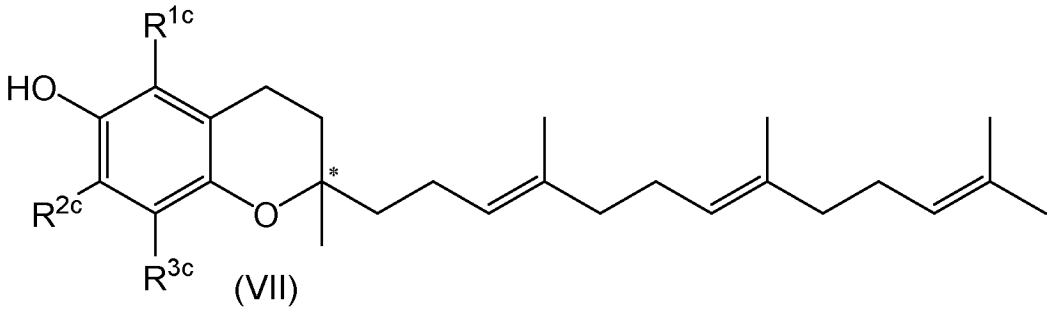


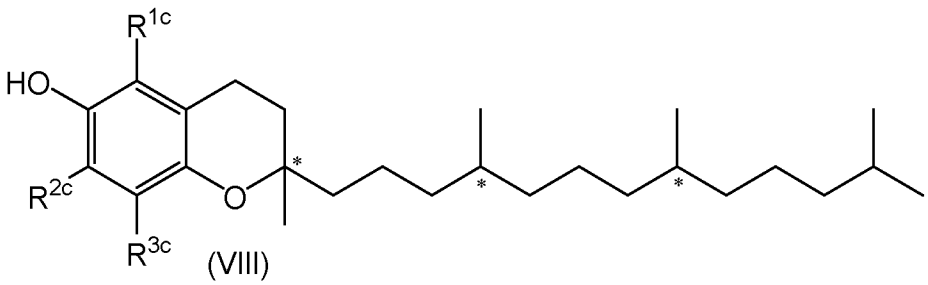
(VI-1)



The asterisks * mark each a chiral/stereogenic center, i.e. all possible isomers having any configuration at said centers are encompassed by the term “compound of formula (VI-1)” and “compound of formula (VI-2)”, respectively.

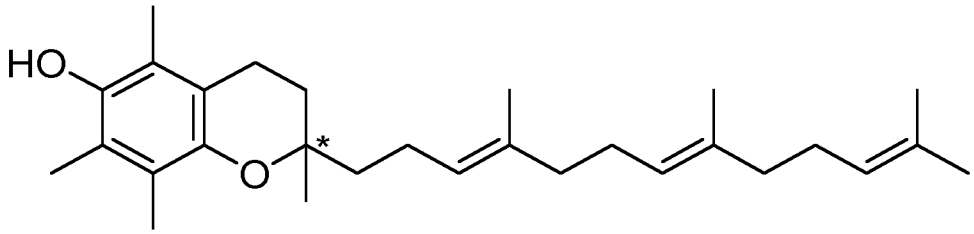
Also, suitable antioxidants are compounds of the following formulae (VII) and (VIII) with R^{1c}, R^{2c} and R^{3c} being independently from each other H or C_{1-4}-alkyl as published in WO 2019/185942 and WO 2019/185888, respectively. Preferred examples thereof are tocotrienols and tocopherols of the formulae (20) to (27) as shown below.



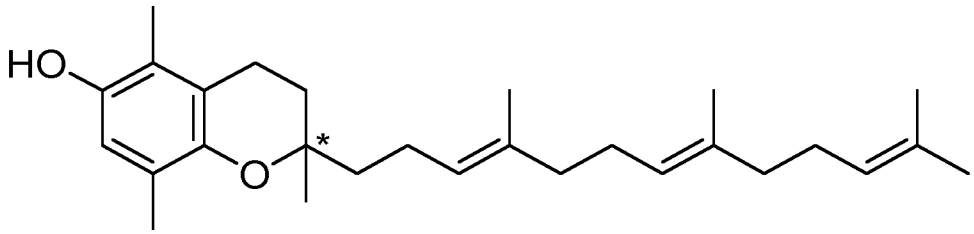


The asterisks * mark each a chiral/stereogenic center. The term “compound of formula (VII)/(VIII)” encompasses all possible isomers having any configuration at said centers.

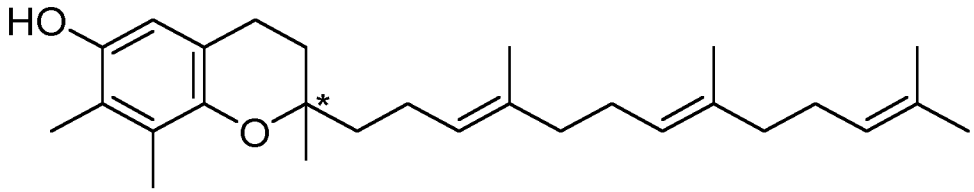
Especially preferred examples of the compound of formula (VII) are the following compounds of formulae (20) (= alpha-tocotrienol), (21) (= beta-tocotrienol), (22) (= gamma-tocotrienol) and (23) (= delta-tocotrienol), whereby all possible diastereomers and enantiomers are included.



