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COSMETIC CONTAINING PHOSPHOLIPIDS AND FLUOROCARBON COMPOUNDS

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(56) Prior Art Documents
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(57) Claim

1. Phospholipid- and fluorocarbon-containing cosmetic, characterised in that it consists of
(a) a carrier suitable for cosmetic use; and
(b) asymmetric lamellar aggregates of phospholipids, which have a phosphatidylcholine content in the range from 30 to 99 % by weight and fluorocarbons laiden with oxygen in the range from 0.2 to 100 % (weight/volume); having a skin penetration depending on the critical solubility temperature of the fluorocarbons or fluorocarbon mixtures selected.

10. Process for the preparation of a phospholipid- and fluorocarbon-containing cosmetic, characterised in that phospholipids having a phosphatidylcholine content of 30 to 99 % by weight are incorporated with a fluorocarbon or fluorocarbon mixture laiden with oxygen after preemulsification at relatively high rotational speeds and subsequent high pressure emulsification into a carrier which is suitable for cosmetic use and does not

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interact with the asymmetric lamellar aggregates, the amount of fluorocarbon being in the range from 0.2 to 100 % (weight/volume) and the particle size of the asymmetric lamellar aggregates being 50 to 1000 µm.

14. Use of a phospholipid-containing cosmetic for control of the oxygen supply to the skin by applying a system containing an asymmetric lamellar oxygen carrier, containing phospholipids having a phosphatidylcholine content of 30 to 99 % by weight and fluorocarbons in the range from 0.2 to 100 % weight/volume, the penetration into the skin being controlled by means of the carrier structure of the phospholipid aggregates and the critical solubility temperature of the fluorocarbons (in n-hexane), and the system being distributed in a carrier which is customary for cosmetic use, such as ointments, creams, lotions, waters, alcoholic extracts, pastes, gels, powders or tinctures, or optionally present on a dressing or a plaster or as a spray.

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(54) Title: COSMETIC CONTAINING PHOSPHOLIPIDS AND FLUOROCARBON COMPOUNDS

(54) Bezeichnung: PHOSPHOLIPIDE UND FLUORCARBONE ENTHALTENDES KOSMETIKUM

(57) Abstract

A cosmetic is disclosed for aiding the transport of oxygen in the skin, as well as a process for preparing the same and its use. The problem with known cosmetics is the insufficient oxygen supply to the skin and adjacent tissues. The object of the invention provides a means to go beyond the stratum corneum of the skin and the epiderm by penetration processes in order to increase the oxygen concentration in the corial zone and adjacent tissues and to activate the metabolic processes. For that purpose, a cosmetic with asymmetrical lamellary aggregates consists of phospholipids and an oxygen-loaded fluorocarbon compound or a fluorocarbon compound mixture. The proportion of fluorocarbon compound lies in a range from 0.2 to 100 % by weight/volume, and it is contained in an excipient appropriate for dermatological uses. This cosmetic is prepared by emulsifying its components and is used in salves, creams, lotions, liquids, alcoholic extracts, pastes, powders, gels, tinctures on or plasters and bandages, or in a spray.

(57) Zusammenfassung

Die Erfindung betrifft ein Kosmetikum zur Unterstützung des Sauerstofftransportes in der Haut, ein Verfahren zu seiner Herstellung sowie die Verwendung desselben. Problem bei den bekannten Kosmetika ist die unzureichende Sauerstoffversorgung der Haut und des angrenzenden Gewebes. Erfindungsaufgabe ist es daher, das Stratum corneum der Haut und die Epidermis durch Penetrationsvorgänge zu überwinden, um im corialen Bereich und angrenzendem Gewebe die Sauerstoffkonzentration zu erhöhen und Stoffwechselvorgänge zu aktivieren. Erfindungsgemäß erfolgt dies durch ein Kosmetikum mit asymmetrischen lamellaren Aggregaten, bestehend aus Phospholipiden und mit Sauerstoff beladenem Fluorcarbon oder Fluorcarbongemisch, wobei der Anteil an Fluorcarbon im Bereich von 0,2 bis 100 % Gewicht/Volumen liegt, in einem für die dermatologische Anwendung geeigneten Träger. Die Herstellung erfolgt durch Emulgierung der entsprechenden Bestandteile und die Verwendung in Salben, Cremes, Lotionen, Wässern, alkoholischen Auszügen, Pasten, Pudern, Gelen, Tinkturen oder auf Verbänden und Pflastern bzw. in einem Spray.

Phospholipid- and fluorocarbon-containing cosmetic

The invention relates to a phospholipid- and fluorocarbon-containing cosmetic having an activity which improves the oxygen supply to the skin.

It is known to employ particular structures in the form of aqueous phospholipid liposomes as cosmetic preparations. Structure-regenerating effects and an improvement in the capacity of resistance of the skin are ascribed to the liposomes prepared from natural phospholipids, e.g. soya lecithin, having a lamellar bilayer structure corresponding to the cell membrane structure. The liposomes penetrate the horny layer and fix to weakened sites of the epidermis and improve the interstitial cell structure.

An increase in the activity of liposomes is achieved by the encapsulation of active compounds and the preparation of liposomal cosmetics. DE-A-3242385 (L'OREAL) protects a liposomal composition which in the liposome phase contains polypeptide extracts, plant extracts (almondermin) and UV light protection filters.

The company Dior markets the face gel "Capture", which contains 5 % thymus extract, 1 % collagen and elastin peptides and 0.1 % hyaluronic acid in liposomes of 100 nm diameter made of soya lecithin. Use is effected by means of a pump disperser [sic].

