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(54) **PREPARATION COSMETIQUE DE PRINCIPES ACTIFS A
FACTEUR ELEVE DE PROTECTION CONTRE LES
RADICAUX LIBRES**

(54) **COSMETIC PREPARATION OF ACTIVE SUBSTANCES WITH
HIGH PROTECTION FACTOR AGAINST FREE RADICALS**

(57) Cette préparation cosmétique de principes actifs protège la peau d'une manière particulièrement efficace contre l'agression des radicaux libres, seule ou en association avec d'autres principes actifs. La préparation comporte un extrait d'écorce de Quebraco blanco contenant au moins 90 % en poids d'oligomères de proanthocyanidine, un extrait de ver à soie contenant le peptide cécropine, des aminoacides et un mélange vitaminique, un hydrogel non ionique cationique ou anionique, des phospholipides et de l'eau, et peut également contenir d'autres principes actifs tels que des dérivés vitaminiques et des extraits végétaux d'acérolox, d'algues, d'agrumes, d'oranges amères, de cerises, de papayes, de thé, de grains de café, de Minosa tenuiflora et d'angélique. Ces préparations présentent des facteurs de protection contre les radicaux libres atteignant 10000, et les compositions cosmétiques contenant lesdites préparations possèdent des facteurs de protection compris entre 40 et 200, en fonction de la proportion de la préparation.

(57) The disclosed cosmetic preparation of active substances protects the skin in a particularly effective way against free radical aggression, both alone and in combination with other active substances. The preparation consists of a Quebraco blanco bark extract containing at least 90 wt.% proanthocyanidin oligomers, a silkworm extract containing the peptide cecropin, amino acids and a vitamin mixture, a non-ionic, cationic or anionic hydrogel, phospholipids and water, and may also contain further active substances such as vitamin derivatives and plant extracts of acerola, sea weed, citrus, bitter orange, cherry, papaya, tea, coffee beans, Mimosa tenuiflora and angelica. The preparations have protection factors against free radicals of up to 10000, and the cosmetic compositions containing these preparations have protection factors of between 40 and 200, depending on their proportion of the preparations.

ABSTRACT

The disclosed cosmetic preparation of active substances protects the skin in a particularly effective way against free radical aggression, both alone and in combination with other active substances. The preparation consists of a *Quebraco blanco* bark extract containing at least 90 wt.% proanthocyanidin oligomers, a silkworm extract containing the peptide cecropin, amino acids and a vitamin mixture, a non-ionic, cationic or anionic hydrogel, phospholipids and water, and may also contain further active substances such as vitamin derivatives and plant extracts of acerola, sea weed, citrus, bitter orange, cherry, papaya, tea, coffee beans, *Mimosa tenuiflora* and angelica. The preparations have protection factors against free radicals of up to 10000, and the cosmetic compositions containing these preparations have protection factors of between 40 and 200, depending on their proportion of the preparations.

PCT/DE99/01851

Cosmetic preparation of active substances with high protection factor against free radicals

5 The disclosed cosmetic preparation of active substances protects the skin in a particularly effective way against free radical aggression, both alone and in combination with other active substances.

10 Free radicals such as superoxide ions, hydroxy radicals, oxides are known as a major factor of degeneration and thus the ageing of the skin. They destruct the proteins and lipids of the cellular membrane, affect the DNA and also decompose the hyaluronic acid, a key substance of the skin. Under normal biological conditions there is an equilibrium ratio between the
15 free radicals coming up and their embankment by endogenous chemical or enzymatic systems. Additional outside stress factors such as aggressive atmosphere, tobacco smoke, ultraviolet radiation etc. may overload these inherent immune systems and shift the equilibrium in favour of the free radicals.
20 Inflammation or ageing phenomena of the skin may occur, indicating a need for compensation by cosmetic products.

 There has already been proposed a series of products for this purpose, most of them containing mixtures of the vitamins A, C and E or additives of superoxide dismutase or extracts of
25 certain plants or animals. Thus a cosmetic compound containing ultrasound decomposition products of yeast and other cellular dispersions is known from US-A-5,629,185. From WO96/29048 a cosmetic containing condensed decomposition products of plants or animals is known. There is also a number of publications
30 describing the use of pure plant extracts for cosmetic purposes, such as WO97/45100, where a mixture of seven different extracts is described for anti-cellulite treatment.

The search for other effective substances is a major element of cosmetic research. Another problem of many of these products is that the substances which are effective against free radicals often do not keep their catching properties within the ready cosmetic compound, i.e. it requires special formulations to permanently maintain the effectiveness of the radical catchers.

On the other hand it seems that it has not become widely known in the cosmetic industry yet that there is a possibility of measuring the antioxidant potential of the skin (DE 4328639) and recently also of determining the radical protection coefficient of a cosmetic preparation by using a relatively simple method and to purposefully add materials to such a preparation.

It is an object of the present invention to provide a cosmetic preparation of active substances which has a particularly high radical protection potential.

Another objective of the invention is to provide a preparation of active substances that keeps its radical protection potential over a long period of time.

Another objective of the invention is to provide special cosmetic compounds containing this preparation of active substances and especially such preparations of active substances which achieve further improvement of properties, in particular with regard to opening the pores of the skin.

According to the invention, the cosmetic preparation of active substances with a high radical protection factor is characterised by comprising

a) a product obtained by extraction of the bark of Quebracho blanco and subsequent enzymatic hydrolysis, containing at least 90 percent by weight of proanthocyanidine oligomers and up to 10 percent by weight of gallic acid, wherein the content of (a), which is available in a concentration of 2 percent by weight linked to a microcapsules, ranges from 0.1 to 10 percent by weight;

(b) an extract of the silkworm obtained by extraction,

containing the peptide Cecropine, amino acids and a vitamin mix, wherein the content of (b) may range from 0.1 to 10 percent by weight;

5 (c) a non-ionic, cationic or anionic hydrogel or mixture of hydrogels, wherein the content of (c) may range from 0.1 to 5 percent by weight;

(d) one or several phospholipids comprising 0.1 up to 30 percent by weight;

10 (e) up to 100 percent by weight of water related to the total weight of the active substance preparation each.