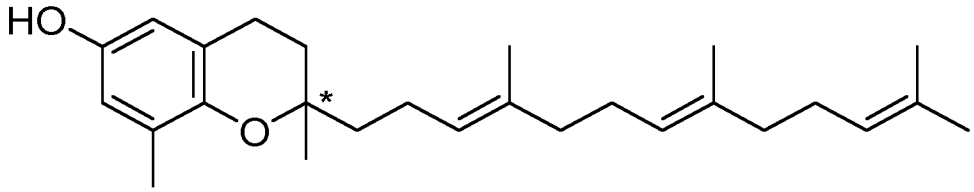
(20)



(21)

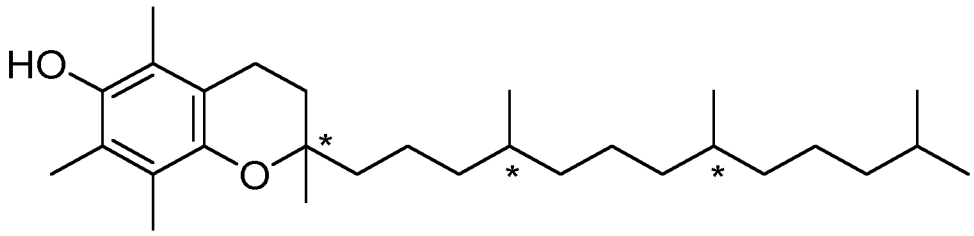


(22)

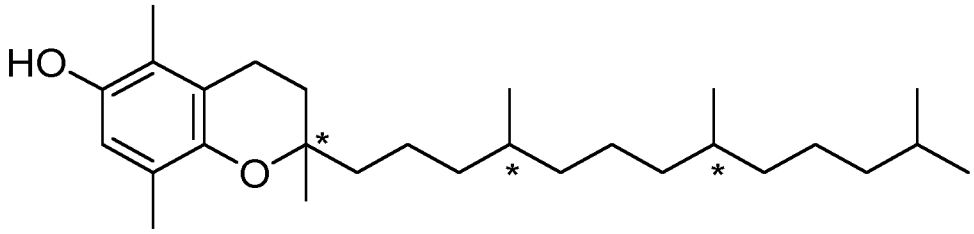


(23)

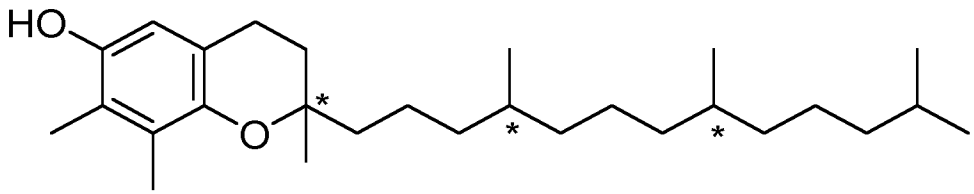
Especially preferred examples of the compound of formula (VIII) are the following compounds of formulae (20) (= alpha-tocopherol), (21) (= beta-tocopherol), (22) (= gamma-tocopherol) and (23) (= delta-tocopherol), whereby all possible diastereomers and enantiomers are included.



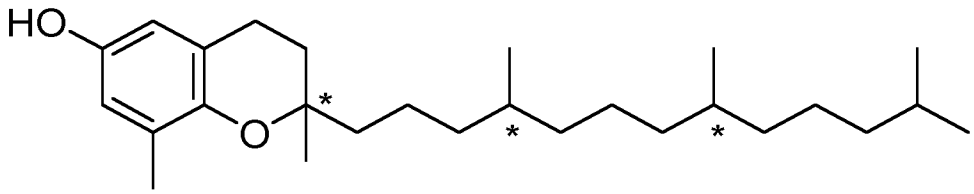
(24)



(25)



(26)



(27)

The asterisks * mark each a chiral/stereogenic center. The term "compound of formula (20)/(21)/(22)/(23)/(24)/(25)/(26)/(27)" encompasses all possible isomers having any configuration at said centers.

Polyphenols

Examples of suitable polyphenols are 2,4,5-trihydroxybutyrophenone, epigallo-catechin gallate ("EGCG"), epigallo-catechin, gallo-catechin, hydroxytyrosol, resveratrol, carnosol, 2-(3,4-dihydroxyphenyl)acetic acid and C_{1-6} alkyl esters thereof, and any mixture thereof.

Further suitable polyphenols are derivatives, preferably esters and (earth) alkali metal salts, of hydroxybenzoic acids such as e.g. gallic acid (= 3,4,5-trihydroxybenzoic

acid) and syringic acid (= 4-hydroxy-3,5-dimethoxy-benzoic acid). Examples of preferred esters are C_{1-20} alkyl esters of gallic acid such as e.g. propyl gallate, octyl gallate or dodecyl gallate, and C_{1-20} alkyl esters of syringic acid.

Also, derivatives, preferably esters and (earth) alkali metal salts, of cinnamic acid and hydroxycinnamic acids such as e.g. ferulic acid (= 3-(4-hydroxy-3-methoxyphenol)prop-2-enoic acid), caffeic acid (= 3,4-Dihydroxycinnamic acid), dihydrocaffeic acid (= 3-(3,4-dihydroxyphenyl) propanoic acid), chlorogenic acid (= the ester of caffeic acid and (-)-quinic acid), o-, m-, p-coumaric acid (= 2-/3-/4-hydroxycinnamic acid), rosmarinic acid (= a caffeic acid ester of 3-(3,4-dihydroxyphenyl)lactic acid), or sinap(in)ic acid (= 3,5-dimethoxy-4-hydroxycinnamic acid) may be used as antioxidants in the present invention.

