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(54) Benevnelse **SOLUBILISATE COMPRISING CURCUMIN AND AT LEAST ONE CANNABINOID AS A FURTHER ACTIVE AGENT**

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SOLUBILISATE COMPRISING CURCUMIN AND AT LEAST ONE CANNABINOID AS A FURTHER ACTIVE AGENT

Description

The invention relates to a solubilizate comprising curcumin and at least one cannabinoid. Furthermore, the invention relates to a fluid containing such a solubilizate, to a capsule filled with such a solubilizate or fluid, and to a dietary supplement and/or pharmaceutical drug containing such a solubilizate.

Curcumin is discussed as an active substance based on various potential pharmacological properties. For example, there are indications for the antioxidant and also for the anti-inflammatory effect of curcumin as well as for the effectiveness against viruses and bacteria and against cancer. Indications could therefore be, for example, Parkinson's, Alzheimer's, diabetes, colorectal tumors, pancreatic cancer, and liver dysfunction.

Cannabinoids are transformation products and synthetic analogues of some terpene phenols that are mainly found in hemp plants (*Cannabis*).

The term “hemp plant” or “cannabis plant” encompasses the wild species *Cannabis sativa* and also variants thereof, including *Cannabis chemovar*, which naturally contain different amounts of the various cannabinoids, *Cannabis sativa* subspecies *indica*, and also plants that are the result of genetic crosses, self-crosses, or hybrids thereof.

The cannabisΔ plant contains at least 113 cannabinoids from the group of terpene phenols. These cannabinoids include, inter alia, Δ9-tetrahydrocannabinol (THC), Δ8-tetrahydrocannabinol, cannabidiol (CBD), cannabichromene (CBC), cannabigerol (CBG), cannabinol (CBN), Δ9 tetrahydrocannabivarine (THCV), cannabicyclol (CBL), cannabielsoin (CBE), cannabitriol (CBT), and cannabinodiol (CBND).

Tetrahydrocannabinol (THC) as a psychoactive substance is thought to mainly cause the psychedelic effect of cannabis products. The plant naturally contains THC in the form of two THC acids which are converted into THC by heating the plant material.

In addition to the psychedelic effect, THC is ascribed considerable medical properties such as pain-relieving and relaxing, appetizing, antioxidant, and neuroprotective effects as well as alleviating glaucoma.

Cannabidiol (CBD) is a non-psychoactive cannabinoid which also has antispasmodic, anti-inflammatory, anti-anxiety, immunosuppressive, neuroprotective and antioxidant effects and an anti-nausea effect, inter alia. In addition, CBD is thought to lower high blood sugar levels and stimulate bone formation. Together with THC a synergistic effect can arise.

Like CBD, cannabichromene (CBC) does not have a psychedelic effect. It is in particular thought to have an antifungal, antidepressant effect. Cannabinol (CBN) is an oxidation product of THC and has a psychedelic effect. In addition to analgesic, relaxing, and calming effects, it is thought to have an appetizing and antibacterial, anti-inflammatory, and anti-asthmatic effect. Cannabigerol (CBG) is not psychoactive and is said to in particular have a greater analgesic effect than THC. Tetrahydrocannabivarin (THCV) has a lower psychoactive effect compared to THC and has an appetite-suppressing and metabolism-stimulating effect, inter alia.

Cannabis furthermore contains a variety of non-cannabinoids with diverse pharmacological properties. There are some indications that cannabinoids such as cannabinol (CBN), cannabidiol (CBD) and others modify the effects of Δ9-THC.

Synthetic cannabinoids may be produced semi-synthetically, i.e. from natural cannabinoids, or else fully synthetically from simple raw materials. There are also other plants that can produce active substances which are effective in the human body through the same mechanisms as the cannabinoids of the hemp plant.

In the context of the present application, the term "cannabinoid" encompasses not only natural and synthetic cannabinoids, but also phytocannabinoids. These include, for example, N-isobutylamides from *Echinacea*, and beta-caryophyllene, which is contained in various aromatic plants, as well as yangonin from the kava plant (*Piper methysticum*), and various catechins from the tea plant (*Camellia sinensis*).

In order to be able to enter the bloodstream after oral intake, the active substance must pass through the small intestinal blood barrier, is then

metabolized in the liver and enters the hepatic vein as a bioavailable fraction. The rest of the total active substance ingested and released in the body is either degraded microbially in the intestine or eliminated with the faeces or bile.

WO 2018/061007 A1 addresses the bioavailability of cannabinoids which is to be improved and in this regard describes formulations of cannabinoids which contain at least one oil, at least one hydrophilic emulsifier, at least one coemulsifier and/or co-solvent and at least 0,1 wt.% of a cannabinoid. Such formulations can contain both cannabinoids and curcumin.

WO 2016/022936 describes an oral dosage form of cannabinoids or standardized marijuana extracts which is improved with regard to gastrointestinal passage. The active ingredient constituents are dissolved in an oily medium with at least one emulsifier to promote self-emulsification.

The publication by H. Rosenkrantz et al.: “Oral and parenteral formulation of marijuana constituents” in the Journal of Pharmaceutical Sciences, vol. 61, no. 7, pp. 1106 to 1112 also describes emulsions containing THC in a content of less than or equal to 10 wt.% in a formulation with sesame oil and polysorbate 80.

The inventor has already created a curcumin solubilizate which has significantly increased bioavailability compared to native curcumin. This solubilizate is described in international patent application WO 2014094921 A1. Surprisingly, it has been found in several studies that due to its high bioavailability, this curcumin solubilizate in its specific formulation also has an unexpectedly greater effect on the reduction of disease symptoms which are in particular associated with inflammation or cancer.

A toxicity due to the micellization of the active substance according to the invention in comparison to the native form could be ruled out on the basis of studies with MTT assays for cell viability. The verification of cell vitality by MTT assay is based on the reduction of the yellow water-soluble dye 3 (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) into a blue-violet water-insoluble formazan.

The inventor has therefore set himself the task of providing a formulation which makes available for the human or animal organism the health-promoting or curative properties of curcumin with regard to a combination with at least

cannabinoid as a further active substance. In particular, it is an object of the invention to provide a highest possible bioavailability of curcumin in combination with at least one cannabinoid.

A further object of the invention is to provide nutritionally and/or pharmacologically acceptable cannabinoids. More particularly, it is an object of the invention to provide cannabinoids in a form that, when mixed with water, gives a mixture free of turbidity for the human eye.

These objects are achieved in a surprisingly simple way with a solubilizate according to Claim 1. This solubilizate consists of curcumin in a content of less than or equal to 10 wt.%, preferably less than or equal to 8 wt.%, more preferably 3 wt.% to 7 wt.%, most preferably 1 wt.% to 3 wt.%, and at least one cannabinoid as a further active substance, and polysorbate 80 or a mixture of polysorbate 80 and polysorbate 20 or of polysorbate 80 and at least one sucrose ester of edible fatty acids (approved in the EU as food additive E 473).

The invention also provides a solubilizate consisting of at least one cannabinoid, in particular CBD and/or THC, in a content of less than or equal to 10 wt.%, preferably less than or equal to 5 wt.%, most preferably 0,3 wt.% to 3 wt.%, and polysorbate 80 or a mixture of polysorbate 80 and polysorbate 20 or of polysorbate 80 and at least one sucrose ester of edible fatty acids.