For improved supply of the skin with oxygen, it has already been proposed to use peroxides such as hydrogen peroxide in order to stimulate the cell metabolism of the skin via the nascent oxygen formed. The considerable side effects such as the skin irritations, however, are an obstacle to use. DE-A-2534315 claimed an O_2-containing cosmetological formulation which is composed of an O_2-saturated gaseous fluorocarbon and a surfactant in aqueous phase in an aerosol container. Borgarello (EP-A-296661) developed an isotropic single phase system for the cosmetic sector, in which halogenated compounds are intended to act as oxygen carriers. A typical composition consists of 34 % of a

mixture of perchloro-1-butyltetrahydrofuran and polyfluoro-1-propyltetrahydrofuran, 7 % isopropanol, 49 % water and 10 % emulsifier. The emulsifiers used are very highly surface-active fluorosurfactants, e.g. of the perfluoroalkanesulphonamide type, which are known to be extremely toxic on i.p. administration in the mouse (LD_{50} 0.1 to 0.2 g/kg) and also have an irritant effect on the skin. Other possible solutions concern the use of a haemolymph extract of molluscs or of an extract of proteins and proteides from cattle spleen.

A convincing and physically detectable toning and invigoration of the skin surface cannot be achieved with the preparations and methods mentioned.

The invention is based on the object of improving the oxygen supply to the skin with the aid of a cosmetic composition containing phospholipids such that a detectable effect is achieved.

According to the invention, the phospholipid-containing cosmetic consists of asymmetric lamellar aggregates, which consist of phospholipids and oxygen-laden fluorocarbon or fluorocarbon mixture, the amount of fluorocarbon being in the range from 0.2 to 100 % w/v (w/v = weight/volume), in a carrier suitable for cosmetic use.

A plurality of fluorocarbons can be employed, e.g. aliphatic straight-chain and branched fluoroalkanes, mono- or bicyclic and optionally fluoroalkyl-substituted fluorocycloalkanes, perfluorinated aliphatic or bicyclic amines, bis(perfluoroalkyl)ethenes, perfluoropolyethers or mixtures thereof. Particularly preferred fluorocarbons are those such as perfluorodecalin, F-butyltetrahydrofuran, perfluorotributylamine, perfluorooctyl bromide, bis-fluoro(butyl)ethene or bis-fluoro(hexyl)ethene or C_6-C_9-perfluoroalkanes.

The amount of fluorocarbons here is in the range from 20 to 100 % w/v, preferably in the range from 40 to 100 %. A particularly preferred range is that from 70 to 100 % w/v.

The term "fluorocarbons" used here is understood

as meaning perfluorinated or highly perfluorinated carbon compounds or mixtures, which are able to transport gases such as O_2 and CO_2. Highly fluorinated hydrocarbon compounds within the meaning of this invention are those in which most of the hydrogen atoms are replaced by fluorine atoms, so that on further replacement the capability for gas transport is not necessarily increased. This is usually achieved if approximately up to 90 % of the hydrogen atoms are replaced by fluorine atoms. Preferred fluorocarbons within the meaning of the present invention are those in which at least 95 % of the hydrogen atoms are replaced, more preferably 98 % and most preferably 100 %.

The phospholipids employed according to the invention are natural phospholipids such as soya lecithin and egg lecithin, synthetic phospholipids and also hydrogenated lecithins, e.g. phospholipone H or partially hydrogenated phospholipids. In these phospholipids, the content of phosphatidylcholine according to the invention is in the range from 10 to 99 % by weight, preferably 30 to 99 % and in particular 70 to 90 %.

In addition to phosphatidylcholine, lysolecithins can also be present in the concentration range from 0.1 to 10 % by weight and/or charged phospholipids such as phosphatidylethanolamine, n-acetylphosphatidylethanolamine or phosphatidic acid in the concentration range 0.1 to 30 % by weight.

In contrast to the known aqueous liposomes (vesicles), the phospholipid-stabilised aggregates according to the invention carry in their core hydrophobic fluorocarbons which are capable of the transport of oxygen. Their interfacial chemical stabilisation is effected primarily by a monolayer having inverse arrangement and optionally a structure of bilayer films attached thereto. Because of the peculiarity of their structural arrangement, these novel aggregates are designated as asymmetric lamellar oxygen carriers. Their exceptional colloid chemical stability can presumably be traced back to the lamellar structure and to the surface

charge of the aggregates. The latter can be traced back to the choice of suitable phospholipids or their mixtures of natural as well as of synthetic origin. Phospholipids, in particular phosphatidylcholine in the said concentration range from 10 to 99 % in combination with lysolecithins of concentration from 0.1 to 10 % and/or charged phospholipids in the concentration range 0.1 to 30 % by weight are primarily responsible for an advantageous action in this sense. The claimed action of the phospholipids is verified by appropriate negative zeta potentials and by the measurement of charge densities (on titration with a cationic polyelectrolyte).

The advantage of the phospholipid dispersions according to the invention is that as a result of an additional oxygen supply mediated via the fluorocarbon, the circulation and thus the metabolic processes in the epidermal layer are promoted and the general status of breathing of the skin is increased. With the increase in cell respiration, the natural defence potential of the skin is increased and the elimination of skin toxins is promoted. Moreover, as a result of the use of the cosmetic in a phospholipid-stabilised form, the moisture-giving action and skin-smoothing properties associated with it come to bear because of the water-carrying lamellar layer structures.

In contrast to the known preparations mentioned at the beginning, the compositions according to the invention show that the chemically inert fluorocarbons can supply the skin with oxygen advantageously and in metered form on account of their exceptionally high oxygen-dissolving power when used topically in the form of asymmetric lamellar aggregates. It was possible for the first time to confirm the penetration of the asymmetric lamellar aggregates by a spectroscopic process as a confirmation of the effect according to the invention using a labelled phospholipid dispersion of physiologically intact isolated skin.