Examples of derivatives of cinnamic acid are Z-ethoxyethyl p-methoxycinnamate, ethylhexyl p-methoxycinnamate, 2-ethylhexyl 4-methoxycinnamate, methyl diiso-propylcinnamate, isoamyl 4—methoxycinnamate, and diethanolamin 4-methoxy-cinnamate.

The most preferred antioxidants used in the formulation of the present invention are DL-alpha-tocopherol, as well as a mixture of DL-alpha-tocopherol and sodium ascorbate, a mixture of DL-alpha-tocopherol and ascorbic acid and a mixture of DL-alpha-tocopherol and ascorbyl palmitate.

The weight ratio of DL-alpha-tocopherol to sodium ascorbate and of DL-alpha-tocopherol to ascorbic acid is preferably ranging from 5:1 to 1:5, more preferably from 3:1 to 1:3, even more preferably from 2:1 to 1:2, most preferably from 1.1:1 to 1:1.1.

Surprisingly the total amount of the antioxidant(s) in the formulations of the present invention is lower than in gelatin-based formulations already being on the market.

Preferably the total amount of the antioxidant(s) is chosen in such a way so that its/their final amount in the formulation is preferably ≤ 4.8 weight-%, more preferably its/their final amount is in the range of from 0.1 to 4.5 weight-% and from 0.2 to 4.0 weight-%, even more preferably its/their final amount is in the range of from 0.3 to 3.5 weight-% and from 0.5 to 3.0 weight-%, most preferably its/their final amount is in the range of from 0.6 to 2.8 weight-% and from 0.8 to 2.5 weight-%, based on the total weight of a) to e) in the formulation. By disclosing these ranges any combination of any lower value with any higher value to a range is also disclosed, i.e. at least 0.5 and at most 4.8 weight-%, 0.6 to 4.5 weight-%; etc.

In the following **Table I** the preferred amounts for specific antioxidants in addition to the ranges above are given:

Table I: All amounts are given in weight-% and are based on the total weight of a), b), c), d) and e) in the formulation.

Antioxidant	**Preferred amount, based on the total weight of the formulation**	**More preferred amount, based on the total weight of the formulation**	**Most preferred amount, based on the total weight of the formulation**
DL-alpha-tocopherol	0.1-3.0	0.2-2.5	0.4-1.6
DL-alpha-tocopherol and ascorbic acid	0.6-2.5	0.8-2.2	1.4-2.1
DL-alpha-tocopherol and sodium ascorbate	0.6-2.5	0.8-2.2	1.4-2.1

Also, within a row any value may be combined with any value of another column.

It is assumed that the amount of other tocopherols or analogues thereof, as well as of tocotrienols and analogues thereof is in a similar range as for DL-alpha-tocopherol.

Anti-caking agent

Suitable organic anti-caking agents are corn starch, as well as starches from other botanical sources such as e.g. as waxy corn, wheat, tapioca, pea and potato, as well as derivatives thereof such as pre-gelatinised starch, starch ethers (e.g. carboxymethyl starch), starch esters (e.g. starch monophosphate, alkenyl-succinated starch, especially octenyl-succinated starch), cross-linked starch and oxidized starch and any mixture thereof. Other suitable organic anti-caking agents are talc, cellulose, microcrystalline cellulose, cellulose derivatives or fibres, ferric ammonium citrate, sodium salts of fatty acids such as e.g. sodium stearate, potassium salts of fatty acids such as e.g. potassium stearate, calcium salts of fatty acids such as e.g. calcium stearate, magnesium salts of fatty acids such as e.g. magnesium stearate, aluminum salts of fatty acids such as e.g. aluminum stearate, ammonium salts of fatty acids such as e.g. ammonium stearate, and any mixture of any of them.

Other suitable anti-caking agents are inorganic anti-caking agents such as e.g. silicic acid $H_{2n+2}Si_nO_{3n+1}$ and alkaline/earth alkali metal salts thereof, precipitated silicic acid, silica (= silicon dioxide), modified silica, hydrophobically modified silica, precipitated silica, magnesium oxide, dicalcium diphosphate, tricalcium phosphate, magnesium phosphate, sodium carbonate, potassium carbonate, calcium carbonate, magnesium carbonate, calcium oxide, magnesium oxide, potassium silicate, calcium silicate, magnesium silicate, magnesium trisilicate, aluminum silicate, sodium aluminum silicate, potassium aluminum silicate, calcium aluminum silicate, zeolithe (aluminosilicates), disodium sulfate or mixtures thereof. Further suitable inorganic anti-caking agents are bentonite and kaolin.

Also, mixtures of organic and inorganic anti-caking agents may be used.

The preferred anti-caking agents used in the formulations of the present invention are anti-caking agents with a particle size D(v,50%) from 100 nm to 10 μm, preferably from 100 nm to 9 μm, more preferably from 150 nm to 5 μm, measured as dry dispersion with a Malvern MasterSizer 3000 (laser diffraction).

The particle size of the anti-caking agent can be determined with a laser diffraction system e.g. Malvern MasterSizer 3000, either as dry dispersion or as wet dispersion in oil or Volasil (a mixture of volatile and cyclic silicones such as octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane). The particle size can also be determined with electron microscopy.

The more preferred anti-caking agents are silicic acid $H_{2n+2}Si_nO_{3n+1}$, silica, microcrystalline cellulose, as well as any mixture thereof.