Such a solubilizate can be used in mixtures with curcumin solubilizates. These may also contain further active substances. The cannabinoid solubilizate per se moreover offers the advantage of providing cannabinoids in a form that can be administered orally, for example in beverages or as a filling of capsules. The solubilization of the cannabinoid, in particular of the CBD, according to the invention provides an efficient protection against oxidation for this active substance. In particular CBD is otherwise prone to oxidation, which means that its active substance content might decrease during the shelf life of CBD-containing products. This is prevented by the invention. With the improved oxidative protection of the cannabinoid active substance, the invention enables products with a longer shelf life to be provided.

In an advantageous embodiment, the solubilizate is provided in a form that can be administered orally, in particular in a curcumin dose in the range from 0,5

mg/kg body weight to 1 mg/kg body weight, preferably in a dose of 0,81 mg/kg body weight, in particular once a day.

For the purposes of the present application, the term “active substance” refers to a substance that is provided in a pharmaceutically effective concentration and is preferably added for the purpose of having a pharmaceutical effect. Here, the name of the respective active substance is understood to encompass also substances that are converted in the body into the active substance and/or into its biologically active form.

One active substance in the context of the present application is a cannabinoid. “Active substances” in the sense of the present application include secondary phytochemicals which are produced as chemical compounds by plants, neither in energy metabolism nor in anabolic or catabolic metabolism. One group of secondary phytochemicals and thus active substances in the sense of the present application are flavonoids. The active substances in the sense of the present application also include natural polyphenols such as resveratrol or the polyphenols from licorice, and natural phenols, in particular chalcones such as xanthohumol. Also encompassed are plant extracts, i.e. substances that were extracted from plants or parts of plants using an extractant. These include extracts from hops. The active substance is referred to as an “extract” even if it is still dissolved in the extractant. Also the term “essence” can be used for an extract.

The “active substances” in the sense of the present application also include enzymes. One example of an enzyme as an “active substance” in the present application is serrapeptase. However, the application is not limited to this enzyme.

The extract from the resin of the frankincense tree, *Boswellia serrata* extract, contains several pentacyclic triterpenes which together are often referred to as total boswellic acids (“total BAs”). The term "boswellic acids” refers to a group of chemical compounds naturally occurring in the resin of the frankincense trees mentioned above. The two basic structures are α-boswellic acid and β boswellic acid. Also, some derivatives of the boswellic acids are known, in particular compounds which carry a keto group at position 11 and/or which are acetylated at position 3. Boswellic acids that are currently considered to be significant in terms of pharmacological effects in particular include α-boswellic acid (αBA) and β-

boswellic acid (βBA) and their derivatives 11 keto-β-boswellic acid (KBA; CAS 17019-92-0) and 3-O-acetyl-11-keto-β-boswellic acid (AKBA; CAS 67416-16-9), and 3-O-acetyl-α-boswellic acid (AαBA), and 3-O-acetyl-β-boswellic acid (AβBA). In particular the derivative AKBA is considered to have an anti-inflammatory effect.

In the context of the present application, the term “Boswellia”, in particular in the term “Boswellia solubilizate” is used in the sense that the term “Boswellia” refers to the active substances from the resin of the frankincense tree, i.e. to at least one boswellic acid and/or at least one derivative of a boswellic acid. The term “boswellic acid solubilizate” refers to a micellar formulation of at least one boswellic acid which may also contain at least one boswellic acid derivative.

Xanthohumol is a flavonoid naturally occurring in hops. It is a prenylated plant polyphenol which is assigned to the chalcones and has only been identified in hops so far. The bitter hop varieties have a significantly higher content of xanthohumol than aroma varieties. In tests, xanthohumol was found to be effective against the emergence and development of cancer cells. In laboratory experiments, it was moreover found that xanthohumol is capable of protecting the nerve cells of the brain and thus could possibly help to slow down the course of diseases like Alzheimer's or Parkinson's.

Serratia peptidase or serrapeptase is a proteolytic enzyme produced by the bacterium Serratia which lives in the intestine of the silkworm. Serrapeptase is said to have beneficial effects in relieving pain, inflammation, traumatic swelling, and excess mucus secretion by the organism. It is said to be effective like an anti-inflammatory and analgesic similar to acetylsalicylic acid, ibuprofen or other non-steroidal analgesics. It is also said to induce fibrinolytic anti-inflammatory and anti-oedematous activity in the tissue. Like all enzymes, serrapeptase is sensitive to the acids produced by the stomach. Therefore, the provision in a formulation that allows gastric passage is an object of the invention.

The solubilizate according to the invention may contain one or more boswellic acids and/or one or more boswellic acid derivatives in a content of less than or equal to 10 wt.%, preferably less than or equal to 5 wt.%, most preferably 2 wt.% to 4 wt.%.

Due to the high proportion of Boswellia, the invention envisages, in an advantageous embodiment thereof, that the solubilizate contains an extract obtained from the resin of the plant *Boswellia serrata* by extraction using ethyl acetate as a source of the one or more boswellic acids and/or one or more boswellic acid derivatives, with boswellic acids being contained in a concentration of at least 85 wt.% in this extract.

The solubilizate according to the invention may contain xanthohumol in an amount of less than or equal to 10 wt.%, preferably less than or equal to 5 wt.%, most preferably 1 wt.% to 3 wt.%.

Due to the high proportion of xanthohumol, the invention contemplates, in an advantageous embodiment thereof, that the solubilizate contains an ethanolic extract of hard resins from hops as a source of xanthohumol, with a xanthohumol concentration in this extract in a range between 65 wt.% and 95 wt.%, preferably in a concentration in a range from 80% to 92 wt.%. In particular the products “Xantho-Flav Pure” or “Xantho-Flav” that will be discussed in more detail below can be used as a xanthohumol source in the context of the invention.

The solubilizate according to the invention may contain serrapeptase in a range of up to 3 wt.%, preferably in a range between 0,1 wt.% and 2 wt.%, most preferably in a range between 0,18 wt.% and 0,35 wt.%.

Even a solubilizate consisting of curcumin and at least one cannabinoid as a further active substance may be provided or employed advantageously within the context of the invention for use as a pharmaceutical drug in the treatment and/or prevention of diseases involving inflammation, cancer, Alzheimer's, Parkinson's, obesity, high cholesterol, elevated blood sugar, diabetes, metabolic syndrome, and/or autoimmune diseases, multiple sclerosis (MS), for reducing visceral fat, for thermogenesis, for lowering cholesterol, in particular LDL cholesterol, and/or glucose in the blood and/or triglycerides in the blood, for improving macular pigment density, for reducing oxidative stress and/or for reducing the accumulation of fat in the hepatocytes, in particular as a pharmaceutical drug for treating and/or preventing fatty liver disease, Friedreich's ataxia, lysosomal diseases, in particular Tay-Sachs disease, arteriosclerosis, heart diseases, arthritis.