As applicable, the active substance preparation may also contain:

15 (f) an ultrasound decomposition product of a yeast containing at least 150 units of superoxide dismutase per ml, wherein the content of the decomposition product (f) is in the range from 0 to 4 percent by weight;

20 (g) an extract of acerola fruits Malpighia punidifolia, wherein the content (g) is in the range from 0 to 20 percent by weight; and

(h) a mixture of 0.1 percent by weight of liposomal Micrococcus luteus extract, retinyle palmitate and tocopherylacetate prepared with phospholipids and free retinyle palmitate related to the total weight of the active substance preparation
25 each.

For one embodiment of the invention comprising the active substance component (h) the portions of the preparation related to the total weight of the cosmetic are as follows: capsules of the active substance according to (a) ranging from 0.1 to
30 10 percent by weight,

hydrogel according to (b) ranging from 0.1 to 5 percent by weight,

encapsulated retinyle palmitate according to (h) 0.001 to 5 percent by weight

35 encapsulated tocopherylacetate according to (h): 0.001 to 2 percent by weight

free retinyle palmitate according to (h): 0.1 to 5 percent by weight

phospholipids: 0.2 to 5 percent by weight,

water as the remaining portion up to 100 percent by weight

5 and/or other auxiliary or carrier substances.

The Quebracho bark extract according to the invention or its hydrolysis product has a very high portion of proanthocyanidines representing condensed tannins. These compounds appearing as oligomers and the low portion of gallic acid in
10 this combination and in a concentration between 1 and 10 percent by weight shows a clear radical protection effect, which by far exceeds the effect of superoxide dismutase (SOD). The activity against free radicals was compared with that of SOD and found to be 42% for a 1 percent by weight solution of
15 the extract (SOD 4%), 83 % for a 2.5 % by weight solution (SOD 15%) and 100 % for a 5 % by weight solution (SOD 38 %).

Preferably the extract (a) contains at least 95 percent by weight of proanthocyanidine oligomers and up to 5 percent by weight of gallic acid, in particular at least 99 percent by
20 weight of proanthocyanidine oligomers and up to 1 percent by weight of gallic acid.

The content of (a) is 1 to 10 percent by weight, wherein the active substance from the Quebracho bark is enclosed in microcapsules. The microcapsules may consist of petrolatum,
25 sodium tristearat, agar, phenonip and water.

The silkworm extract (b) is obtained by extraction of the silkworm (Bombyx mori) with 1,2-propylene glycol and contains vitamins, amino acids and the Cecropine peptide, which has a special antibacterial functionality. A range of studies of the
30 haemolymph and the cuticular matrix of the silkworm carried out during the last years showed that it does not only contain antibacterial peptides but also inhibitors, in particular fungal protease inhibitors. Such extracts also show oxygen-consuming properties, thus activating the cellular metabolism,
35 and they have moisture-keeping properties, a clear curative effect on lesions in the skin by reducing healing time and a

skin-smoothing effect.

Preferably, the extract (b) includes the amino acids aspartinic acid, asparagine, threonine, serine, glutaminic acid, proline, glycine, alanine, valine, cysteine, methionine, 5 isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, arginine.

Preferably extract (b) also contains a vitamin mixture including vitamins B₁, B₂, B₅, B₆, B₈, B₉, B₁₂, PP, A, E and C.

10 The concentration of components (a) and (b) in the active substance preparation preferably ranges from 0.1 to 3 percent by weight each, in particular from 0.5 to 3 percent by weight.

The gel contained according to the invention, which may also be a mixture of different gels, is a hydrogel soluble in water at temperatures above 40 up to 50 °C, approximately, and 15 which takes the gel structure at low temperatures between 10 and 30 °C. Examples of such gels are non-ionic polymers such as polyvinyl alcohol, polyvinyl pyrrolidone-modified maize starch and hydroxyethylcellulose, cationic polymers such as cationic Guar, cationic cellulose, synthetic cationic polymers 20 or gels such as gelatine, carrageenan, bentonite gels, copolymeric gels such as carbomer.

The phospholipids contained according to the invention have been selected among phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl inositol, phosphatidyl serine, 25 phosphatidic acid and lysolecithines as well as mixtures thereof. Known products are Phoslipon®, for example. The contents of phospholipids ranges from 0.1 to 30 percent by weight, preferably 0.5 to 20 percent by weight.

The components (a) and (b) of the active substance 30 preparation and the phospholipids (d) presumably form association-like configurations of different molecules which again are accumulated mostly homogeneously in the generating structure of the gel (c) + (e), the whole being called "association complex". This may also include portions of the 35 SOD-containing yeast decomposition product and of the acerola extract as well as certain plant extracts.

The encapsulated mixture of 0.1 percent by weight of Micrococcus luteus extract, retinyle palmitate and tocopheryl-acetate is present as liposome prepared with phospholipids, wherein the content of retinyle palmitate and tocopherylacetate
5 may preferably range from 0.001 to 1 percent by weight. The portion of phospholipids in this encapsulated mixture generally ranges between 5 and 40 percent by weight.

Additionally, the preparation of the active substance as an association complex may contain a mixture of the vitamins
10 A, B and C as well as additional SOD and/or extracts of acerola fruits. However, the complete preparation of the cosmetic preparation may also contain vitamins and other antioxidants.