The most preferred anti-caking agents are hydrophilic precipitated silicic acid $H_{2n+2}Si_nO_{3n+1}$, hydrophilic precipitated silica and any mixture thereof.

The amount of the anti-caking agent is chosen in such a way so that its final amount in the formulation is preferably ranging from 1 to 10 weight-%, more preferably ranging from 3 to 9 weight-% and from 4 to 8 weight-%, most preferably ranging from 4.5 to 7.5 weight-%, based on the total weight of a), b), c), d) and e). By disclosing these ranges any combination of any lower value with any higher value to a range is also disclosed, i.e. 1-7.5 weight-%, 4.5-10 weight-% etc.

Characteristics of the formulations of the present invention

The formulations of the present invention show preferably a bulk density ranging from 0.58-0.67 g/cm^3, more preferably a bulk density ranging from 0.60-0.65 g/cm^3.

Furthermore, the formulations of the present invention show preferably a tap density ranging from 0.6-0.7 g/cm^3, more preferably a tap density ranging from 0.64-0.69 g/cm^3, most preferably a tap density ranging from 0.65-0.68 g/cm^3.

The bulk density and the tap density are measured as follows:

A 250 ml glass cylinder is filled with the sample. The volume and the weight are measured. Bulk density is the weight divided by the volume.

For measuring the tap density the sample is tapped with a 2000 Taps with a Stampfvolumeter JEL STAV II (J. Engelsmann AG). The tapped volume is measured. Tap density is the weight divided by the tapped volume.

Preferably the formulations of the present invention show besides the bulk density and/or tap density above, also the particle sizes and/or particle size distribution as cited below, which results in a very good homogeneity when mixed into feed.

The amount of residual moisture in the final formulation is preferably ranging from 0.1-8.0 weight-%, more preferably ranging from 0.5 to 7.0 weight-%, most preferably ranging from 1.0 to 6.0 weight-%, based on the total weight of the formulation, i.e. the total weight of a), b), c), d), e) and f). By disclosing these ranges any combination of any lower value with any higher value to a range is also disclosed, i.e. 1.0-8.0 weight-%, 0.5-6.0 weight-% etc.

When step E) of the process according to the present invention is performed the moisture content is lower than without step E) being performed.

Particle size and measurement

To determine the particle size of the solid formulation of the present invention a sieve test can be performed with filters of 850 µm pores (mesh 20), 425 µm pores (mesh 40) and 150 µm pores (mesh 100).

Furthermore, the particle size of the solid formulation may also be determined by laser diffraction analytic whereby the dry dispersion of the sample is measured with a Malvern Mastersizer 2000 or 3000 and Fraunhofer calculation.

The particle sizes of the formulation, when determined with laser diffraction with a Malvern Mastersizer 3000 and Fraunhofer calculation, are as follows:

D(v,10%) = 200-280 μm;

D(v, 50%) = 290-370 μm;

D(v, 90%) = 400-500 μm.

Synonyms of "D(v,10%)" are "d(v,10%)", "d(v,10)", "d(v,0.1)", "D(v,10)" and "D(v,0.1)". This applies in an analogous manner for "D(v,50%)" and "D(v,90%)".

Process for the manufacture of the formulation

The formulation of the present invention is preferably manufactured according to a process comprising the following steps:

A) Dissolving gelatin b) and, if present, a water-soluble antioxidant c) in water to obtain a matrix;

B) Heating the fat-soluble vitamin a), the fat-soluble antioxidant c) and, if present, the oil to obtain an active phase;

C) Emulsifying the active phase obtained in step B) into the matrix obtained in step A) to obtain a dispersion;

D) Spray-drying the dispersion obtained in step C) in presence of an anti-caking agent to obtain the formulation.

The single steps are disclosed in more detail below. Further details, that may also be generalized, are given in the examples.

Step A)

The amounts of the gelatin b), and if present, the water-soluble antioxidant c) are chosen so that the final amounts of these compounds in the solid formulation after having performed steps A) to D) and A) to E), respectively, is as described above.

Step A) is preferably performed at a temperature ranging from 40 to 80°C, more preferably ranging from 50 to 75°C, most preferably ranging from 55 to 70°C.

Step B)

The amounts of the fat-soluble vitamin a), the fat-soluble antioxidant c) and, if present, the oil are chosen so that the final amounts of these compounds in the solid formulation after having performed steps A) to D) and A) to E), respectively, is as described above.

Step B) is preferably performed at a temperature to bring the components a) and c) into a liquid state.

When vitamin D, preferably vitamin D_3, is present in the formulation of the present invention, the vitamin D is preferably added to the other fat-soluble vitamin and the fat-soluble antioxidant as oily suspension, whereby the weight ratio of vitamin D to the oil is preferably ranging from 1:1 to 1:10, more preferably from 1:2 to 1:5.

If only vitamin D, preferably vitamin D_3, is present in the formulation of the present invention, the vitamin D is preferably added to the fat-soluble antioxidant as oily suspension, whereby the weight ratio of vitamin D to the oil is preferably ranging from 1:1 to 1:10, more preferably from 1:2 to 1:5

Step C)

Preferably this step is performed at a mixing temperature in the range of from 40 to 75°C, more preferably at a mixing temperature in the range of 50 to 70°C, even more preferably at a mixing temperature in the range of 55°C to 65°C to obtain a dispersion.

The homogenization can be achieved by using a rotor-stator device or a high-pressure homogenizer or both. Other devices known to the person skilled in the art may also be used.