In particular, the invention provides the solubilizates as described above for use as an anti-inflammatory drug and/or as an antibiotic and/or as a pharmaceutical drug with an effect against cancer, Alzheimer's, Parkinson's, obesity, high cholesterol, elevated blood sugar, diabetes, metabolic syndrome, and/or autoimmune diseases, multiple sclerosis (MS), for lowering visceral fat, for thermogenesis, as a cholesterol-lowering pharmaceutical drug, in particular with respect to LDL cholesterol, and/or as a pharmaceutical drug with an effect for lowering glucose in the blood and/or triglycerides in the blood, for improving macular pigment density, for reducing oxidative stress and/or for reducing the accumulation of fat in the hepatocytes, in particular as a pharmaceutical drug with an effect against fatty liver, Friedreich's ataxia, lysosomal diseases, in particular Tay-Sachs disease, arteriosclerosis, heart diseases, arthritis.

Depending on the further components that are contained in the solubilizate, in order to provide stable micelles of the active substances, the emulsifier content, in particular the polysorbate content, may be at least 70 wt.%, preferably in the range between 75 wt.% and 95 wt.%, most preferably in the range between 79 wt.% and 88 wt.% within the context of the invention.

Depending on the specific application case, the solubilizate of the invention may contain up to 20 wt.%, preferably up to 15 wt.% of ethanol, for example, and/or up to 25 wt.%, preferably between 12 wt.% and 20 wt.%, most preferably up to 10 wt.% of glycerol, and/or additionally up to 10 wt.%, preferably up to 7 wt.% of water. The addition of ethanol allows to reduce the content of emulsifier, in particular the content of polysorbate, which is an advantage in view of the ADI value for polysorbate (25 mg/kg body weight) as recommended by WHO. The content of emulsifier, in particular the content of polysorbate may also be reduced by adding glycerol.

The solubilizates of the invention have a narrow particle size distribution with small mean particle sizes, even under the physiological conditions of a gastric passage; the diameter distribution of the micelles in a dilution of the solubilizate with distilled water in a ratio of 1:500 at pH 1,1 and 37°C ranges from about d_{10} = 6 nm to about d_{90} = 20 nm. These values were determined from a volume distribution. Details of particle size analysis of the micelles of the solubilizates will be explained below.

An indication of the improved bioavailability compared to compositions of at least one cannabinoid or of curcumin and at least one cannabinoid as a further active substance that have not been micellated according to the invention is obtained by a measurement of turbidity of the solubilizate, which is much more easily accessible to measurement techniques. As a result of the formulation according to the invention, the turbidity of the solubilizate is preferably less than 25 FNU, more preferably less than 3 FNU, as measured by scattered light measurement using infrared light in compliance with the specifications of the ISO 7027 standard at a dilution of the solubilizate in a ratio of 1:50 in water under physiological conditions (pH 1,1 and 37°C).

In order to facilitate oral application of a solubilizate of the invention in a more simple and convenient way for the consumer or patient, the invention also provides a capsule filled with a solubilizate as described above, wherein the capsule is in the form of a soft gelatin capsule or a hard gelatin capsule or a soft gelatin-free capsule or a hard gelatin-free capsule, for example a cellulose capsule.

Moreover, in the context of the invention, the solubilizate according to the invention may be incorporated into other fluids, in particular liquids. The active substance-filled small micelles will be retained when doing so. Thus, the invention also provides a fluid containing the solubilizate as described above, wherein the fluid is selected from the group comprising foods, dietary supplements, beverages, cosmetics, and pharmaceutical products. In the context of the invention, the fluid may in particular comprise an aqueous dilution of the solubilizate.

For producing a solubilizate according to the invention comprising curcumin and at least one cannabinoid as a further active substance, it is possible either to mix together individually prepared solubilizates, or to directly prepare a solubilizate that contains curcumin and at least one cannabinoid as the further active substance.

The invention furthermore provides a method for producing a solubilizate as described above. If co-micellization of curcumin and at least one cannabinoid as a further active substance is desired, the invention provides the following first variant of a preparation method, with the following steps

a) providing polysorbate 80 or a mixture of polysorbate 80 and polysorbate 20 or of polysorbate 80 and at least one sucrose ester of edible fatty acids,

b) adding the at least one cannabinoid, in particular in the form of CBD oil and/or THC oil,

c) adding curcumin powder,

wherein step a) comprises heating to a temperature in the range from 40°C to 62°C, preferably to a temperature in the range from 45°C to 57°C, most preferably to a temperature in the range between 48°C and 52°C;

and wherein step b) comprises heating to a temperature in the range from 82°C to 97°C, preferably to a temperature in the range from 83°C to 92°C, most preferably to a temperature in the range from 85°C to 89°C; wherein this temperature is maintained in step c).

This preparation method makes it possible to produce a solubilizate which, in an aqueous dilution, is able to form micelles loaded with curcumin and with at least one cannabinoid as a further active substance. For this purpose, it is also possible to mix the at least two active substances with one another in a preparatory step under appropriately adapted temperature control, and then to add them in combined form, as a mixture.

In the context of the invention, the at least one cannabinoid is in particular used in the form of CBD oil, THC oil, or a mixture of the two. In principle, any formulation can be used as a source of cannabinoids within the scope of the invention. For example it is possible to use oils, in particular those known as "full-spectrum" oils, pastes, powders, crystalline forms, and/or isolates, with all of the formulations mentioned containing at least one cannabinoid. In principle, it is also possible to use extracts of at least one cannabinoid in order to obtain a solubilizate according to the invention. The formulations mentioned may be those that essentially contain one cannabinoid, for example CBD in the case of what is known as "CBD oil". However, it is also possible to provide mixtures of at least two cannabinoids in a cannabinoid formulation that is used as a cannabinoid in the context of the invention.

During step b), even further active substances such as for example *Boswellia serrata* extract and/or xanthohumol may also be incorporated.

Additionally or alternatively, further active substances such as for example serrapeptase may be incorporated in step c). In addition or as an alternative to further active substances, MCT oil can be added in step c).

In particular in this case, before step b) a step

b1) adding water at a temperature in the range from 40°C to 62°C, preferably at a temperature in the range from 45°C to 57°C, most preferably at a temperature in the range from 48°C to 52°C, can be carried out.

Additionally or alternatively, in step b1) also the addition of ethanol can be carried out at a temperature in the range from 40°C to 62°C, preferably at a temperature in the range from 45°C to 57°C, most preferably at a temperature in the range from 48°C to 52°C.

The invention also relates to solubilizates which exhibit in aqueous dilution both micelles loaded with curcumin alone or else with another active substance alone, at least immediately after their preparation. The invention thus also provides a method for producing a solubilizate as described above by mixing a curcumin solubilizate and at least one cannabinoid solubilizate, in particular in a quantitative ratio of 1:1.

To this end, the invention provides for a method for producing a cannabinoid solubilizate with the following steps:

a) providing polysorbate 80 or a mixture of polysorbate 80 and polysorbate 20 or of polysorbate 80 and at least one sucrose ester of edible fatty acids,

b) adding the at least one cannabinoid, for example in the form of CBD oil and/or THC oil,

wherein in step a) a heating to a temperature at least in a range from 40°C to 62°C, preferably to a temperature in a range from 45°C to 57°C, most preferably to a temperature in a range from 48°C to 52°C is carried out,

and wherein in step b) a heating to a temperature in a range from 82°C to 97°C, preferably to a temperature in a range from 83°C to 92°C, most preferably to a temperature in a range from 85°C to 89°C, is carried out.