According to the invention, the active substance preparation may also contain, in addition to the basic components (a)
15 through (e), different plant extracts such as citrus peel or leaf extracts (Citrus bigaradia, Citrus hystrix, Citrus aurantifolia, Citrofurtunella microcarpa, Citrus aurantium, Citrus reticulata), petitgrain extract (peel or fruit), extract
20 of the Spanish cherry, kiwi extract (Actinidia chinensis), papaya fruit- extract (Caricae papayae), tea extract [leaves of green or black tea, leaves or bark of new jersey tea (Ceanthus velutinas)], coffee bean extract (INCI name: coffee bean extract; of green or roasted beans), prunus extract
25 (Prunus armeniaca, Prunus dulcis, Prunus persica, Prunus domestica, Prunus spinosa, Prunus serotina, Prunus virginiana), extracts of the bark of the Mexican skin tree (Mimosa tenuiflora), angelica root extract (Angelica archangelica). Such plant extracts are commercially available, e.g. from DRAGOCO,
30 Holzminden; Germany.

The content of these plant extracts may range from 0 to 40 percent by weight, preferably from 0.1 to 40 percent by weight, in particular 0.5 to 20 percent by weight, where the mixture may also contain mixtures of these extracts as well as
35 mixtures with the components (f) and (g) of the active substance preparation.

Depending on the plant and the added quantity, the addition of the above plant extracts may increase the radical protection factor several times, presumably with the occurrence of synergistic interactions, the correlation between which we have not been able to find out yet completely.

The antioxidants that may be used in the invention include vitamins such as vitamin C and derivatives of it, such as ascorbylacetates, phosphates and palmitates; vitamin A and its derivatives; folic acid and its derivatives, vitamin E and its derivatives, such as tocopherylacetate; flavones or flavonoides; amino acids such as histidine, glycine, tyrosine, tryptophan and derivatives of it; carotinoids and carotenes, such as β -carotin, α -carotin; uric acid and derivatives; α -hydroxy acids such as citric acid, lactic acid, malic acid; stilbenes and their derivatives etc.

Vitamins may also be contained in a mixture with enzymes as another portion in the active substance preparation or in the cosmetic composition apart from the active substance preparation. The content may be at least be 0.5 percent by weight of a mixture of enzymes and vitamins containing at least 150 units/ml (U/ml) of superoxide dismutase (SOD).

Preferably, the used mixture of enzymes and vitamins is an ultrasound decomposition product of a yeast, where the decomposition product contains SOD, protease, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin D₂ and vitamin E. Preferably, it contains at least 150 U/ml of SOD, protease and the vitamins B and D, where the proportion between SOD and protease as international units at least ranges from 3:1 to 8:1.

Of special advantage for making the enzyme / vitamin mixture is an ultrasound-based decomposition method described in DE 4241154C1, where a cellular dispersion or suspension is passed through a continuous ultrasound irradiation cell, where the sonotrode protects up to half or two thirds of its length into the cell and is submerged in the medium to be exposed to ultrasound-irradiation. The sonotrode has an angle of 80.5 to 88.5 degrees, and the correlation between the submerged length

in mm of the sonotrode and the exposed volume in ml is set to a value ranging from 1:1.1 o 1:20. The portion of solid particles in the medium to be exposed to acoustic irradiation ranges from 1:0.02 to 1:2.2 percent by weight.

5 Yeasts such as baker's yeast, brewing yeast, wine yeast as well as specially treated yeasts such as SOD-enriched yeasts can be used as cellular dispersions. For instance, a cellular dispersion that can be preferably used may contain *Saccharomyces cerevisiae*.

10 The addition, for instance, of 1 percent by weight of such a yeast decomposition product of baker's yeast as an optional portion of the association complex may nearly double a radical protection factor, which itself is high already, from 1620 to 3150. Further remarks on the radical protection factor will be
15 made below.

 In addition to the above components the active substance preparation in the form of the association complex may also contain an extract of acerola fruits (Malpighia punidifolia). Acerola is a small tree indigenous to the West Indies, to
20 northern South America, to Central America, Florida and Texas, which is rich in vitamin C and other active substances such as Vitamin A, thiamine, riboflavine and niacine, which may develop a complex activity together with different other components such as phosphor, iron, calcium. The aqueous acerola extract
25 is normally available as a powdered product.

 As another active substance in the complete composition of the cosmetic preparation and in addition to the above active substance complex an especially preferred embodiment may contain one or several of the following components:

30 (1) extracts or treated extracts of plants binding free radicals or moisture, selected among acerola fruits (*Malpighia punidifolia*), *Camellia oleifera*, *Colunsonia canadensis* and *Hibiscus sabdariffa*;

 (2) extracts or treated extracts of algae binding free radicals
35 or moisture, selected among omega plankton with a high content of cerebrosid stimulants,

micro algae of the chlorella species and macro algae of the ulva species associated with byssus (mussel silk) as biotechnological protein fraction and subsequently associated with dextrine, wherein the product appears in the mixture with peptide derivates derived from α -MSH and associated with xanthin.

(3) natural and synthetic polymers selected among chitosanglycolate, condensed products of desiccated milk, and activated fatty acids,

(4) magnetically hard single crystals of bariumhexaferrite having a coercitive field strength of 3000-5000 Oe and a grain size of 50-1200 nm intercalated in or mixed with asymmetric lamellar aggregates for phospholipids and fluorocarbons as well as

(5) other active substances and carriers selected among hyaluronic acid, omega CH activator, behentrimonium chloride, passion flower oil as well as modified kaolin.

The mentioned modified kaolin is contained according to WO96/17588 and has been modified with spherical TiO_2 or SiO_2 particles having a size of $< 5 \mu\text{m}$, wherein the spherical particles' share in the kaolin mixture ranges from 0.5 to 10 percent by weight. This is what makes the preparation feel very smooth on the skin and gives it additional anti-inflammatory functionality. The modified kaoline may amount to a content ranging from 0.1 to 6 percent by weight of the total quantity of the cosmetic.