Step D)

The dividing and drying of the mixture of the oil-in-water preparation to produce the solid formulation according to the present invention can be done in any conventional way, such as spray cooling, modified spray cooling, spray drying,

spray-drying in combination with fluidized bed granulation, modified spray drying or sheet drying and crushing, see e.g. WO 91/06292 A1.

Preferably the conversion to the solid formulation is achieved by a powder-catch technique, whereby the sprayed dispersion droplets are caught by the anti-caking agent (so-called "catch media"), and dried.

Step E)

It is advantageous to treat the powder obtained after having performed step D) thermally. Hereby preferably temperatures of up to 125°C are applied, more preferably the thermal treating is carried out at a temperature ranging from 80-120°C, even more preferably the thermal treating is carried out at a temperature ranging from 100 to 120°C, most preferably the thermal treating is carried out at a temperature ranging from 110 to 120°C. Hereby the amount of moisture in the formulation is decreased.

Preferably the process for the manufacture of the formulation according to the present invention does neither comprise a crosslinking step performed by exposure to radiation nor does it comprise a crosslinking step performed by using an enzyme.

Further embodiments of the present invention

Use

The present invention is also directed to the use of the formulation according to the present invention with the preferences as given above as additive to feed or premixes.

Feed additive, premix and feed according to the present invention

The present invention is also directed to a feed additive, a premix and a feed comprising the formulation according to the present invention with the preferences as given above. Feed (or 'feedingstuff') means any substance or

product, including additives, whether processed, partially processed or unprocessed, intended to be used for oral feeding to animals.

Feed in the context of the present invention is especially feed for broilers including starter, grower, finisher; broiler breeders including starter, grower (pullets), layers and male breeders, for layers and other poultry such as e.g. hens and duck layers, layers breeders, ducks and geese, partridges, quails and pheasants, ostrich and emu, for turkeys including starter, grower, finisher; for turkey breeders including starter, grower, layers and male breeders, for ruminants including calves, milk replacer, heifers, beef cattle, breeding bulls, sheep and goats; for horses, especially foals, leisure horses, race horses, mares and stallions, for rabbits, for mick and foxes, for swine including fattening pigs: pre-starter, starter, grower, finisher; breeders: replacement gilts, sows, boars, and feed for companion animals, especially for dogs and cats.

The amount of the formulation and the fat-soluble vitamin respectively follows the regulatory guidelines in the regions depending on the specific animal species and its age.

In the Supplementation Guidelines the amount of the vitamins A and D_3 is given in International Units ("I.U.").
To ensure that the active content in the feed is communicated in a systematic way, "I.U." is used as a universal unit for fat soluble vitamins because there are different forms of the vitamins with varying amounts of fat-soluble vitamins.

The formulation according to the present invention is usually added to feed in form of a premix, i.e. a mixture with other micro-nutrients such as other vitamins or their formulations and minerals. The premix inclusion in feed is < 1 weight-% for many species.

The amount of the formulation according to the present invention needed to be included into the feed is calculated based on the active content of the feed and the

targeted dosage of the fat-soluble vitamin in the final feed considering said inclusion level.

The conversion factors of the fat-soluble vitamins are as follows:

1 I.U. Vitamin A corresponds to 0.344 µg of Vitamin A acetate;
1 I.U. Vitamin D_3 corresponds to 0.025 µg of Vitamin D_3.

The following **Table IV** shows the amounts of the fat-soluble vitamins added per kg of air-dry feed. The exact amount is depending on several factors such as phase/age of the animal, animal species and legal local limits.

Table IV

Animal	**Vitamin A [I.U.]**	**Vitamin D_3 [I.U.]**	**HyD [mg]**
Broilers	10000-15000	3000-5000	—
Turkeys	6000-15000	3000-5000	0.092
Layers & other poultry	8000-16000	3000-5000	0.069
Swine	5000-20000	1000-2000	0.05
Ruminants	20000-150000	400-40000	—
Horses	25000-80000	3500-8500	—
Rabbits	8000-12000	800-1200	—
Mink & Foxes	10000-15000	1500-2000	—
Dogs	7100-23000	640-1100	—
Cats	9000-25000	750-1300	—
Fish & Shrimps	4000-12000	1500-6500	—

Below are given non-limiting examples of feed to which the formulations of the present invention may be added.

Feed for poultry

The feed for poultry differs from region to region. In the following **Tables V and VI** typical examples for diets in Europe and Latin America are given. These diets include cereals such as wheat, rye, maize/corn, minerals such as NaCl, vegetable oils such as soya oil, amino acids and proteins.

Thus, the present invention is also directed to feed for poultry comprising the formulation according to the present invention; preferably to feed for poultry comprising the formulation according to the present invention and cereals, minerals, vegetable oils, amino acids and proteins.