It is also possible in step a) to increase the temperature to a value in a range from 82°C to 97°C, preferably to a temperature in a range from 83°C to 92°C, most preferably to a temperature in a range from 85°C to 89°C. In preparation for this, it is possible to perform a step

a1) mixing glycerol and cannabinoid, for example in the form of CBD oil, to produce a solution; wherein in step a1) a heating to a temperature in a range from 82°C to 97°C, preferably to a temperature in a range from 83°C to 92°C, most preferably to a temperature in a range from 85°C to 89°C, is carried out.

It is also possible within the scope of the invention, in preparation thereof, to perform a step

a11) mixing water and at least one sucrose ester of an edible fatty acid, wherein in step a11) a heating to at least a temperature in a range from 40°C to 62°C, preferably to a temperature in a range from 45°C to 57°C, most preferably to a temperature in a range from 48°C to 52°C is carried out;

and a step

a12) addition of polysorbate 20 and/or polysorbate 80 to the mixture produced in step a11) is carried out, wherein in step a12) a heating to a temperature in a range from 82°C to 97°C, preferably to a temperature in a range from 83°C to 92°C, most preferably to a temperature in a range from 85°C to 89°C is carried out.

Following step a1) or following step a11) or following step a12), the cannabinoid is added in step b).

The invention will now be explained in more detail by way of exemplary embodiments. The following components were used:

Curcumin

The product named “Turmeric Oleoresin Curcumin Powder 95%” with the product code EP-5001 from Green Leaf Extraction Pvt Ltd., Kerala, India, was used as the curcumin. The curcumin powder has CAS Number 458-37-7. It is a natural product obtained by solvent extraction of the rhizomes of *Curcuma longa*. The curcumin content of the powder is at least 95%, according to manufacturer specifications. This curcumin content is determined by ASTA method 18,0.

As an alternative to the “oleoresin turmeric 95%” curcumin powder from Green Leaf mentioned above, it is also possible for the exemplary embodiments described below to use, as the curcumin, 95% curcumin extract by Neelam Phyto-Extracts, Mumbai, India, or curcumin BCM-95-SG or curcumin BCM-95-CG from eurochem GmbH, Gröbenzell, Germany, or Curcuma Oleoresin 95% from Henry Lamotte OILS GmbH, Bremen, Germany, for example.

CBD

CBD oil was used as the source for a cannabinoid, in particular for example the product "CBD Drops PRM BLK 24%" from the manufacturer Pharmahemp. Furthermore, a CBD isolate with the brand name Cannapure® from the manufacturer Arevipharma GmbH was used, which contains at least 98% synthetic cannabidiol.

Boswellia

In the context of the present application, the term “Boswellia” in particular refers to an extract from the resin of the frankincense plant. Specifically, an extract of the species *Boswellia serrata* has been used, which was an extract obtained by extraction with ethyl acetate from the resin of the plant with the botanical name *Boswellia serrata* with the product code “HC22519” manufactured by Frutarom Belgium N.V., Londerzeel, Belgium. A solubilizate containing this extract is also referred to as “boswellic acid solubilizate” because of its content of boswellic acids.

Besides extracts from the resin of the frankincense plant, it is also possible to use boswellic acids and/or derivatives of boswellic acids for the purposes of the solubilizates according to the invention. In particular, the following may be considered: alpha-boswellic acid (CAS number 471-66-9), beta-boswellic acid (CAS number 631-69-6) and their derivatives, 3-O-acetyl-alpha-boswellic acid

(CAS number 89913-60-0), 3-O-acetyl-beta-boswellic acid (CAS number 5968-70-7), 11-keto-beta-boswellic acid (KBA, CAS number 17019-92-0), and 3-O-acetyl-11-keto-beta-boswellic acid (AKBA, CAS number 67416-61-9).

Xanthohumol

The products “Xantho-Flav” or “Xantho-Flav Pure” of the brand “Hopsteiner” by Simon H. Steiner, Hopfen, GmbH, Mainburg, Germany were used as the xanthohumol source. Both are natural products produced from hops. The active substance is the hop polyphenol xanthohumol. This is a yellow colored powder with a xanthohumol content between 65% and 85% in “Xantho-Flav” and at least 85% in “Xantho-Flav Pure”, according to manufacturer specifications.

The concentrations of xanthohumol and isoxanthohumol in “Xantho-Flav Pure” are quantified by the manufacturer according to UV spectrophotometric analysis or HPLC EBC 7,8 using external calibration standard pure XN (370 nm) or IX (290 nm). “Xantho-Flav Pure” contains the prenylated flavonoid xanthohumol in a very high concentration. For the exemplary embodiments in the context of the present application, “Xantho-Flav Pure” of batch number 9432 was used.

Serrapeptase

The product named Serratiopeptidase 20.000 U/mg from Shaanxi Pioneer Biotech Co. Ltd. with batch number PBD 20170708 was used as the serrapeptase. This is a greyish white to light-brown powder. The enzyme unit (U) is a unit which has since been replaced by the katal to indicate enzymatic activity. Since the numerical values change when katal is used, the enzyme unit (U) continues to be used in medicine and clinical chemistry. One enzyme unit U corresponds to one micro-mole substrate conversion per minute.

Polysorbate 80

The source of polysorbate 80 was the material “TEGO SMO 80 V FOOD” with the specification code “K04 EU-FOOD” from Evonik Nutrition & Care GmbH, Essen, Germany. The product complies with the EU requirements for food additive E 433. As an alternative to the TEGO SMO 80 V from Evonik mentioned above, it is also possible to use TEGO SMO 80 V from InCoPA Gmbh, Illertissen, Germany, or

Crillet 4/Tween 80-LQ-(SG) from CRODA GmbH, Nettetal, Germany, or Lamesorb SMO 20 and Kotilen-O/1 VL from Univar or from Kolb Distributions AG, Hedingen, Switzerland, as the polysorbate 80 in the exemplary embodiments described below.

Polysorbate 20

The source of polysorbate 20 was the material “TEGO SML 20 V FOOD” with the specification code “K09 EU-FOOD” from Evonik Nutrition & Care GmbH, Essen, Germany. The product complies with the EU requirements for food additive E 432. As an alternative to the TEGO SML 20 from Evonik mentioned above, it is also possible to use Crillet 1/Tween 20-LQ-(SG) from CRODA GmbH, Nettetal, Germany, as the polysorbate 20 within the context of the invention.

Sucrose esters of edible fatty acids

A sucrose ester with the product designation “DUB SE 15 P” from the manufacturer Stéarine Dubois was used as the sucrose ester of edible fatty acids. This ester is approved in the EU as food additive E473.

Ethanol

In the context of the present application, ethanol was purchased from Berkel Pfälzische Spritfabrik GmbH & Co. KG. According to the specification for “undenatured neutral alcohol 1411U taxed”, the content of ethanol of this product is about 92,6 to 95,2 wt.%.

Glycerol

The product used as glycerol in the context of the present application was “Glycamed 99,7%” from Glaconchemie GmbH, Merseburg, Germany. The glycerol content of this product is at least 99,5%, according to manufacturer specifications.

Medium-chain triglycerides

Medium-chain triglycerides (MCTs) are triglycerides that contain medium-chain fatty acids. Medium-chain fatty acids include caproic acid, caprylic acid, capric acid and lauric acid. These are saturated fatty acids which naturally occur in tropical vegetable fats such as coconut oil and palm kernel oil. To a small extent

they are also contained in milk fat. There is no pure MCT oil in nature; however, pure MCT oils can be obtained synthetically.