Use as a cosmetic is not restricted to the face parts of the person, but relates to all epidermal areas

of other body, including fatty tissue with deficient circulation affected by cellulitis and the scalp area, in this case in particular the hair cells.

The topical use of fluorocarbon-containing phospholipid-stabilised aggregates on the skin was unknown until now. Fluorocarbons themselves are chemically and biologically inert organic liquids having a high oxygen-dissolving power. Because of these properties, they were proposed as gas carriers in blood substitute emulsions and also put into use in humans (K. C. Lowe: Blood substitutes, Ellis-Horwood, Chichester, GB., 1988). Like soya or egg lecithin, the naturally occurring phospholipids are also toxicologically acceptable and moreover known as skin-compatible and good for the skin.

The fluorocarbons can be selected for O_2 solubility, partial vapour pressure and lipid solubility according to the specific intended application. The critical solubility temperature of the fluorocarbons (CST) in n-hexane correlates with their solubility in lipids, e.g. cell membranes, and is thus a measure of the rate of release through the skin. Thus, e.g. perfluorodecalin and perfluorooctyl bromide having small CST values are released relatively rapidly, while on the other hand F-tributylamine having a high CST value of 59°C also has a high half-life of release. It was found that fluorocarbons behave ideally when mixed and their CST values depend linearly on the composition. It is thus possible by mixing various fluorocarbons to set defined CST values which are often not realisable by means of individual compounds. This result offers the possibility of employing fluorocarbon mixtures specifically to affect the penetration rate into the skin and their residence time in a positive manner.

The invention also relates to a process for the preparation of a phospholipid-containing cosmetic, which consists in emulsifying phospholipids with a fluorocarbon or a fluorocarbon mixture which is loaded with oxygen, the amount of fluorocarbon being in the range from 0.2 to

100 % w/v, and the asymmetric lamellar aggregates having a mean particle size from 50 to 3000 nm obtained in this way being incorporated into a carrier suitable for cosmetic use. A preemulsification of the crude dispersion by addition of the fluorocarbon to an aqueous phospholipid solution at a temperature corresponding to the starting substances employed is effected here. The preemulsification is appropriately effected at relatively high speeds of rotation, e.g. 12,000 to 15,000 rpm. The actual homogenisation is then effected using a high-pressure homogeniser. The diameters of the aggregates are in the order of magnitude from 50 to 3000 nm, preferably 140 to 320 nm. The particle size distributions can be rendered uniform or separated by centrifugation. Heat sterilisation in an autoclave is possible without an effect on the particle sizes. To avoid autoxidation processes in the unsaturated fatty acid radical of native lipids, antioxidants, e.g. α-tocopherol, can be added.

The lipid fraction employed according to the process contains phosphatidylcholine according to the invention in an amount from 0.1 to 99 % by weight, preferably 30-99 % and in particular 70 to 90 %.

The incorporation of the asymmetric lamellar aggregates as an active substance in ointments, creams, lotions and other aqueous or alcoholic cosmetic formulations is effected depending on the intended application, it being possible to vary the fluorocarbon content and thus the O_2 availability within wide limits. Before incorporation into all cosmetic systems, e.g. gels, pastes, powders, ointments, creams, lotions and waters or alcoholic extracts, the aggregates can be partially loaded or saturated with gaseous oxygen. Even saturation with the oxygen in the atmospheric air by the establishment of equilibrium which customarily takes place according to Henry's law offers a higher oxygen capacity than all comparable known systems.

According to the invention, the content of asymmetric lamellar phospholipid aggregates in the cosmetic preparations can be in the range from 0.05 to 80 %

by weight, preferably in the range from 0.05 to 60 % and in particular in the range from 1 to 50 % by weight. It is particularly to be emphasised that, after processing, the asymmetric lamellar phospholipid aggregates according to the invention are present in the cosmetic preparations unaffected by the accompanying substances, which says something for their particular stability.

The invention will be illustrated in greater detail below by means of examples. In the associated drawings

Fig. 1 is a diagram of the critical solubility temperatures (CST) of perfluorocarbon mixtures in n-hexane using perfluorodecalin as a starting point

Fig. 2 is a diagram of the critical solubility temperatures of perfluorocarbon mixtures in n-hexane using F-octylbromide as a starting point.

Some selected fluorocarbons and their O_2 solubility, their vapour pressure and their critical solubility temperature are shown in Table 1. Starting from these values, the desired characteristics for the penetration of the skin with the aid of a cosmetic composition can be selected for mixtures of fluorocarbons.

Table 1

Fluorocarbon	O_2 solubility [ml of O_2/100 ml of Fc]	Vapour Pressure $P_{37°C}$ [mm Hg]	CST [°C]
Perfluorooctyl bromide	50	14	-24.5
Perfluorodecalin	40	12.5	22
Bis-F(butyl)ethene	50	12.6	22.5
F-cyclohexylmethyl-morpholine	42	4	38.5
F-tripropylamine	45	18.5	43
F-dihexyl ether	45	2	59
F-tributylamine	40	1	59
Perfluorodecalin-F-tributylamine 1:1	40	7	42
Perfluorobutyl-tetrahydrofuran	52	51	29
F-methylcyclohexane	57	180	8.2
F-hexane	58	414	20

Example 1

50 ml of a 10 % strength aqueous phospholipid solution (soya lecithin, 80 % phosphatidylcholine (PC)) are homogenised together with 80 g of a highly pure fluorocarbon mixture containing no H atoms (90 % perfluorodecalin, 10 % F-dibutylmethylamine, critical solubility temperature 26°C) using an ultrasonic disintegrator with ice-cooling until the particles have a mean diameter of 244 nm. The multilamellar structure of the aggregates of fluorocarbon and phospholipid can be detected from ^{31}P-NMR measurements by the typical signal width as well as from electron micrographs.