Table V: European diet

Ingredients (%)	**Starter Period (day 0-21)**	**Grower Period (day 22-36)**
Wheat	20.00	22.50
Rye	12.00	12.00
Soybean meal	34.00	28.50
Maize	27.00	28.50
Vegetable Oil	3.10	4.20
NaCl	0.10	0.10
DL Methionine	0.24	0.24
L-Lysine	0.15	0.15
Limestone	0.85	0.85
Dicalcium Phosphate	1.50	1.90
Vitamin & Mineral mix	1.00	1.00
Coccidiostat (Avatec)	0.06	0.06
TiO_2	-	0.10
calculated Provision		
apparent metabolizable energy, MJ/kg	12.5	12.90
apparent metabolizable energy, kcal/kg	2986	3082

crude Protein, %	21.2	19.1
Methionine + Cysteine, %	0.89	0.83
Lysine, %	1.23	1.09
Calcium, %	0.83	0.91
total phosphorus, %	0.68	0.73
available phosphorus, %	0.35	0.40

Table VI: Latin American diet

Ingredients (%)	**Starter**	**Grower**
Corn	53.0	57.1
Soybean meal	38.5	34.2
Calcium	0.70	0.70
Phosphorus	2.40	2.00
$NaHCO_3$	0.23	0.24
NaCl	0.20	0.20
Methionine	0.30	0.10
Lysine	0.21	0.00
Soya Oil	3.50	4.50
Premix	1.00	1.00
Calculated provision (%)		
Crude protein	22.4	20.4
apparent metabolizable energy, (MJ/kg)	12.7	13.2
apparent metabolizable energy, (kcal/kg)	3034	3154
Total phosphorus	0.86	0.76
Calcium	1.00	0.85
Available phosphorus	0.44	0.38
d-Lysine	1.25	0.98
d-Methionine + Cysteine	0.91	0.68
d-Threonine	0.77	0.71
Na	0.18	0.18
Cl	0.20	0.19

Pet food

Pet foods are formulated to meet nutrient specifications using combinations of multiple ingredients to meet the targeted nutrient specification.

The nutrient specifications for a complete and balanced dog or cat food will meet or exceed the guidelines provided by AAFCO (American Association of Feed Control Officials). The ingredient composition of pet-food can include any legal feed ingredient so number of combinations are not quite infinite but close. Some examples of ingredient used in dog and cat foods can be found in **Table VII** below:

Table VII:

Ingredient Class/Ingredient	**Use rates**
1 ANIMAL MEALS	**10-35%**
Chicken	
Turkey	
Duck	
Poultry Br-Product	
Lamb	
Venison	
Beef	
Pork	
Meat & Bone	
Fish	
2 FRESH MEATS	**3-20%**
Chicken	
Turkey	
Duck	
Lamb	
Venison	

Beef	
Pork	
Fish	
3 VEGETABLE PROTEINS	**8-20%**
Soybean Meal	
Corn Gluten Meal	
Pea Protein	
Potato Protein	
Soy Protein Conc/Isolates	
4 GRAINS	**0-70%**
Corn/Maize	
Wheat	
Brown Rice/Brewers Rice	
Oatmeal/Oat Groats	
Barley	
Millet	
Milo/Sorghum	
Rye	
Corn Gluten Feed	
Wheat Middlings	
5 FIBER SOURCES	**2-8%**
Beet Pulp	
Corn Bran	
Wheat Bran	
Cellulose	
Tomato Ponace	
Potato Fiber	
Pea Fiber	
6 FATS & OILS	**1 - 15%**
Animal Fat	
Poultry Fat	
Chicken Fat	

Beef Tallow	
Sunflower Oil	
Canola Oil	
7 MICRONUTRIENTS	**0.10-1%**
Vitamins	
Minerals	
Others (e.g. Fructooligosaccharides (FOS) used as a pre-biotic)	
8 PALATANTS (FLAVORS)	**0-5%**
9 Other non-basic ingredients	
Dried Egg Product	1-15%
Fish Oil	0.5-2%
Fish Meal	1-4%
Flaxseed	1-4%
Dried Peas	5-30%
Dried Chickpeas	5-30%
Dried Lentils	5-10%
Dried Potatoes	5-20%
Dried Sweet Potatoes	5-20%
Tapioca Starch	5-15%
Potato Starch	5-15%
Pea Starch	5-15%

Thus, the present invention is also directed to pet food comprising the formulation according to the present invention; preferably to pet food comprising the formulation according to the present invention and animal meals and/or fresh meats, vegetable proteins, grains, fiber sources, fats and/or oils, micronutrients, palatants and optionally other non-basic ingredients.

Feed for Swine

Reference is made here to the NATIONAL SWINE NUTRITION GUIDE, 2010, whereby two non-limiting examples are given below.

Table VIII: Corn and Soybean Meal Diet

DIET	PERCENTAGE, %
Corn, yellow	70.99
Soybean meal, solv. extr., CF<4%, CP<48%	25.19
Corn oil	1.00
Calcium carbonate	0.95
Monocalcium phosphate	0.78
Salt (NaCI)	0.37
L-Lysine HCI	0.17
DL—Methionine	0.04
L-Threonine	0.02
Vitamin and trace mineral premix	0.50
Total	100%

Table IX: High fiber ingredient diet

DIET	PERCENTAGE, %
Corn, yellow	37.48
Corn DDGS, <4% oil	30.00
Wheat middlings	19.00
Soybean meal, solv. extr., CF<4%, CP<48%	7.11
Corn oil	3.52
Calcium carbonate	1.28
Salt (NaCI)	0.39
L-Lysine HCI	0.57
DL—Methionine	0.03
L-Tryptophan	0.04
L-Threonine	0.10

Vitamin and trace mineral premix	0.50
Total	100%

Thus, the present invention is also directed to feed for swine comprising the formulation according to the present invention; preferably to feed for swine comprising the formulation according to the present invention and corn, soybean meal, minerals, vegetable oils, amino acids, further vitamins and trace mineral premixes.

The invention is now further illustrated in the following non-limiting examples.

Examples

The following example 1 illustrates the manufacture of the formulation of the present invention.

Example 1 (Table 1)

The matrix components, i.e. gelatin and the water-soluble antioxidant are dissolved in water at approximately 65°C to obtain the "matrix".