The following aspects relating to the use of medium-chain triglycerides are not according to the invention and are merely illustrative. Individual MCTs or a mixture of different MCTs can be used as medium-chain triglycerides in solubilizates. Medium-chain triglycerides were used in the form of MCT oil Delios VK Kosher, manufactured by Cognis GmbH, Monheim, Germany, or in the form of MCT oil (70/30) Rofetan GTCC 70/30 manufactured by DHW Deutsche Hydrierwerke Rodleben GmbH, Dessau-Roßlau, Germany, CAS number 73-398-61-5.

Furthermore, medium-chain triglycerides can be used in the form of the product ROFETAN DTCC 70/30 (Ph. Eur.). This is a caprylic/capric acid triglyceride with CAS number 73398-61-5. The product corresponds to the monograph “medium-chain triglycerides” of the European Pharmacopoeia valid at the filing date. Manufacturers are Ecogreen Oleochemicals DHW, Deutsche Hydrierwerke GmbH, Rodleben, Germany.

If **water** is added in the preparation of a solubilizate, distilled water is used.

The particle size analyses of the micelles in aqueous dilutions of solubilizates according to the invention were measured according to the principle of dynamic light scattering using laser light of 780 nm wavelength, unless stated otherwise. The particle size measurements were performed using the ParticleMetrix NANO-flex backscatter particle analyzer. The measuring principle is based on dynamic light scattering (DLS) in a 180° heterodyne backscattering setup.

For the experimental determination of turbidity of the solubilizates according to the invention, the turbidity meters are calibrated with a standard suspension. Thus, instead of measured light intensity, the concentration of the calibration suspension is indicated. So, when any arbitrary suspension is measured, the indication means that the respective liquid causes the same light scattering as the standard suspension at the indicated concentration. The internationally defined turbidity standard is formazine. The most common units include the indication FNU, i.e. Formazin Nephelometric Units. This is the unit used in water treatment, for example, for measuring at 90° in compliance with the requirements of the ISO 7072 standard.

For preparing a solubilizate according to the invention including the active substances curcumin and at least one cannabinoid as a further active substance it is possible either to mix individually prepared solubilizates with one another or to directly prepare a solubilizate that contains curcumin and at least one cannabinoid or several further active substances.

Curcumin solubilizates

By way of example, a 7% curcumin solubilizate is prepared. To this end,

925 g	polysorbate 80
75 g	curcumin powder 95% (= 71,2 g of curcumin)

are used. The polysorbate 80 is heated to between 48 and 52°C. The curcumin powder is added to the polysorbate under stirring, while further heating to a temperature in the range from 95 to 97°C. The powder is added at an appropriate rate so as to be evenly drawn into the emulsifier during stirring. After cooling to a temperature below a maximum of 60°C, the curcumin solubilizate is bottled. This solubilizate was used for the preparation of a curcumin and Boswellia solubilizate.

At a dilution ratio of 1:500 in water at pH 1,1 and a temperature of 37°C, the 7% curcumin solubilizate exhibits an average turbidity of 0,9 FNU.

However, it should be noted that the curcumin content can be further increased without having to accept adverse consequences, for example in terms of the stability of the micelles.

Also, the polysorbate 80 may be entirely or partially replaced by polysorbate 20 or by sucrose esters of edible fatty acids. For example, for preparing a curcumin solubilizate with polysorbate 20 alone, 894 g of polysorbate 80 and 106 g of 95% curcumin powder can be used. The polysorbate 20 is heated to between about 63°C and about 67°C. While stirring, the curcumin powder is slowly added to the polysorbate 80. While adding the curcumin powder, heating is continued to between about 83°C and about 87°C. The resulting solubilizate is slowly cooled to below about 45°C and is then ready for being bottled.

Otherwise, the preparation of these variants corresponds to that described above. Solubilizates of up to about 11% can be produced in this way.

For preparing a

2,4% CBD solubilizate (free of water),

the following is used:

900 g	polysorbate 80, and
100 g	CBD oil (CBD Drops PRM BLK 24%, = 24 g CBD).

. The polysorbate 80 is heated to between 48 and 52°C. The CBD oil is added to the polysorbate under stirring, while the temperature is further increased to a range between 85°C and 89°C. After cooling to a temperature below a maximum of 60°C, the CBD oil solubilizate is bottled.

At a dilution ratio of 1:50 in water at pH 1,1 and a temperature of 37°C, the anhydrous 2,4% CBD oil solubilizate exhibits a turbidity of 2,9 FNU.

An anhydrous CBD solubilizate according to the invention, in particular one according to the above example, is particularly suitable as a filling for capsules.

A further example of a cannabinoid solubilizate according to the invention is a

2,4% CBD solubilizate,

for which the following is used:

100 g	CBD oil (CBD Drops PRM BLK 24%, = 24 g CBD).
27 g	sucrose ester of edible fatty acids,
54 g	water
22,5 g	glycerol, and
796,5 g	polysorbate 80

. Water and glycerol are mixed and heated to a temperature in the range from 48°C to 52°C. The sucrose ester is incorporated under vigorous stirring. The stirring is performed vigorously enough so that the sucrose ester dissolves in water and glycerol. Polysorbate 80 is added while stirring and is homogenized while heating to a temperature of 85°C to 89°C. The stirring is performed vigorously enough so that the polysorbate 80 is evenly distributed. After having been cooled to a temperature below 60°C while stirring, the CBD oil is incorporated under vigorous stirring and is completely homogenized while re-heating to a temperature of 85°C to 89°C. The stirring is performed vigorously enough so that the CBD oil is evenly distributed. The product is then cooled to a temperature below 60°C and bottled. It is then stored in the dark at not more than 25°C.

At a dilution ratio of 1:50 in water at pH 1,1 and a temperature of 37°C, the 2,4% CBD oil solubilizate exhibits a turbidity of 3,6 FNU. It is particularly suitable as an additive for beverages.

3% CBD solubilizate (free of water)

The following is used:

31,2 g	CBD isolate (Cannapure® at least 98%, = 30,5 g CBD),
62 g	glycerol, and
906,8 g	polysorbate 80

. Glycerol and CBD isolate are mixed and heated to a temperature in the range from 85°C to 89°C. Heating takes place at a rate sufficient for the CBD to completely dissolve in the glycerol and to obtain a clear solution. Polysorbate 80 is added at a temperature between 85°C and 89°C during stirring. The stirring is performed vigorously enough so that the polysorbate 80 is evenly distributed. The product is then cooled to a temperature below 60°C and bottled. It is then stored in the dark at not more than 25°C.

At a dilution ratio of 1:50 in water at pH 1,1 and a temperature of 37°C, the 2,4% CBD oil solubilizate exhibits a turbidity of 2,7 FNU. It is particularly suitable as a filling for capsules.