The aggregation dispersion can be mixed with suitable alcohols for the purpose of sterilisation without problems and without affecting its stability. Addition of 30 ml of ethanol produces sterility, the resulting dispersion having the following composition: 62 % w/v fluorocarbons; 9.7 % phospholipids; 19 % ethanol

The zeta potential of minus 61 mV verifies a negative surface charge produced by the phospholipids with an electrostatic stabilisation of the dispersion. After saturation with gaseous oxygen, the dispersion is incorporated into an ointment base which is tolerable and non-interacting with the asymmetric lamellar aggregates. The cosmetic obtained in this way has the following composition:

20 ml of phospholipid dispersion
(5 g of fluorocarbon, 2.2 g of phospholipid)
65 ml of aqueous phase
(polyacrylic gel, glycerol, polyethylene glycols, methylparaben)
15 ml of oily phase
(mineral oil, cetyl alcohol, triglycerides).

The asymmetric lamellar phospholipid aggregates in the cream are unaffected by the accompanying substances.

Example 2

18 g of lyophilised phospholipid of the composition [60 % PC, 20 % PE (phosphatidylethanolamine)] are dissolved in 90 ml of sterilised water and treated with 16 ml of undenatured ethanol. Using a mechanical high-speed stirrer (Ultra-Turrax, 15,000 rpm), the dispersion is stirred and at the same time perfluorodecalin (CST 22°C) is added successively to the stirring container, which is temperature-controlled at 20°C. The crude dispersion is homogenised at 500 atm in a stream of inert gas in a high-pressure homogeniser of the Manton Gaulin type. At the start of the last but one passage, α-tocopherol acetate is added to 0.1 % to the dispersion to avoid autoxidation processes and as a scavenger for free radicals.

The measurements carried out using the photon correlation spectrometer N-4 MD (Coultronics) confirm the presence of a unimodal particle size distribution and a mean particle diameter of 128 nm. The asymmetric lamellar phospholipid aggregates are present in concentrically

arranged uneven-numbered layers, as can be clearly detected from cryoelectron micrographs. Electron microscopy investigations using "negative staining" are in agreement with this. According to ^{31}P-NMR investigations, the asymmetric lamellar aggregates are present in the unilamellar state with a zeta potential of minus 76 mV. The composition of the dispersion is

48 % w/v perfluorodecalin
13 % phospholipids
9 % ethanol.

Example 3

80 g of n-F-hexane, which is present in a mixture with its perfluorinated isomers (CST 20°C) were mechanically preemulsified with 9.5 grams of egg yolk 3-sn-phosphatidylcholine in 47 ml of deionised and sterilised water under inert gas conditions with the addition of 0.2 % of dl-alpha-tocopherol to give a crude emulsion. The crude emulsion was homogenised in a pressure homogeniser at pressures of 500 atm under a suitable temperature regime and with checking of the particle sizes. The dispersion obtained has a medium viscosity and a particle diameter of 294 nm. After addition of 8 ml of propylene glycol, stability and sterility (microorganism count less than 100 microorganisms/g) were observed in a long-term experiment at room temperature. Dilution, e.g. in the preparation of lotions, is possible without problems without a change of important colloid-chemical parameters.

Investigations of the dispersion in polarised light using a light microscope indicate the presence of an isotropic single phase system, in which liquid-crystalline structures are non-existent.

Example 4

In vivo detection of liposome penetration

A freshly isolated physiologically intact skin was fixed by its inside to an O_2 sensor (Clark electrode) and the epidermis was wetted with an O_2-transporting

dispersion containing asymmetric lamellar aggregates. Under these conditions, the electrode does not indicate an O_2 partial pressure. After a penetration period of 57 minutes, the aggregates had reached the dermal skin section in the measuring area of the electrode. The O_2 partial pressure rose to a value of 159 mm Hg. The penetration rate into the skin is dependent on the type and size of the aggregates.

Examples 5 to 19

The following examples describe cosmetic formulations for specific uses. The data in per cent contained therein are percentages by weight.

Example 5 Emulsion (body lotion)

Polyacrylic acid	0.30 %
TEA	0.30 %
p-Methylhydroxybenzoate	0.20 %
p-Propylhydroxybenzoate	0.10 %
Imidazolidinyl urea	0.20 %
Na-EDTA	0.06 %
Cetyl/stearyl alcohol	1.00 %
Stearic acid	1.00 %
Isopropyl myristate/palmitate	3.00 %
Liquid paraffin	4.00 %
Jojoba oil	2.00 %
Asymmetric lamellar phospholipid aggregates	10.00 %
Perfume oil	1.00 %
Demineralised water	q.s.

Example 6 Emulsion (cream)

Polyacrylic acid	0.30 %
Propylene glycol	5.00 %
TEA	0.30 %
Emulsifier 1	6.00 %
Emulsifier 2	4.50 %
Aloe vera	2.00 %
Rice husk oil	1.50 %
Cetyl/stearyl alcohol	1.00 %

Jojoba oil	1.50 %
p-Methylhydroxybenzoate	0.20 %
p-Propylhydroxybenzoate	0.10 %
Imidazolidinylurea	0.20 %
Asymmetric lamellar phospholipid aggregates	50.00 %
Perfume oil	1.00 %
Demineralised water	q.s.