Vitamin A acetate and the fat-soluble antioxidant are heated at approximately 65°C under stirring until complete melting of vitamin A acetate ("active phase"). They are then emulsified into the matrix.

Hereby, the amounts of the ingredients are chosen in such a way that their concentrations in the final formulation are as disclosed in **Table 1**.

After thorough mixing the resulting dispersion is sprayed into a spray tower in the presence of an anti-caking agent to form droplets of the desired size. The solidified droplets are then dried by an drying air of various temperatures (5-75°C). The dried powder is separated from the majority of the anti-caking agent and sieved through 150 µm and 600 µm filters.

The powder is further treated at a temperature of up to 120°C in a mixer or in a fluid bed, whereby it is made partially water-insoluble.

The particle size of the dried and thermically-treated powder is determined with laser diffraction analytic with a Malvern Mastersizer 3000. The sample is hereby dry dispersed. By applying the Fraunhofer theory the particle size distribution of the sample is calculated.

Furthermore, the bulk and the tap density are measured according to the procedures as described above.

Ingredients / Example	**Example 1**
a) Vitamin A acetate [weight-%]	19.6
b) Gelatin [weight-%]	71.4
c) DL-alpha-tocopherol [weight-%]	1.0
c) Sodium ascorbate [weight-%]	1.0
d) Anti-caking agent [weight-%]	7.0 (silica)
e) Residual moisture [weight-%]	2.1
Particle size d(v,10%) [µm]	228
Particle size d(v,50%) [µm]	326
Particle size d(v,90%) [µm]	449
Bulk density [g/cm3]	0.60
Tap density [g/cm3]	0.65

The single amounts a), b) c) and d) are based on the total weight of a), b), c) and d) together. The amount of residual moisture e) is based on the total weight of a), b), c), d) and e) together.

Claims

1. A formulation with a self-heating temperature ≥ 120°C, whereby said formulation **consists of**

a) a fat-soluble vitamin in an amount of at least 10 weight-%, whereby the fat-soluble vitamin is vitamin A or a derivative thereof and optionally vitamin D or a derivative thereof;

b) gelatin in an amount of at least 60 weight-%;

c) at least one antioxidant in an amount of ≤ 5 weight-%;

d) an anti-caking agent;

e) optionally an oil;

f) optionally residual moisture;

whereby all amounts a) to e) sum up to 100 weight-% and are based on the total weight of a), b), c), d) and e) together.

2. The formulation according to claim 1, whereby said anti-caking agent d) is silicic acid $H_{2n+2}Si_nO_{3n+1}$, silica, microcrystalline cellulose, as well as any mixture thereof.

3. The formulation according to claim 1 and/or 2, whereby the amount of gelatin is at least 62 weight-%, preferably at least 65 weight-%, more preferably at least 68 weight-%, most preferably at least 70 weight-%, based on the total weight of a) to e).

4. The formulation according to any one or more of the preceding claims, whereby said formulation has a bulk density ranging from 0.58-0.67 g/cm^3.

5. The formulation according to any one or more of the preceding claims, wherein the formulation has a particle size D(v,50%) ranging from 290 to 370 μm, measured as dry dispersion with a Malvern MasterSizer 3000 (laser diffraction).

6. The formulation according to any one or more of the preceding claims, wherein said anti-caking agent d) has a particle size D(v,50%) ranging from 100 nm to 10 μm, measured as dry dispersion with a Malvern MasterSizer 3000 (laser diffraction).

7. The formulation according to any one or more of the preceding claims, wherein the fat-soluble vitamin a) is vitamin A acetate or a mixture of vitamin A acetate and vitamin D3, preferably in a weight ratio of vitamin A acetate to vitamin D3 from 1:1 to 100:1, more preferably from 10:1 to 85:1

8. The formulation according to any one or more of the preceding claims, whereby said antioxidant c) is a tocopherol or a mixture of a tocopherol with a water-soluble antioxidant.

9. A container with a volume ranging from 450 l to 3000 l comprising a formulation according to any one or more of the preceding claims.

10. The container according to claim 9, whereby the container has a volume ranging from 480 to 2000 l, preferably ranging from 500 to 1500 l, more preferably ranging from 500 to 1000 l, most preferably ranging from 600 to 800 l.

11. The container according to claim 9 and/or 10, whereby the container is a flexible intermediate bulk container.

12. A process for the manufacture of a formulation according to any one or more of the claims 1-8 comprising the following steps:

A) Dissolving gelatin b) and, if present, a water-soluble antioxidant c) in water to obtain a matrix;
B) Heating the fat-soluble vitamin a), the fat-soluble antioxidant c) and, if present, the oil e) to obtain an active phase;

C) Emulsifying the active phase obtained in step B) into the matrix obtained in step A) to obtain a dispersion;

D) Spray-drying the dispersion obtained in step C) in presence of an anti-caking agent d) to obtain the formulation.

13. The process according to claim 12 further comprising an additional step:

E) Thermal treating the formulation obtained after step D).