In particular for beverages, it is also possible within the scope of the invention to prepare the following

3% CBD solubilizate,

with a reduction in the amount of polysorbate. To this end,

31,5 g	CBD isolate (Cannapure® at least 98%, = 30,5 g CBD),
27 g	sucrose ester of edible fatty acids,
54 g	water
22,5 g	glycerol, and
865 g	polysorbate 80

are used. Water and glycerol are mixed and heated to a temperature in the range from 48°C to 52°C. Polysorbate 80 is added while stirring and is homogenized while heating to a temperature of 85°C to 89°C. The stirring is performed vigorously enough so that the polysorbate 80 is evenly distributed. This is followed by cooling to a temperature below 60°C during stirring. Separately, glycerol and the CBD isolate are mixed together and slowly heated to a temperature between 85°C and 89°C and completely homogenized, i.e. until a clear solution has been obtained. Subsequently, the polysorbate-sucrose ester mixture is incorporated into the CBD-glycerol mixture under vigorous stirring. While re-heating to a temperature between 85°C and 89°C, stirring is performed vigorously enough to achieve an even distribution. The product is then cooled to a temperature below 60°C and bottled. It is then stored in the dark at not more than 25°C.

At a dilution ratio of 1:50 in water at pH 1,1 and a temperature of 37°C, this 3% CBD oil solubilizate exhibits a turbidity of 4,1 FNU. It is particularly suitable as an additive for beverages.

Besides the use of CBD oil, it is also possible within the scope of the invention to prepare and use cannabinoid solubilizates with THC oil and/or with oils or isolates or other sources of other cannabinoids as well, additionally or alternatively.

12% boswellic acid solubilizate

The following is used:

76 g	80% *Boswellia serrata* extract (= 60,8 g boswellic acid),
24 g	water
400 g	polysorbate 20

.

The water is mixed with the boswellia powder while being heated to a temperature in the range from 87 to 93°C. While maintaining the temperature, polysorbate 20 is incorporated. The emulsifier is added at such a rate, while stirring, that the fluids homogenize stably to form a solubilizate. Heavy foaming may occur during the preparation. This can be ignored if a clear solubilizate can be seen at the bottom of the collection vessel during bottling.

The following exemplary embodiment of a 1,5% serrapeptase solubilizate is not according to the invention and is for illustrative purposes only.

<u>1,5% serrapeptase solubilizate</u>

The following is used:

15 g	serrapeptase: serratiopeptidase 20.000 U/mg = 300.000.000 U,
15 g	water
16,5 g	MCT oil
953,5 g	polysorbate 80

.

At a temperature in the range between 18 and 22°C, water is mixed with serrapeptase, and the mixture is homogenized. This means that the serrapeptase is distributed as evenly as possible in the water. This creates the conditions for the serrapeptase to be largely completely dissolved in the water. While heating to a temperature in the range from 83 to 87°C, MCT oil is

incorporated into the water-serrapeptase mixture under constant stirring. The stirring is performed vigorously enough for the serrapeptase to dissolve evenly in the water. At unchanged temperature, polysorbate 80 is added under stirring and is homogenized. The stirring is performed vigorously enough so that the polysorbate 80 is evenly distributed. The product is then cooled to a temperature below 60°C and bottled. It is then stored in the dark at not more than 25°C.

300.000 U/g corresponds to 15 mg/g of 1,5% serrapeptase in enzymatic units. At a dilution in water of 1:50, the turbidity of this solubilizate was determined under physiological conditions at pH 1,1 and 37°C. The resulting value was 1,8 FNU.

10% Xantho-Flav solubilizate (corresponding to 7.5% xanthohumol) with ethanol

For this variant of a xanthohumol solubilizate according to the invention, the following is used:

100 g	Xantho-Flav (≙ 75 g xanthohumol),
150 g	ethanol (96%) of neutral alcohol grade 1411U,
and	
750 g	polysorbate 80

.

First, the Xantho-Flav powder is dissolved in ethanol while being heated to a temperature in the range between 48 and 52°C. A homogeneous solution is created. Polysorbate 80 is then added into the solution of Xantho-Flav in ethanol while heating to between 83 and 87°C. The adding is done at a rate such that the two fluids homogenize well under stirring. The resulting solubilizate is cooled to below 60°C and is bottled and stored in the dark and cool, i.e. at temperatures below 25°C.

The solubilizates described above can be used to prepare the solubilizate according to the invention comprising curcumin and at least one a further active substance by mixing. This will be described below with reference to exemplary embodiment 1.

In the context of the present application, a verification about whether the homogenization of the components to form a solubilizate according to the invention

has been sufficiently completed in the preparation of any solubilizates is obtained by measurements of the clarity of the product, which indicates complete micellization, using a laser beam. Such a laser beam measurement may be performed, for example, by illuminating the sample using a commercially available laser pointer, in particular with a wavelength in the range between 650 nm and 1700 nm (spectral color red), and subsequent visual inspection of the illuminated or irradiated solubilizate. The verification is not achieved by sampling and thus outside the reaction vessel, but in the reaction vessel. The laser beam is directed through a sight glass which is located on the front of the reaction vessel, perpendicularly to the reaction vessel. If merely a point of light appears on the rear inner surface of the reaction vessel, completely free of scattering, the resulting particle structures in the reaction vessel are smaller than the wavelength of the visible light, which is thus a visual confirmation that the process of micellization has been completed.

The following exemplary embodiments 1 and 2 are not according to the invention with respect to the serrapeptase solubilizate with MCT and are for illustrative purposes only.

Exemplary embodiment 1

Solubilizate of 1,4% curcumin / 2,4% boswellic acid / 1,5% xanthohumol / 0,48% CBD / 0,3% serrapeptase

The following is used:

200 g	7% curcumin solubilizate,
200 g	12% Boswellia solubilizate,
200 g	7,5% xanthohumol solubilizate, and
200 g	2,4% water-free CBD solubilizate,
200 g	1,5% serrapeptase solubilizate

.

All five solubilizates can be heated to a temperature in the range from 50°C to 60°C to lower their viscosity and thus enhance flowability. Then they are mixed

together by stirring. Once a homogeneous complete product is obtained, it is optionally cooled to a temperature below 60°C and bottled.

Prior to further processing such as filling into capsules, it is favorable to again stir the product to homogenize it, and if necessary to this end to heat it moderately, i.e. to a temperature of about 40°C to 50°C.

At a dilution ratio of 1:50 in water at a pH 1,1 and a temperature of 37°C, the solubilizate exhibits an average turbidity of 3,4 FNU.

Exemplary embodiment 2

Directly prepared solubilizate of 1,4% curcumin / 2,4% boswellic acids / 1,5% xanthohumol / 0,048% CBD / 3% serrapeptase

The following is used:

15 g	95% curcumin powder,
30,4 g	*Boswellia serrata* extract (24,3 boswellic acid),
20 g	Xantho-Flav powder (at least 70% xanthohumol = 15 g xanthohumol),
20 g	CBD oil (0,48 g CBD),
3 g	serrapeptase (60.000.000 U),
12,6 g	water
20 g	ethanol
3,3 g	MCT oil
160 g	polysorbate 20, and
715,7 g	polysorbate 80

.

Polysorbate 80 and polysorbate 20 are mixed at a temperature in the range between 48°C and 52°C while stirring vigorously enough so that a homogeneous mixture is obtained. Water and ethanol are added while stirring vigorously enough so that a homogeneous mixture is obtained at a temperature in the range from 48°C to 52°C. Xanthohumol and Boswellia are slowly admixed under consistent stirring.