Example 7 Emulsion (cleaning emulsion)

Polyacrylic acid	0.10 %
Propylene glycol	3.00 %
TEA	0.10 %
Emulsifier 1	5.00 %
Emulsifier 2	2.50 %
Linalol oil	1.30 %
Avocado oil	2.00 %
Jojoba oil	1.50 %
p-Methylhydroxybenzoate	0.20 %
p-Propylhydroxybenzoate	0.10 %
Imidazolidinylurea	0.20 %
Asymmetric lamellar phospholipid aggregates	0.10 %
Perfume oil	0.25 %
Demineralised water	q.s.

Example 8 Emulsion (mask)

Polyacrylic acid	0.30 %
Emulsifier 1	5.00 %
Emulsifier 2	6.00 %
TEA	0.30 %
Aloe vera	1.50 %
Jojoba oil	1.50 %
p-Methylhydroxybenzoate	0.20 %
p-Propylhydroxybenzoate	0.10 %
Imidazolidinylurea	0.20 %
Asymmetric lamellar phospholipid aggregates	40.00 %
Perfume oil	0.50 %
Demineralised water	q.s.

Example 9 Gel (gel mask)

Polyacrylic acid	1.30 %
Hydroxyethyl cellulose	0.20 %
Propylene glycol	10.00 %
Asymmetric lamellar phospholipid aggregates	40.00 %
TEA	0.10 %
p-Methylhydroxybenzoate	0.20 %
Imidazolidinylurea	0.30 %
Perfume oil	0.50 %
Demineralised water	q.s.

Example 10 Sunscreen

Emulsifier system consisting of asymmetric lamellar phospholipid aggregates, stabilisers, polyglycerol esters, polyoxyethylene esters, isopropyl palmitate	
Glycerol	5.00 %
$MgSO_4.7H_2O$	0.50 %
UV filter 1	3.00 %
UV filter 2	3.00 %
p-Methylhydroxybenzoate	0.20 %
p-Propylhydroxybenzoate	0.10 %
Imidazolidinylurea	0.30 %
Perfume oil	1.00 %
Demineralised water	q.s.

Example 11 Shampoo

Sodium lauryl ether sulphate	35.00 %
Fatty acid amidoalkyl betaine	10.00 %
Pearl lustre concentrate	5.00 %
Alkyl amidosulfosuccinate	5.00 %
Asymmetric lamellar phospholipid aggregates	7.50 %
Luviquat	1.00 %
Protein hydrolysate	1.00 %
Preservative	0.40 %
Citric acid	0.05 %
Perfume	0.50 %
Rock salt	0.50 %

Demineralised water	q.s.

Example 12 Shower bath

Sodium lauryl ether sulphate	45.00 %
Fatty acid amidoalkyl betaine	10.00 %
Pearl lustre concentrate	5.00 %
Asymmetric lamellar phospholipid aggregates	12.00 %
Citric acid	0.05 %
Preservative	0.40 %
Perfume	1.50 %
Rock salt	1.50 %
Demineralised water	q.s.

Example 13 Hair treatment

Polyacrylic acid	0.50 %
Chelaplex	0.006 %
TEA	0.50 %
Propylene glycol	6.50 %
Asymmetric lamellar phospholipid aggregates	20.00 %
Preservative	0.50 %
Perfume	1.50 %
Demineralised water	q.s.

Example 14 Deodorant cream

Emulsifier 1	8.00 %
Emulsifier 2	4.00 %
Jojoba oil	5.00 %
Aloe vera	5.00 %
Propylene glycol	6.00 %
Menthol	0.10 %
Polyacrylic acid	0.15 %
TEA	0.13 %
Preservative	0.50 %
Asymmetric lamellar phospholipid aggregates	25.00 %
Perfume in the deodorant active compound	1.50 %
Demineralised water	q.s.

Example 15 Aftershave balsam

Polyacrylic acid	0.20 %

Chelaplex	0.006 %
TEA	0.20 %
Wax	1.00 %
Glycerol	4.00 %
Jojoba oil	4.00 %
Rice husk oil	4.00 %
Ethanol	10.00 %
Asymmetric lamellar phospholipid aggregates	37.00 %
Preservative	0.50 %
Perfume	1.50 %
Demineralised water	q.s.

Example 16 Make-up

Emulsifier system consisting of polyglycerol esters, paraffin, polyoxyethylene esters, isopropyl palmitate, waxes	25.00 %
Aloe vera	2.00 %
Glycerol	5.00 %
$MgSO_4.7H_2O$	0.50 %
Preservative	0.50 %
Asymmetric lamellar phospholipid aggregates	37.00 %
Colorant 1	8.50 %
Perfume oil	1.00 %
Demineralised water	q.s.

Example 17 Eye make-up

Carbopol	0.20 %
TEA	0.20 %
Sorbitol	10.30 %
Preservative	0.50 %
Liquid paraffin	2.50 %
Asymmetric lamellar phospholipid aggregates	8.00 %
Emulsifier	3.70 %
Mineral oil	2.90 %
Ethanol	5.00 %
Colorant	8.00 %
Demineralised water	q.s.

Example 18 Eyeshadow compressed with light protection factor

Talc	40.00 %
Mg carbonate	1.50 %
Mg stearate	2.50 %
Kaolin	2.20 %
Colorants	15.80 %
Pearl lustre pigment	21.50 %
Perfume oil	1.50 %
Silk protein	5.00 %
Emulsion as processing means	
Emulsifier	4.50 %
Silicone oil, volatile	2.50 %
Asymmetric lamellar phospholipid aggregates	2.50 %
UV filter	2.00 %
Preservative	0.30 %
Demineralised water	q.s.