The mentioned magnetically hard particles for stimulating the circulation of the blood may be such as described in WO95/03061 or such with smaller particle sizes and in a mixture with asymmetric lamellar aggregates charged with oxygen up to the saturation pressure, where the content of magnetic particles related to the total composition of the cosmetic may range from 0.01 to 10 percent by weight.

The mentioned asymmetric lamellar aggregates are known from WO94/00098 and consist of phospholipids and fluorocarbon charged with oxygen or a fluorocarbon mixture. The fluorocarbon

content is in the range from 0.2 to 100 percent by weight/volume, wherein the phospholipid has a phosphatidyl choline content of more than 30 up to 99 percent by weight and where these aggregates have a skin penetration depending on the critical solubility temperature of the fluorocarbons.

In addition, the aggregates may also appear alone in the cosmetic preparation only charged with oxygen. The content may range from 2.5 to 20 percent by weight of the total composition of the cosmetic.

These aggregates are oxygen carriers and allow the penetration of the oxygen into the skin, thus improving oxygen supply to the skin.

The preparation according to the invention further contains cosmetic auxiliary substances and carriers as normally used in such preparations, e.g. water, glycerine, propylene glycol, preserving agents, colorants, pigments with colouring effect, thickeners, softening substances, moisture-preserving substances, aromatic substances, alcohols, polyalcohols, electrolytes, polar and non-polar oils, polymers, copolymers, emulsifiers, waxes, stabilisers, tinted plant extracts such as fat-soluble gardenia extract, fat-soluble carrot extract, paprika LS extract, β -carotene, lithospermum extract and active deodorants.

It is also advantageous to add suitable water-soluble and/or oil-soluble UVA or UVB filters or both to the composition according to the invention. Among advantageous oil-soluble UVB filters are 4-aminobenzoic acid derivates such as the 4-(dimethylamino) benzoic acid (2-ethylhexyl)ester, ester of the cinnamic acid such as the 4-methoxycinnamic acid (2-ethylhexyl)ester, benzophenone derivates such as 2-hydroxy-4-methoxybenzophenone, 3-benzylidene camphor derivates such as 3-benzylidene camphor.

Water-soluble UVB filters are for instance sulfonic acid derivates of benzophenone or of 3-benzylidene camphor or salts such as the Na or K salt of the 2-phenylbenzimidazol-5-sulfonic acid.

UVA filters include dibenzoylmethane derivatives such as 1-phenyl-4-(4'-isopropylphenyl)propane-1,3-dione

Preferred solar radiation protection filters are inorganic pigments on the basis of metal oxides such as TiO_2 , SiO_2 , ZnO , Fe_2O_3 , ZrO_2 , MnO , Al_2O_3 , which can also be used as a mixture with each other or with organic filters.

Particularly preferred inorganic pigments are agglomerated substrates of TiO_2 and/or ZnO , having a contents of spherical and porous SiO_2 particles, wherein the SiO_2 particle size ranges from 0.05 μm to 1.5 μm and where apart from the SiO_2 particles there are inorganic particle-type substances of a spherical structure, where the spherical SiO_2 particles form defined agglomerates with other inorganic substances having a particle size ranging from 0.06 μm to 5 μm .

Particularly advantageously used SiO_2 particles are highly monodisperse, non-porous, spherical SiO_2 particles according to DE 3616133, produced by hydrolytic polycondensation of tetraalkoxy silane in an aqueous alcoholic-ammoniacal medium, where a sol of primary particles is generated, which subsequently brings the contained SiO_2 particles to the desired particle size of about 0.05 up to 10 μm by continuously adding tetraalkoxy silane proportioned in a controlled way, depending on the reaction.

Pigments, pigment mixtures or powders with pigment-like functionality, also comprising those having a pearlescent effect, may also comprise substances such as: mica, kaolin, talcum powder, mica-titanium oxide, mica-titanium oxide-iron oxide, bismuth oxychloride, nylon globules, ceramic globules, expanded and non-expanded synthetic polymer powders, powdery natural organic compounds such as pulverized hard algae, encapsulated and non-encapsulated cereal starches and mica-titanium oxide-organic dye.

Normally, a wide range of compounds may be used as softeners, such as stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, 1,2-propanediol, 1,3-butandiol, cetylic alcohol, isopropyl isostearate, stearic acid, isobutyl

palmitate, oleyl alcohol, isopropyl laurate, decyloleate, 2-octadecanol, isocetylic alcohol, cetylic palmitate, silicon oils such as dimethylpolysiloxane, isopropyl myristate, isopropyl palmitate, polyethylene glycol, lanoline, cacao
5 butter, vegetable oils such as maize oil, cotton seed oil, olive oil, mineral oils, butyl myristate, palmitic acid etc.

Cosmetic preparations with the preparation of the active substance according to the invention may exist as O/W or W/O emulsions. Suitable emulsifiers for O/W emulsions are for
10 instance addition products of 2-30 mol ethylene oxide to linear C_8 - C_{22} fatty alcohols, to C_{12} - C_{22} fatty acids and to C_8 - C_{15} alkylphenols; C_{12} - C_{22} fatty acid monoesters and diesters of addition products of 1-30 mol ethylene oxide to glycerine ; Glycerine monoesters and diesters as well as sorbitan monoester
15 and diester of C_6 - C_{22} fatty acids, polyol- and polyglycerin-ester; addition products of ethylene oxide to castor oil; betaines such as coconut alkyl dimethyl ammonium glycinate or coconut acylaminoethylhydroxyethylcarboxymethylglycinate (CTFA: cocamidopropyl betaines) as well as ampholytic tensides.

20 Suitable emulsifiers for W/O emulsions are for instance addition products of 2-15 mol ethylene oxide to castor oil, esters of C_{12} - C_{22} fatty acids and glycerine, polyglycerin, pentaerythrite, sugar alcohols (e.g. sorbite), polyglucosides (e.g. cellulose), polyalkylene glycols, wool alcohols,
25 copolymers of polysiloxan polyalkyl polyether.