The temperature is then increased to 63°C to 67°C under vigorous stirring. Subsequently, curcumin, serrapeptase, CBD oil, and MCT oil are incorporated into the mixture. Care is taken to ensure good mixing and homogeneity of the product. If appropriate, pauses are taken between the addition of a substance and the addition of the next substance. The adding is conducted slowly enough, while stirring, so that the particular ingredient to be added is evenly incorporated into the preparation.

The temperature is further increased to a value in the range between 85°C and 89°C. The heating is conducted under constant stirring and slowly enough to ensure that the mixture that is being heated remains homogeneous and so that a clear product is obtained. After cooling to a temperature below 60°C, the product is bottled. It is dark and viscous and is stored in the dark at temperatures of not more than 25°C. Prior to further processing such as filling into capsules, it is favorable to again stir the product to homogenize it and, if necessary to this end, to heat it moderately, i.e. to a temperature of about 40°C to 50°C.

At a dilution ratio of 1:50 in water at a pH of 1,1 and a temperature of 37°C, the solubilizate exhibits a turbidity of 3,4 FNU.

Exemplary embodiment 3

Solubilizate of 3% curcumin / 3,2% boswellic acid / 1,6% xanthohumol / 1% CBD oil

The following is used:

40,5 g	80% *Boswellia serrata* extract (32,4% boswellic acid),
31,5 g	95% curcumin powder (29,925 g of curcumin),
20,7 g	Xantho-Flav powder containing at least 80% of xanthohumol (16,5 g xanthohumol),
54,3 g	water
45 g	ethanol
315 g	polysorbate 20
483 g	polysorbate 80
10 g	CBD oil: 30% cannabidiol.

. Cannabidiol (CBD) is a barely psychoactive cannabinoid derived from the female hemp *Cannabis sativa* or *Cannabis indica*. A non-THC-free CBD oil was used, which means that it may contain traces of THC. Tetrahydrocannabinol (THC) is responsible for the psychedelic effects of hemp plants.

While heating to a temperature in the range from 48 to 52°C, polysorbate 20 and polysorbate 80 are homogenized with each other while being dissolved in each other, under stirring. While maintaining the temperature, the emulsifier mixture is mixed with the water and ethanol, while stirring is performed vigorously enough so that the water and the ethanol are dissolved evenly in the emulsifier solution. At unchanged temperature, the Boswellia serrata extract and the xanthohumol are incorporated into the water-diluted emulsifier mixture while stirring. The adding is performed at a rate slow enough so that the Boswellia serrata extract and the xanthohumol are evenly drawn into the dilute emulsifier solution under stirring. Subsequently, the temperature is increased to a range between 63°C and 67°C under vigorous stirring. The curcumin powder is incorporated while stirring. The temperature is further increased to a value in the range between 85°C and 89°C while stirring vigorously enough so that the curcumin is evenly distributed in the preparation and homogenized. Subsequently, the CBD oil is incorporated into the mixture while stirring vigorously enough so that the CBD oil is evenly distributed in the preparation and homogenized.

This is followed by cooling to a temperature of less than or equal to 45°C. The dark-yellow viscous preparation comprising a solubilizate of curcumin and boswellic acid and xanthohumol and CBD oil is then bottled and stored in the dark and cool, i.e. below 25°C. The solubilizate and an aqueous solution thereof are stably homogeneous and soluble in crystal clear form.

It will be apparent to a person skilled in the art that the invention is not limited to the examples described above, but rather can be varied in various ways. It is in particular possible to combine or swap the features of the individually illustrated examples. This applies in particular to the emulsifier composition and the composition of active substances of the solubilizate according to the invention.

PATENTKRAV

1. Solubilisat, som består av

kurkumin i et innhold på mindre enn eller lik 10 vekt-%, fortrinnsvis mindre enn eller lik 8 vekt-%, mer foretrukket 3 vekt-% til 7 vekt-%, mest foretrukket 1 vekt-% til 3 vekt-%;

og minst ett kannabinoid som minst ett ytterligere aktivt stoff; og

polysorbat 80 eller en blanding av polysorbat 80 og polysorbat 20, eller av polysorbat 80 og minst én sukroseester av spiselige fettsyrer,

hvori solubilisatet eventuelt inneholder

opptil 20 vekt-%, fortrinnsvis opptil 15 vekt-% etanol; og/eller

opptil 25 vekt-%, fortrinnsvis mellom 12 vekt-% og 20 vekt-%, mest foretrukket opptil 10 vekt-% glyserol; og/eller

i tillegg opptil 10 vekt-%, fortrinnsvis opptil 7 vekt-% vann.

2. Solubilisatet ifølge krav 1,

karakterisert ved at

solubilisatet omfatter som minst ett ytterligere aktivt stoff ett stoff eller flere stoffer valgt fra gruppen omfattende

sekundære fytokjemikalier, spesielt flavonoider, naturlige fenoler, spesielt chalconer som xantohumol, planteekstrakter, spesielt fra harpiksen til røkelsestreet, og enzymer, spesielt serrapeptase.

3. Solubilisat, som består av

minst ett kannabinoid, spesielt kannabidiol CBD og/eller tetrahydrokannabinol THC, i et innhold på mindre enn eller lik 10 vekt-%, fortrinnsvis mindre enn eller lik 5 vekt-%, mest foretrukket 0,3 vekt-% til 3 vekt-%,

og polysorbat 80 eller en blanding av polysorbat 80 og polysorbat 20 eller av polysorbat 80 og minst én sukroseester av spiselige fettsyrer,

hvori solubilisatet eventuelt inneholder

opptil 20 vekt-%, fortrinnsvis opptil 15 vekt-% etanol; og/eller

opptil 25 vekt-%, fortrinnsvis mellom 12 vekt-% og 20 vekt-%, mest foretrukket opptil 10 vekt-% glyserol; og/eller

i tillegg opptil 10 vekt-%, fortrinnsvis opptil 7 vekt-% vann.

4. Solubilisatet ifølge et hvilket som helst av de foregående kravene,

for anvendelse i behandlingen og/eller forebyggingen av sykdommer som involverer betennelse, kreft, Alzheimers, Parkinsons, fedme, høyt kolesterol, forhøyet blodsukker, diabetes, metabolsk syndrom og/eller autoimmune sykdommer, multippel sklerose (MS), for å redusere visceralt fett, for termogenese, for å senke kolesterol, spesielt LDL-kolesterol, og/eller glukose i blodet og/eller triglyserider i blodet, for å forbedre makulær pigmenttetthet, for å redusere oksidativt stress og/eller for å redusere akkumuleringen av fett i hepatocyttene, spesielt farmasøytisk produkt for behandling og/eller forebygging av fettleversykdom, Friedreichs ataksi, lysosomale sykdommer, spesielt Tay-Sachs sykdom, arteriosklerose, hjertesykdommer, leddgikt.

5. Solubilisatet ifølge et hvilket som helst av kravene 1 til 3,

for anvendelse som et antiinflammatorisk kosttilskudd og/eller som et farmasøytisk legemiddel med en effekt mot kreft, Alzheimers, Parkinsons, fedme, høyt kolesterol, forhøyet blodsukker, diabetes, metabolsk syndrom, og/eller autoimmune sykdommer, multippel sklerose (MS), for å senke visceralt fett, for termogenese, som et kolesterolsenkende farmasøytisk legemiddel, spesielt med hensyn til LDL-kolesterol, og/eller som et farmasøytisk legemiddel med en effekt for senkning av glukose i blodet og/eller triglyserider i blodet, for å forbedre makulær pigmenttetthet, for å redusere oksidativt stress og/eller for å redusere akkumuleringen av fett i hepatocyttene, spesielt farmasøytisk produkt med en

effekt mot fettleversykdom, Friedreichs ataksi, lysosomale sykdommer, spesielt Tay-Sachs sykdom, arteriosklerose, hjertesykdommer, leddgikt.