Example 19 Make-up - transparent powder compressed with light protection factor

Talc	70.50 %
Kaolin	10.00 %
Mg carbonate	2.50 %
Mg stearate	1.50 %
Silk protein	2.50 %
Colorants	4.50 %
Lustre pigments	7.50 %
Perfume oil	1.00 %
Emulsion as processing means	
Emulsifier	4.50 %
Silicone oil, volatile	2.50 %
Asymmetric lamellar phospholipid aggregates	2.50 %
UV Filter	2.00 %
Preservative	0.30 %
Demineralised water	q.s.

Patent Claims

1. Phospholipid- and fluorocarbon-containing cosmetic, characterised in that it consists of

(a) a carrier suitable for cosmetic use; and

(b) asymmetric lamellar aggregates of phospholipids, which have a phosphatidylcholine content in the range from 30 to 99 % by weight and fluorocarbons laiden with oxygen in the range from 0.2 to 100 % (weight/volume); having a skin penetration depending on the critical solubility temperature of the fluorocarbons or fluorocarbon mixtures selected.

2. Cosmetic according to Claim 1, characterised in that the lamellar aggregates have an asymmetric, preferably 3-layer structure, originating from their fluorocarbon core.

3. Cosmetic according to Claim 1 or 2, characterised in that the fluorocarbons are selected from the group which are selected from [sic] aliphatic straight-chain and branched fluoroalkanes, mono- or bicyclic, optionally fluoroalkyl-substituted, fluorocycloalkanes, perfluorinated aliphatic or bicyclic amines, bis(perfluoroalkyl)ethenes, perfluoropolyethers and mixtures thereof.

4. Cosmetic according to Claim 3, characterised in that the fluorocarbons are selected from the group which consists of perfluorodecalin, F-butyltetrahydrofuran, perfluorotributylamine, perfluorooctyl bromide, bisfluoro(butyl)ethene and C_6-C_9-perfluoroalkanes.

5. Cosmetic according to one of Claims 1 to 4, characterised in that the amount of fluorocarbons is in the range from 20 to 100 % weight/volume, preferably in the range from 40 to 100 %, in particular in the range from 70 to 100 %.

6. Cosmetic according to one of Claims 1 to 5, characterised in that the phospholipids are selected from the group consisting of natural phospholipids such as soya lecithin and egg lecithin and also synthetic phospholipids and/or partially hydrogenated phospholipids.

7. Cosmetic according to one of Claims 1 to 6, characterised in that the lipid fraction used contains phosphatidylcholine in an amount from 70 to 99 % by weight.

8. Cosmetic according to one of Claims 1 to 7, characterised in that, in addition to phosphatdylcholine [sic], lysolecithins are present in the concentration range from 1 to 10 % by weight.

9. Cosmetic according to one of Claims 1 to 8, characterised in that, to achieve a slow skin penetration, it contains fluorocarbons or fluorocarbon mixtures having a relatively high critical solubility temperature.

10. Process for the preparation of a phospholipid- and fluorocarbon-containing cosmetic, characterised in that phospholipids having a phosphatidylcholine content of 30 to 99 % by weight are incorporated with a fluorocarbon or fluorocarbon mixture laiden with oxygen after preemulsification at relatively high rotational speeds and subsequent high pressure emulsification into a carrier which is suitable for cosmetic use and does not interact with the asymmetric lamellar aggregates, the amount of fluorocarbon being in the range from 0.2 to 100 % (weight/volume) and the particle size of the asymmetric lamellar aggregates being 50 to 1000 µm.

11. Process according to Claim 10, characterised in that the fluorocarbons are selected from the group which are selected from [sic] aliphatic straight-chain and branched fluoroalkanes, mono- or bicyclic, optionally fluoroalkyl- substituted, fluorocycloalkanes, perfluorinated aliphatic or bicyclic amines, bis(perfluoroalkyl)ethenes, perfluoropolyethers and mixtures thereof, and are preferably selected from the group which consists of perfluorodecalin, F-butyltetrahydrofuran, perfluorotributylamine, perfluorooctyl bromide, bis-fluoro(butyl)ethene and C_6-C_9-perfluoroalkanes.

12. Process according to Claim 10 or 11, characterised in that the amount of fluorocarbons is in the range from 20 to 100 % wt./vol., preferably in the range from 40 to 100 %.

13. Process according to Claim 10 or 11, characterised in that the amount of phospholipids in the cosmetic is in the range from 0.9 to 15 % by weight, in particular in the range from 2 to 9 %.

14. Use of a phospholipid-containing cosmetic for control of the oxygen supply to the skin by applying a system containing an asymmetric lamellar oxygen carrier, containing phospholipids having a phosphatidylcholine content of 30 to 99 % by weight and fluorocarbons in the range from 0.2 to 100 % weight/volume, the penetration into the skin being controlled by means of the carrier structure of the phospholipid aggregates and the critical solubility temperature of the fluorocarbons (in n-hexane), and the system being distributed in a carrier which is customary for cosmetic use, such as ointments, creams, lotions, waters, alcoholic extracts, pastes, gels, powders or tinctures, or optionally present on a dressing or a plaster or as a spray.

15. Use according to Claim 14, characterised in that the content of phosphatidylcholine in the lipid fraction employed is in the range from 30 to 99 % and in particular in the range from 70 to 90 %.