The water content of a preparation with the active substance complex may vary within a wide range and is preferably between 5 and 90 percent by weight, where a lower water content of about 0.5-8 percent by weight may be found in
30 particular in lipsticks.

The especially preferable cosmetic preparation with the active substance component (f) is a particularly effective protection against the attack of free radicals on the skin both alone and in combination with other active substances and has
35 a surprising effect on the opening of the pores of the skin, similar to the effect of a cleaning means (peeling). This

increases the efficiency of other properties by further ingredients of the cosmetic preparation, like improved moisturizing and smoothing of the skin, thus improving even more and for a longer time the entire state of the skin.

5 It was also surprising that the retinyle palmitate in both encapsulated and in non-encapsulated form is effective in the upper and lower layers of the skin at the same time and maintains this effectiveness over a longer period of time, thus improving the repair effect of the association complex. The
10 latter seems to be due to the presence of tocopherylacetate, since only in this combination the simultaneous and lasting effect could be observed.

 The preparation of the active cosmetic substance according to the invention, when applied either alone or in combination
15 with other active substances, protects the skin in a particularly efficient way against the attack of free radicals on the skin. It has a high radical protection factor between 100 and 3500×10^{14} Radicals/mg.

 The radical protection factor (RPF) determines the
20 activity of a substance for binding free radicals as compared with a test substance. The test substance consists of a highly reactive, semi-stable radical, which reacts with all known antioxidants. Such radicals include nitroxides such as proxo (2,2,5,5-tetramethyle-1-dihydropyrrolinoxy-nitroxide), tempol
25 (2,2,6,6-tetramethyl-1-piperidinoxy-4-ol-nitroxide), DTBN (di-tert-butyl-nitroxide) or preferably DPPH (1,1-diphenyl-2-picryl-hydrazyl).

 The RPF is determined by measuring the signal amplitude of the test radical by electron spin resonance (ESR/EPR) before
30 and after mixing with an antioxidant and by calculating the RPF on this basis. For a series of standard antioxidants the RPF is a known parameter, so it is 827 for all-trans-retinole, 196 for all-trans retinal acetate, 41200 for DL- α -tocopherol and about 48 for α -tocopherol acetate, each $\times 10^{14}$ radicals/mg.

35 The preparation of the active cosmetic substance alone, if existing as "association complex" of the components (a)

through (e) and in a concentration of 10 percent by weight of (a) and (b) each has an RPF of 1255, which is very high as compared with common active substances in cosmetic formulations with declared radical scavengers, which achieve values of about 4 to 40. This is the case even though the concentration of the active substances themselves in (a) and (b) is only 2 percent by weight, as a maximum.

"High radical protection factor" according to the present invention means a value of 100 or higher, preferably 1000 or higher. In certain combinations of plant extracts and the association complex itself according to the present invention this value may be increased to 10000 and higher. Depending on the portion of the preparation, the corresponding cosmetic compositions with such preparations comprise radical protection factors, for example, from 40 to 200 or higher.

The exact method for measuring the radical protection factor has been described by Herrling, Groth, Fuchs and Zastrow in Conference Materials "Modern Challenges To The Cosmetic Formulation" 5.5.-7-5.97, Düsseldorf, p. 150-155, Verlag f. chem. Ind. 1997. Starting from the known concentration of the test substance (here: DPPH) or the number of its free radicals (radicals per ml) they measure a signal amplitude S_1 with an ESR spectrometer. The test radical and the antioxidant are dissolved in a water/alcohol solution (e.g. 0.1 M) each. The signal amplitude S_2 of the antioxidant is measured. The normalised difference between the two signal amplitudes is the reduction factor RF.

$$RF = (S_1 - S_2) / S_1$$

The result of the radical reduction of the test substance $RC \times RF$ is normalised relative to the quantity of product input PI (mg/ml). Where RC is the amount of the test substance, i.e. the known number of radicals in the test substance. The radical protection factor is calculated by means of the following equation:

15

$$\text{RPF} = \frac{\text{RC [Radicals/ml]} \times \text{RF}}{\text{PI [mg/ml]}}$$

The result is

5 $\text{RPF} = N \times 10^{14}$ [Radicals per mg],
 where N is a positive real number and RPF for simplification
 may be reduced to the value of N. This reduction has been used
 in the examples of the present invention.

10 The radical protection factor may be determined by means
 of a handy and very simple ESR spectrometer (GALENUS GmbH,
 Berlin, Germany) and is a new magnitude for characterising
 cosmetic products as regards their capacity of binding free
 radicals. The method is an in vitro method, where no individual
 properties of the user of the cosmetic are influencing the
 15 antioxidants.

 Other advantageous effects of products with the active
 substance preparation according to the invention, in combina-
 tion with other active substances or carriers are a lasting
 improvement of the general state of the skin, a delayed ageing
 20 process of the skin, lasting improvement of the moisturizing
 and smoothing effect on the skin. The particularly advantageous
 embodiment described above with an additional algae-peptide
 product and magnetically hard single crystals of bariumhexa-
 ferrite comprises a special allergy-reduced risk, according to
 25 allergy and dermatological tests.

 The cosmetic preparation according to the invention may
 be used, for example, in sun creams, sun gels, after-sun
 products, day creams, night creams, masks, body lotions,
 cleansing milk, makeup's, lipsticks, eye cosmetics, hair masks,
 30 hair conditioners, shampoos, shower gels, shower oils, bathing
 oils and other common products. A particular advantage of the
 active substance preparation according to the invention is the
 embodiment with the optional component (f) in a cream, lotion,
 a makeup, fluid, gel or lipstick. Advantageous cosmetic
 35 preparations also include tooth pastes mouthwash, under the
 special aspect of neutralising free radicals in the mouth of
 smokers and also as special cream for the hands and the face

of smokers. Such products are manufactured in a way known by workers skilled in the art. When selecting special carrier substances, the corresponding pharmaceutical preparations may also be made.