6. Solubilisatet ifølge et hvilket som helst av kravene 1 til 3 eller solubilisatet for anvendelse ifølge ett av kravene 4 eller 5,

karakterisert ved at

emulgatorinnholdet, spesielt polysorbatinnholdet, er minst 70 vekt-%, fortrinnsvis i området mellom 75 vekt-% og 95 vekt-%, mest foretrukket i området mellom 79 vekt-% og 88 vekt-%, og/eller

diameterfordelingen av micellene i en fortynning av solubilisatet med destillert vann i forholdet 1:500 under fysiologiske forhold (pH 1,1 og 37 °C) strekker seg fra ca. d_{10} = 6 nm til ca. d_{90} = 20 nm, og/eller

turbiditeten til solubilisatet er mindre enn 25 FNU, fortrinnsvis mindre enn 5 FNU, mest foretrukket mindre enn 3 FNU, målt ved måling av spredt lys ved anvendelse av infrarødt lys i henhold til spesifikasjonene til ISO 7027-standarden ved en fortynning av solubilisatet i et forhold på 1:50 eller 1:500 i vann under fysiologiske forhold (pH 1,1 og 37 °C).

7. Kapsel fylt med et solubilisat ifølge et hvilket som helst av kravene 1 til 3 eller 6, eller kapsel fylt med et solubilisat for anvendelse ifølge et hvilket som helst av kravene 4 til 6,

karakterisert ved at

kapselen er i form av en myk gelatinkapsel eller en hard gelatinkapsel eller en myk gelatinfri kapsel eller en hard gelatinfri kapsel, for eksempel en cellulosekapsel.

8. Fluid, som inneholder et solubilisat ifølge et hvilket som helst av kravene 1 til 3 eller 6, eller kapsel fylt med et solubilisat for anvendelse ifølge ett av kravene 4 til 6, **karakterisert ved at**

fluidet velges fra gruppen omfattende matvarer, kosttilskudd, drikkevarer, kosmetikk og farmasøytiske produkter hvori

fluidet eventuelt omfatter en vandig fortynning av solubilisatet.

9. Fremgangsmåte for fremstilling av et solubilisat ifølge et hvilket som helst av kravene 1, eller 2, eller 6,

med de følgende trinnene

(a) å tilveiebringe polysorbat 80 eller en blanding av polysorbat 80 og polysorbat 20, eller av polysorbat 80 og minst én sukroseester av spiselige fettsyrer;

(b) å tilsette det minst ene kannabinoidet;

(c) å tilsette kurkuminpulver;

hvori

i trinn (a) utføres en oppvarming til en temperatur i et område fra 40 °C til 62 °C, fortrinnsvis til en temperatur i et område fra 45 °C til 57 °C, mest foretrukket til en temperatur i et område fra 48 °C til 52 °C;

og hvori i trinn (b) utføres en oppvarming til en temperatur i et område fra 82 °C til 97 °C, fortrinnsvis til en temperatur i et område fra 83 °C til 92 °C, mest foretrukket til en temperatur i et område fra 85 °C til 89 °C;

hvori trinn c) omfatter å opprettholde denne temperaturen;

hvori, eventuelt, før trinn (b) utføres et trinn (b1) med å tilsette vann ved en temperatur i et område fra 40 °C til 62 °C, fortrinnsvis ved en temperatur i et område fra 45 °C til 57 °C, mest foretrukket ved en temperatur i et område fra 48 °C og til 52 °C;

og/eller hvori eventuelt i trinn

(b1) utføres også å tilsette etanol ved en temperatur i et område fra 40 °C til 62 °C, fortrinnsvis ved en temperatur i et område fra 45 °C til 57 °C, mest foretrukket ved en temperatur i et område fra 48 °C til 52 °C.

10. Fremgangsmåten ifølge krav 9,

hvori i trinn (b) inkorporeres minst ett ytterligere aktivt stoff, spesielt *Boswellia serrata*-ekstrakt og/eller xantohumol.

11. Fremgangsmåten ifølge krav 9 eller 10,

hvori i trinn (c) inkorporeres minst ett ytterligere aktivt stoff, spesielt serrapeptase.

12. Fremgangsmåte for fremstilling av et solubilisat ifølge et hvilket som helst av kravene 1 eller 2 eller 6,

ved å blande et kurkuminsolubilisat og minst ett kannabinoidsolubilisat ifølge krav 3, spesielt i et kvantitativt forhold på 1:1 av de individuelle solubilisatene.

13. Fremgangsmåte for fremstilling av et kannabinoidsolubilisat ifølge et hvilket som helst av kravene 3 eller 6, med de følgende trinnene:

(a) å tilveiebringe polysorbat 80 eller en blanding av polysorbat 80 og polysorbat 20 eller av polysorbat 80 og minst én sukroseester av spiselige fettsyrer;

(b) å tilsette det minst ene kannabinoidet;

hvori i trinn (a) utføres en oppvarming til en temperatur minst

i et område fra 40 °C til 62 °C, fortrinnsvis til en temperatur i et område fra 45 °C til 57 °C, mest foretrukket til en temperatur i et område fra 48 °C til 52 °C;

og hvori i trinn (b) utføres en oppvarming til en temperatur i et område fra 82 °C til 97 °C, fortrinnsvis til en temperatur i et område fra 83 °C til 92 °C, mest foretrukket til en temperatur i et område fra 85 °C til 89 °C.

14. Fremgangsmåten ifølge krav 13,

hvori i trinn (a) økes temperaturen til en verdi i området fra 82 °C til 97 °C, fortrinnsvis til en temperatur i et område fra 83 °C til 92 °C, mest foretrukket til en temperatur i et område fra 85 °C til 89 °C.

15. Fremgangsmåten ifølge krav 13 eller 14,

hvori før trinn (a) utføres et trinn

(a1) å blande glyserol og kannabinoid for å fremstille en løsning,

hvori i trinn (a1) utføres en oppvarming til en temperatur i et område fra 82 °C til 97 °C, fortrinnsvis til en temperatur i et område fra 83 °C til 92 °C, mest foretrukket til en temperatur i et område fra 85 °C til 89 °C

hvori eventuelt før trinn (a) utføres et trinn (a11) å blande vann og minst én sukroseester av en spiselig fettsyre hvori i trinn (a11) utføres en oppvarming til en temperatur minst i et område fra 40 °C til 62 °C, fortrinnsvis til en temperatur i et område fra 45 °C til 57 °C, mest foretrukket til en temperatur i et område fra 48 °C til 52 °C; og et trinn

(a12) å tilsette polysorbat 20 og/eller polysorbat 80 til blandingen fremstilt i trinn (a11) utføres, hvori i trinn (a12) utføres en oppvarming til en temperatur i et område fra 82 °C til 97 °C, fortrinnsvis til en temperatur i et område fra 83 °C til 92 °C, mest foretrukket til en temperatur i et område fra 85 °C til 89 °C.