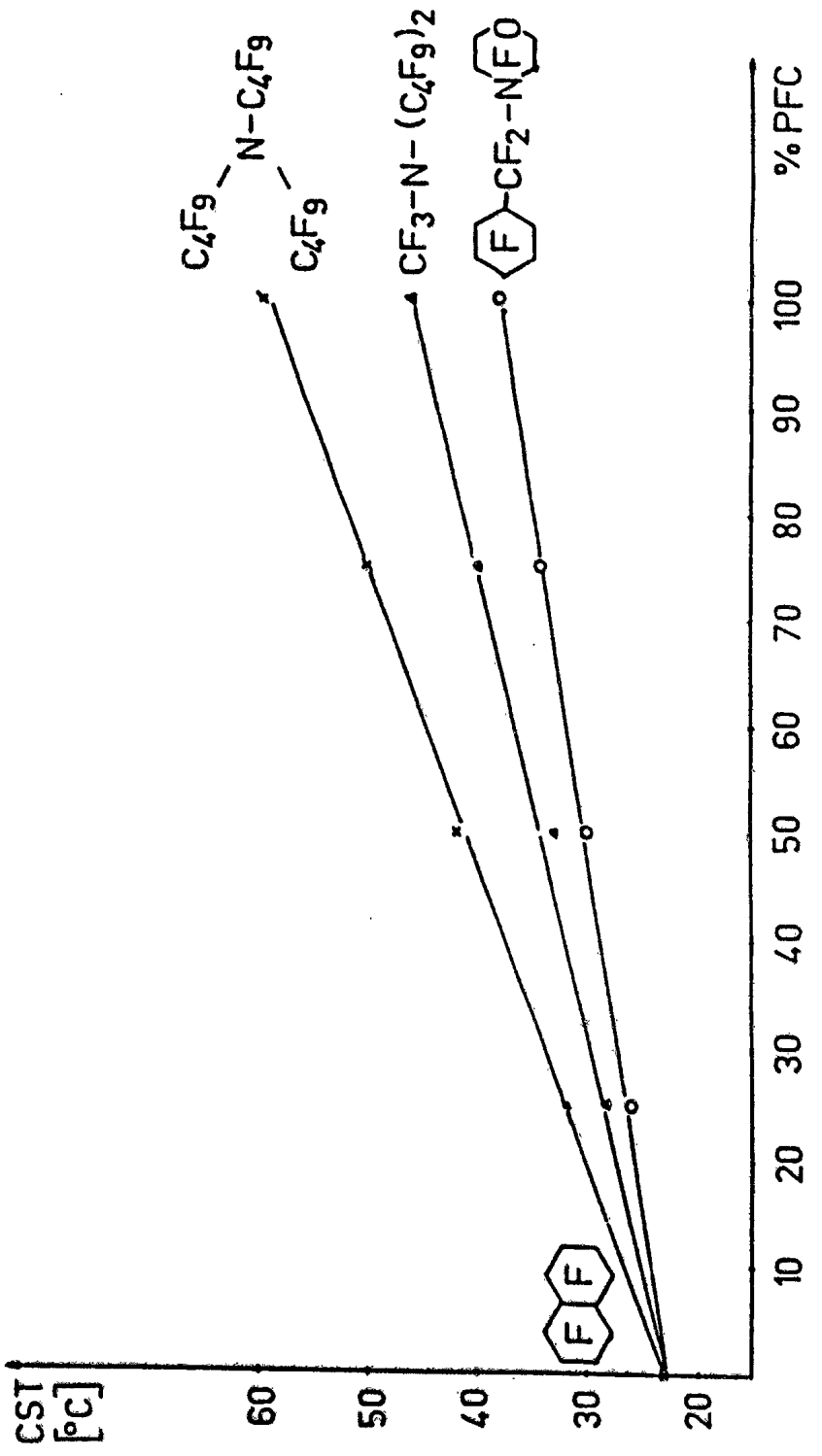
CST [°C]
60
50
40
30
20
10
20
30
40
50
60
70
80
90
100
% PFC
C_4F_9–N–C_4F_9
C_4F_9
CF_3–N–$(C_4F_9)_2$
F–CF_2–NFO
F
F