5 Another subject matter of the invention is a cosmetic preparation comprising a content of plant extract selected from the group comprising citrus extract, petitgrain extract, cherry extract of the Spanish cherry, papaya fruit extract, tea extract, coffee bean extract, prunus extract, skin tree
10 extract, angelica extract and mixtures of them as has been defined more in detail above, with a content of 0.5 to 40 percent by weight as well as 99.5 to 60 percent by weight of other active substances or carriers or mixtures of active substances and carrier substances, each related to the total
15 composition. Active and carrier substances may be the substances mentioned above.

The following examples are to illustrate the invention more in detail. If not otherwise indicated, all measures will be given in percent by weight.

20 Manufacture of the active substance complex

For making the gel basis, gel powder such as carbomer was added to water, homogenised and subsequently neutralised with triethanolamine, for example. Then ethanol and glycerine were added to improve mixing properties, and the mixture was well
25 stirred.

To this gel basis a mixture of phospholipids (Phoslipon®), Quebracho extract and silkworm extract was added and mixed at a temperature of up to 45 °C. Then another portion of the above gel or a second gel such as Guar propyl triammonium chloride
30 was added and stirred well with the whole mixture at increased temperature, but below 45 °C. This way you got the active substance preparation according to the invention, hereinafter called "complex".

In those cases where the active substance preparation
35 contained other ingredients such as yeast decomposition product, acerola extract or extracts of tea, coffee, kiwi,

citrus, cherry, papaya or skin tree, such extract was added to the mixture of phospholipids and mixed with the gel.

Example 1 Day cream

5 phase A: carbomer 0.2; glycerine 2.0; propylene glycol 1,0;

dist. water q.s. ad 100;

phase B: C₁₂-C₁₅-alkyl cetylic alcohol 3,7; stearate 0,5; jojoba oil 1,0;

phase C: triethanolamine 0,2;

10 phase D: active substance complex with (a) through (f) 3.5; perfume 0.5; preservant 0.3

15 Phases A and B were warmed up to 65 ±2 C° while being stirred, and phase B was homogenised in phase A. Then phase C was added and homogenised correspondingly. Subsequently, the mixture was cooled down to 35 °C while being stirred, and phase D was added and mixed thoroughly. The active substance complex contained 1.0 % of an SOD-containing enzyme / vitamin product obtained from baker's yeast using the ultrasound method

20 according to DE 4241154C1.

The added active substance complex contained 1% of dry gel, 7% of phospholipids, 2% of Quebracho extract, 1% of silkworm extract, 1% of SOD from a yeast decomposition product. The radical protection factor of this active substance complex

25 amounted to 1925, and in the formulation the RPF was around 49.

Example 2 Special cream

phase A: glycerine 3.0; dist. water q.s. ad 100;

phase B: Vaseline 22.5; jojoba oil 5.0;

30 phase C: active substance complex with (a) through (f) 5.5; asymmetric lamellar aggregates (AOCS) according to example 2 of WO94/00109 10.5; AOCS with Ba hexaferrite single crystals according to example 1 of WO95/03061, 2.0; modified kaolin according to example 1 of WO96/17588 0,3.

35 Phases A and B were warmed up to 65 ±2 C° while being stirred, and phase B was homogenised in phase A. Subsequently, the mixture was cooled down to 35 °C while being stirred, and

phase C was added and mixed thoroughly.

The active substance complex contained 1.0 % of an SOD-containing enzyme / vitamin product obtained from wine yeast using the ultrasound method according to DE 4241154C1 and in addition 0.5 % of vitamin E and 0.5 % of vitamin C. The basic ingredients of the active substance complex were 0.5% of dry gel, 10% of phospholipids, 1% of quebracho extract, 2% of silkworm extract. The radical protection factor of this active substance complex amounted to 2120, and in the formulation the RPF was around 41.5.

Example 3 Sun gel

phase A: carbomer 1.5; glycerine 3.0; propylene glycol 2.5; dist. water q.s. ad 100;

phase B: triethanolamine 1,5;

phase C: peptide preparation MAP-X® according to PCT/DE97/02941 1,0; ZnO 2.0; TiO₂ 5.0; SiO₂ 1.0; shellac (20 % aqueous solution) 1.0;

phase D: active substance complex with (a) through (f) 3,5;

phase E: perfume 0.5, preservative 0,3.

Phase A was warmed up to 60 ±2 °C while being stirred and homogenised and cooled down to 45 °C. Phase B was homogenised in phase A. After cooling down to about 40 °C, phase C was added and the mixture was well homogenised. Subsequently, the mixture was cooled down to 35 °C while being stirred, and phases D and E were added and mixed and stirred thoroughly.

The active substance complex contained 1.0 % of an SOD-containing enzyme / vitamin product obtained from brewer's yeast using the ultrasound method according to DE 4241154C1 and in addition 0.5 % of vitamins E, vitamin C and vitamin A, each. The basic ingredients of the active substance complex were 0.15% of dry gel, 20% of phospholipids, 5 % of quebracho extract, 3 % of silkworm extract. The radical protection factor of this active substance complex amounted to 3050.

Example 4 Day cream

A composition according to example 1 was made, with the active substance complex containing 20 % of black tea extract

instead of 1 % of SOD of a yeast decomposition. The radical protection factor of this active substance complex amounted to 3100.

Example 5 Sun cream

5 A composition according to example 1 was made, wherein phase A contained an additional 3 % of TiO_2 and 7.5 % of benzophenone-3. Instead of 1 % of SOD of a yeast decomposition, the active substance complex contained 5 % of coffee bean extract of roasted coffee beans and 2% of kiwi extract. The
10 radical protection factor of this active substance complex amounted to 3200.