14. Use of the formulation according to any one or more of claims 1-8 as additive to feed or premixes.

15. Feed additive, premix or feed comprising the formulation according to any one or more of claims 1-8.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2021/083503

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23L33/155 A23K40/10 A23K40/30 A23P10/35 A61K9/16
A61K9/51 A61P3/02 A23K20/174 A23K20/158 A23K50/40
A23K50/75 A23L33/11 A23L33/28 A23K20/147 A23K50/48

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)
A61P C11C A23P A61K A23K A23L

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.
X	EP 0 285 682 A1 (HOFFMANN LA ROCHE [CH]) 12 October 1988 (1988-10-12) claims 1-7; example 1 -----	1-15
X	EP 0 494 417 A2 (BASF CORP [US]) 15 July 1992 (1992-07-15) cited in the application claims 1-6; example 3 -----	12,13
X	US 5 043 170 A (BORENSTEIN BENJAMIN [US] ET AL) 27 August 1991 (1991-08-27) claims 1-23; figure 3 -----	12,13
X	CN 110 250 521 A (WANHUA CHEMICAL GROUP CO LTD ET AL.) 20 September 2019 (2019-09-20) abstract claims 1-10; example 6 -----	12,13

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[X] Further documents are listed in the continuation of Box C.

[X] 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

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"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	Date of mailing of the international search report
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10

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 540 085 B1 (DAVIES HEATHER J [GB]) 1 April 2003 (2003-04-01) column 1, paragraph 3	9-11
A	WO 2018/220340 A1 (MOOTRAL SA [CH]) 6 December 2018 (2018-12-06) page 26, paragraph 2	9
A	US 2020/029596 A1 (LI JIANDONG [CN] ET AL) 30 January 2020 (2020-01-30) claims 1-10	1-15
A	KATOUZIAN IMAN ET AL: "Nano-encapsulation as a promising approach for targeted delivery and controlled release of vitamins", TRENDS IN FOOD SCIENCE AND TECHNOLOGY, ELSEVIER SCIENCE PUBLISHERS, GB, vol. 53, 6 May 2016 (2016-05-06), pages 34-48, XP029579298, ISSN: 0924-2244, DOI: 10.1016/J.TIFS.2016.05.002 the whole document	1-15
A	GONNET M ET AL: "New trends in encapsulation of liposoluble vitamins", JOURNAL OF CONTROLLED RELEASE, ELSEVIER, AMSTERDAM, NL, vol. 146, no. 3, 15 September 2010 (2010-09-15), pages 276-290, XP027260358, ISSN: 0168-3659 [retrieved on 2010-06-25] the whole document	1-15
A	US 5 356 636 A (SCHNEIDER JOACHIM U [DE] ET AL) 18 October 1994 (1994-10-18) claims 1-16	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2021/083503

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0285682 A1	12-10-1988	AT 64527 T	15-07-1991
		EP 0285682 A1	12-10-1988
EP 0494417 A2	15-07-1992	BR 9200039 A	08-09-1992
		DE 69118861 T2	05-09-1996
		DK 0494417 T3	13-05-1996
		EP 0494417 A2	15-07-1992
		JP 3210049 B2	17-09-2001
		JP H0532941 A	09-02-1993
US 5043170 A	27-08-1991	AT 89129 T	15-05-1993
		DE 69001557 T2	19-08-1993
		DK 0383116 T3	07-06-1993
		EP 0383116 A2	22-08-1990
		JP H02245143 A	28-09-1990
		US 5043170 A	27-08-1991
CN 110250521 A	20-09-2019	NONE	
US 6540085 B1	01-04-2003	AT 233206 T	15-03-2003
		AU 751372 B2	15-08-2002
		BE 1011959 A6	07-03-2000
		CA 2306164 A1	22-04-1999
		EP 1021351 A1	26-07-2000
		EP 1302401 A1	16-04-2003
		FR 2769606 A3	16-04-1999
		JP 2001048228 A	20-02-2001
		NL 1010271 C1	12-04-1999
		US 6540085 B1	01-04-2003
		WO 9919224 A1	22-04-1999
WO 2018220340 A1	06-12-2018	AR 110945 A1	22-05-2019
		AR 111986 A1	11-09-2019
		AU 2017416351 A1	12-12-2019
		AU 2018276117 A1	12-12-2019
		BR 112019025372 A2	16-06-2020
		BR 112019025388 A2	16-06-2020
		CA 3064811 A1	06-12-2018
		CA 3065004 A1	06-12-2018
		CN 110708965 A	17-01-2020
		CN 110944517 A	31-03-2020
		EP 3629756 A1	08-04-2020
		EP 3629757 A1	08-04-2020
		JP 2020521500 A	27-07-2020
		JP 2020521503 A	27-07-2020
		KR 20200012969 A	05-02-2020
		KR 20200012970 A	05-02-2020
		RU 2019143116 A	09-07-2021
		RU 2019143432 A	09-07-2021
		US 2020138056 A1	07-05-2020
		US 2020170281 A1	04-06-2020
		UY 37351 A	02-01-2019
		UY 37732 A	02-01-2019
		WO 2018220338 A1	06-12-2018
		WO 2018220340 A1	06-12-2018
US 2020029596 A1	30-01-2020	CA 3065840 A1	07-02-2019
		CN 107594597 A	19-01-2018

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2021/083503

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		EP 3607837 A1	12-02-2020
		JP 2020528746 A	01-10-2020
		KR 20190126830 A	12-11-2019
		US 2020029596 A1	30-01-2020
		WO 2019024548 A1	07-02-2019
US 5356636 A	18-10-1994	CA 2083754 A1	15-06-1993
		DE 4141351 A1	17-06-1993
		DK 0547422 T3	01-04-1996
		EP 0547422 A2	23-06-1993
		IL 103866 A	05-12-1996
		JP 2519008 B2	31-07-1996
		JP H0665062 A	08-03-1994
		US 5356636 A	18-10-1994