Example 6 Day cream

A composition according to example 1 was made, wherein phase A contained an additional 1% of TiO_2 and 0.5 % of ZnO .
15 Instead of 1 % of SOD of a yeast decomposition, the active substance complex contained 1 % of green tea extract, 2 % of an extract of green coffee beans, 1% of vitamin C and 1% of vitamin E (tocopherolacetate). The radical protection factor of this active substance complex amounted to 5600.

20 Example 7 Example for comparison purposes

The following components of an active substance complex were mixed with each other:

0.15 % of guar propyl triammonium chloride (gel); 20 % of phospholipids; 0.1 % of triethanolamine; 1.0 % of vitamin E;
25 0.1 % of vitamin C; 78.65 % of water.

The measured radical protection factor of the whole compound was 2.

Example 8 emulsion-based fluid with increased vitamin A content (vitamin A²)

30 phase A: carbomer 0.05, glycerine 2.5, propylene glycol 0,5; dist. water q.s. ad 100;
phase B: C_{12} - C_{15} -alkyl cetylic alcohol 1.5; stearate 0,1; olive oil 1,0;
phase C: triethanolamine 0,05;
35 phase D complex with (a) through (d) containing 2 % of quebracho extract, 2 % of silkworm extract, 0.1 % of carbomer,

0.1 % of TEA, water 0.9%;

as well as (h) retinyle palmitate and tocopherylacetate (1:1) as liposomes with phospholipids and with 0.1 % of Micrococcus luteus extract = 0.1, retinyle palmitate (free) 0.5;

5 phase E: perfume oil 0.2, preservant 0.3.

Phases A and B were warmed up to 65 ± 2 °C while being stirred, and phase B was homogenised in phase A. Then phase C was added at about 50 °C and homogenised correspondingly. Subsequently, the mixture was cooled down to about 30 °C while
10 being stirred, and phases D and E were added and mixed and homogenised thoroughly.

The radical protection factor of the complex amounted to 2100, and in the fluid the RPF was around 20.

Example 9 O/W Antismoke day cream

15 phase A: sorbitan monostearate 4; avocado oil 3;
Oleyl oleate 8;

phase B: water q.s. ad 100; propylene glycol 2, glycerine 5
carbomer 0.2;

phase B1: NaOH 0.4;

20 phase C: preservant 0.4;

phase D: active substance complex with (a) through (f) with
vitamins A,E,C,B 5;

phase E: perfume oil 0,5.

Phases A and B were made separately at 80 °C while
25 stirring intensively and subsequently mixed, stirred and homogenised. After cooling down to 60 °C, phase B1 was added for neutralisation. After cooling down to 50°C, phase C was added. At 30 °C phases D and E were added to the mixture one after another and homogenised; RPF = 39.

30 Example 10 Antismoke night cream

The cream provides a repair effect to a smoker's skin while at the same time having a prophylactic effect for the day.

phase A: Vaseline 8.5; jojoba oil 3.0; stearic acid 3.8;

phase B: water q.s. ad 100; glycerine 5; carbomer 0.3;

35 phase C: triethanolamine 0,3;

phase D: preservant 0.4;

phase E: active substance complex (a) through (f) with vitamins A, E, C, B and 2 % aloe vera 10.0; perfume oil 0.1.

The procedure was the same as in example 9; RPF = 48.

Example 11 Hand cream against brown smoker's fingers

5 phase A: cetylic alcohol 8.5; stearic acid 3.8;

phase B: water q.s. ad 100; glycerine 2, carbomer 0.9;

phase C: triethanolamine 0,3;

phase D: vitamin E 1.0; aloe vera 1.0; preservant 0.4; active substance complex with (a) through (f) with vitamins A, E, C

10 5.0; perfume oil 1.4; whitening complex 1,0.

The procedure was the same as in example 9; RPF = 35.

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Claims

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1. Cosmetic active substance preparation with a high radical protection factor, which comprises a content of

10 a) a product obtained by extraction of the bark of Quebracho blanco and subsequent enzymatic hydrolysis, containing at least 90 percent by weight of proanthocyanidine oligomers and up to 10 percent by weight of gallic acid, where the content of (a), which is available in a concentration of 2 percent by weight linked to a microcapsule ranges from 0.1 to 10 wt.%;

15 (b) an extract of the silkworm obtained by extraction, containing the peptide cecropine, amino acids and a vitamin mix, where the content of (b) ranges from 0.1 to 10 wt.%;

(c) a non-ionic, cationic or anionic hydrogel or mixture of hydrogels, where the content of (c) ranges from 0.1 to 5 wt.%;

20 (d) one or several phospholipids in the range of 0.1 up to 30 wt.%;

(e) water.

2. Preparation according to claim 1, characterised by additionally comprising

25 (f) an ultrasound decomposition product of a yeast containing at least 150 units of superoxide dismutase per ml, wherein the content of the decomposition product (f) is in the range from 0 to 4 wt.%, and

30 (g) an extract of acerola fruits Malpighia punidifolia, wherein the content (g) is in the range from 0 to 30 wt.%; related to the total weight of the active substance preparation each.

35 3. Preparation according to claim 1, characterised by additionally comprising

(h) a mixture of 0.1 wt.% of Micrococcus luteus extract,

retinyle palmitate and tocopherylacetate in liposomal form prepared with phospholipids, and additionally free retinyle palmitate and wherein the portions of the components contained
5 in the preparation relative to the total weight of a cosmetic preparation are as follows: active substance capsules according to (a) and (b) ranging from 0.1 to 10 wt.%, hydro gel according to (c) ranging from 0.1 to 5 wt.%, encapsulated retinyle palmitate according to (h) ranging from 0.001 to 5 wt.%,
10 encapsulated tocopherylacetate according to (h) 0.001 to 2 wt.%, free retinyle palmitate according to (h) 0.1 to 5 wt.%, phospholipids 0.2 to 5 wt.%.

4. Preparation according to claim 3, characterised in that the
15 portions of the components lie within the following ranges: active substance capsules according to (a) and (b) ranging from 0.5 to 3 wt.%, hydro gel according to (c) ranging from 0.1 to 3 wt.%, encapsulated retinyle palmitate according to (h) ranging from 0.05 to 2 wt.%, encapsulated tocopherylacetate
20 according to (h) ranging from 0.05 to 1 wt.%, free retinyle palmitate according to (h) ranging from 0.5 to 2 wt.%.

5. Preparation according to claim 1, characterised in a radical protection factor in the range from 100 to 3500, measured by
25 determining the number of free radicals of a solution of a test substance (S_1) by electron spin resonance (ESR) as compared with the ESR measurement result of the cosmetic active substance preparation according to the relationship
$$RPF = (RC \times RF) / PI, \text{ where } RF = (S_1 - S_2) / S_1 ; RC = \text{concentration of the test substance (radicals per ml)}; PI = \text{concentration of the active substance preparation (mg per ml)}.$$

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6. Preparation according to claim 1, characterised in that the extract (a) contains at least 99 wt.% of proanthocyanidine
35 oligomers and up to 1 wt.% of gallic acid.

7. Preparation according to claim 1, characterised in that the amino acids contained in (b) comprise aspartic acid, asparagine, threonine, serine, glutamic acid, proline, glycine, alanine, valine, cysteine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, arginine.
8. Preparation according to claim 1, characterised in that the vitamin mixture included in (b) comprises the vitamins B₁, B₂, B₅, B₆, B₈, B₉, B₁₂, PP, A, E and C.
9. Preparation according to claim 1, characterised in that the active substance preparation contains an additional mixture of the vitamins A, E and C or each of these vitamins individually.
10. Preparation according to claim 1, characterised in that it exists as an association complex between the phospholipids (d), partially comprising the components (a) and (b) and the gel (c) with the water (e).
11. Preparation according to claim 1, characterised in that the active substance preparation exists as cosmetic composition, further comprising one or several of the following components:
- (1) extracts or treated extracts binding free radicals or moisture of
- (1.1) plants selected among acerola fruits (*Malpighia punidifolia*), *Camellia oleifera*, *Colunsonia canadensis* and *Hibiscus sabdariffa*; or
- (1.2) algae selected among omega plankton, providing a high portion of cerebroside stimulants, microalgae of the *Chlorella* species and macro algae of the *Ulva* species associated with byssus (mussel silk) as biotechnological protein fraction and subsequently associated with dextrine, wherein the product appears in the mixture with peptide derivatives derived from α -MSH and associated with xanthin;
- (2) yeast decomposition products selected among baker's yeast, brewer's yeast, wine yeast and made according

- to a non-harming ultrasound treatment of the aqueous yeasts;
- (3) natural and synthetic polymers selected among chitosan-glycolate, condensed products of desiccated milk, and activated fatty acids;
- 5 (4) magnetically hard single crystals of bariumhexaferrite having a coercitive field intensity of 3000 - 5000 Oe and a grain size of 50-1200 nm intercalated in or mixed with asymmetric lamellar aggregates of phospholipids and fluorocarbons ; and
- 10 (5) other active substances selected among chitosanglycolate, hyaluronic acid, omega CH activator, behentrimonium chloride, passion flower oil and carrier substances;
- (6) mixtures thereof.
- 15 12. Preparation according to claim 1, characterised in that the concentration of the components (a) and (b) in the active substance ranges from 0.1 to 3 wt.% each.
- 20 13. Preparation according to claims 1 or 11, characterized in that it comprises an additional portion of 0.1 to 20 wt.% of plant extracts selected from the group consisting of citrus peel or leaf extracts (*Citrus bigaradia*, *Citrus hystrix*, *Citrus aurantifolia*, *Citrofortunella microcarpa*, *Citrus aurantium*, *Citrus reticulata*), petitgrain extract (peel or fruit), extract
- 25 of the Spanish cherry, kiwi extract (*Actinidia chinensis*), papaya fruit extract (*Caricae papayae*), tea extract [leaves of green or black tea, leaves or bark of new jersey tea (*Ceanthus velutinas*)], coffee bean extract (INCI name: coffee bean extract; of green or roasted beans), prunus extract (*Prunus armeniaca*, *Prunus dulcis*, *Prunus persica*, *Prunus domestica*,
- 30 *Prunus spinosa*, *Prunus serotina*, *Prunus virginiana*), extracts of the bark of the Mexican skin tree (*Mimosa tenuiflora*), angelica root extract (*Angelica archangelica*); and the remaining portion of carrier substances or other active
- 35 substances and carrier substances.

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5 14. Cosmetic preparation characterised in a content of 0.5 to
40 wt.% of plant extracts selected from the group comprising
cherry extract of the Spanish cherry, papaya fruit extract
(*Caricae papayae*), tea extract [leaves of black tea, leaves or
10 extract of green or roasted beans, prunus extract (*Prunus*
armeniaca, *Prunus dulcis*, *Prunus persica*, *Prunus domestica*,
Prunus spinosa, *Prunus serotina*, *Prunus virginiana*), angelica
root extract (*Angelica archangelica*)
and 99.5 to 60 wt.% of carrier substances or of other active
15 substances and carrier substances.

15. Use of the cosmetic preparation of active substances with
high protection factor against free radicals according to any
of claims 1 through 13 in combination with other cosmetic
20 substances such as other active substances, auxiliary sub-
stances and carrier substances in cosmetic preparations such
as creams, gels, lotions, masks, make-up, shampoos, sticks,
oils, mascara, corresponding sun protection preparations as
well as toothpastes and mouthwashes.

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AMENDED SHEET