Fig. 1

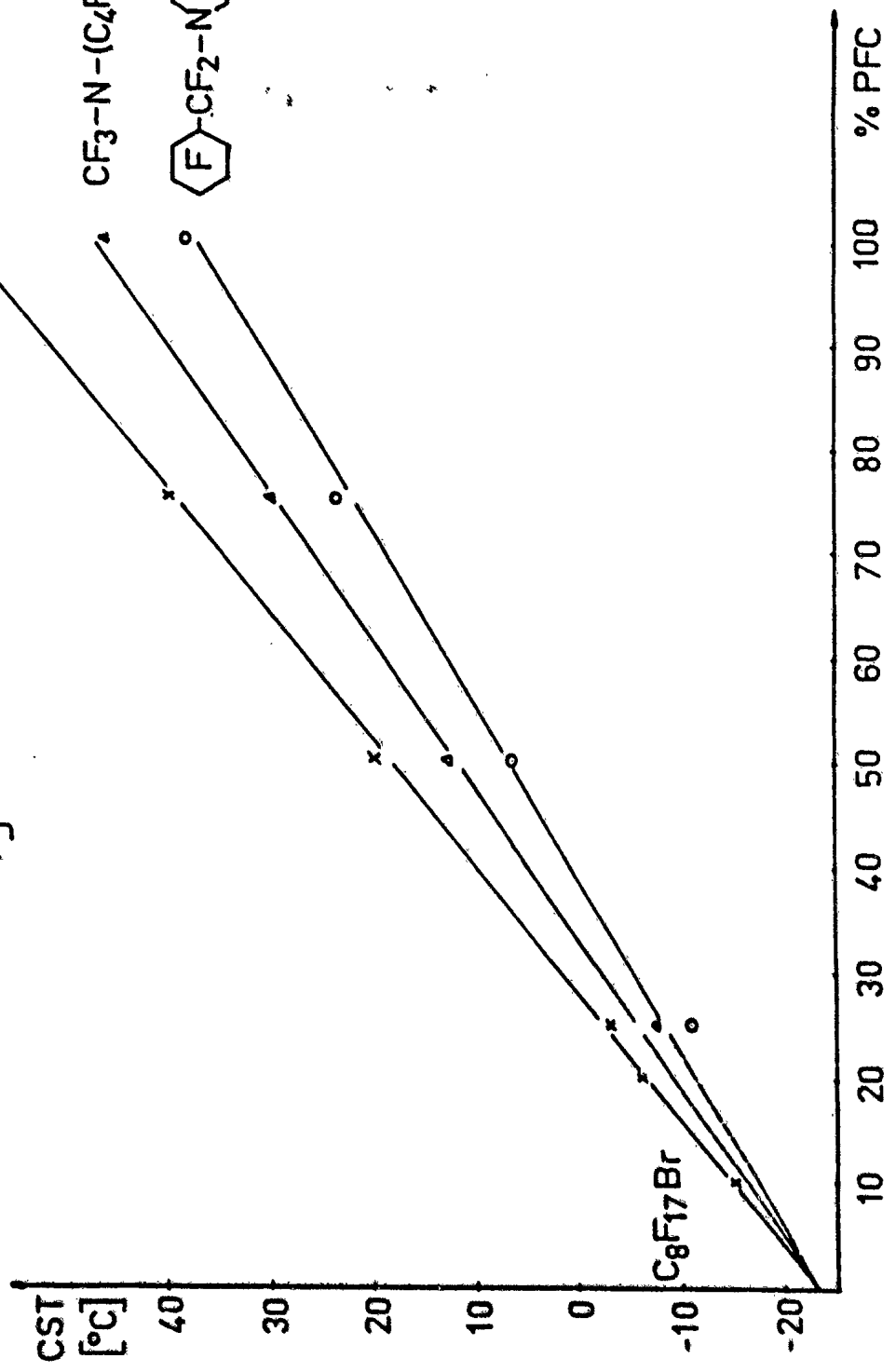
CST [°C]
40
30
20
10
0
-10
-20
10
20
30
40
50
60
70
80
90
100
% PFC
$(C_4F_9)_3N$
$CF_3-N-(C_4F_9)_2$
$F-CF_2-NFO$
$C_8F_{17}Br$

Fig. 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DE 93/00575

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. 5 A61K7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int. Cl. 5 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DE,A,4 127 442 (ZENTRALINSTITUT FUR ANORGANISCHE CHEMIE) 18 February 1993 see the whole document	1-15
Y	WO,A,9 206 676 (MICRO VESICULAR SYSTEMS,INC.) 30 April 1992 see the whole document see page 11 - page 12; example 3	1-15
Y	WO,A,8 908 459 (ALPHA THERAPEUTIC CORPORATION) 21 September 1989 see the whole document	1-15

-/--

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 October 1993 (18.10.93)	26 October 1993 (26.10.93)
Name and mailing address of the ISA/ EUROPEAN PATENT OFFICE Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DE 93/00575

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,9 100 110 (LONG) 10 January 1991 see the whole document see page 13, line 2 - line 33	1-15

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

DE 9300575
SA 76786

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 18/10/93

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE-A-4127442	18-02-93	None		
WO-A-9206676	30-04-92	US-A-	5160669	03-11-92
		AU-A-	8947691	20-05-92
		CA-A-	2093526	17-04-92
		EP-A-	0558571	08-09-93
WO-A-8908459	21-09-89	EP-A-	0417104	20-03-91
		JP-A-	2258050	18-10-90
		US-A-	5061484	29-10-91
WO-A-9100110	10-01-91	EP-A-	0480925	22-04-92

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen PCT/DE 93/00575

I. KLASSIFIKATION DES ANMELDUNGSGEGENSTANDS (bei mehreren Klassifikationssymbolen sind alle anzugeben)[6]

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

Int.Kl. 5 A61K7/00

II. RECHERCHIERTE SACHGEBIETE

Recherchierter Mindestprüfstoff [7]

Klassifikationssystem	Klassifikationssymbole
Int.Kl. 5	A61K

Recherchierte nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Sachgebiete fallen [8]

III. EINSCHLAGIGE VEROFFENTLICHUNGEN [9]

Art.*	Kennzeichnung der Veröffentlichung [11], soweit erforderlich unter Angabe der maßgeblichen Teile [12]	Betr. Anspruch Nr.[13]
P,X	DE,A,4 127 442 (ZENTRALINSTITUT FÜR ANORGANISCHE CHEMIE) 18. Februar 1993 siehe das ganze Dokument ---	1-15
Y	WO,A,9 206 676 (MICRO VESICULAR SYSTEMS, INC.) 30. April 1992 siehe das ganze Dokument siehe Seite 11 - Seite 12; Beispiel 3 ---	1-15
Y	WO,A,8 908 459 (ALPHA THERAPEUTIC CORPORATION) 21. September 1989 siehe das ganze Dokument --- -/--	1-15

* Besondere Kategorien von angegebenen Veröffentlichungen [10]:

"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist

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"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden

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"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

IV. BESCHEINIGUNG

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
18.OKTOBER 1993	26. 10. 93
Internationale Recherchenbehörde	**Unterschrift des bevollmächtigten Bediensteten**
EUROPAISCHES PATENTAMT	BENZ K.F.

III. EINSCHLAGIGE VEROFFENTLICHUNGEN (Fortsetzung von Blatt 2)

Art *	Kennzeichnung der Veröffentlichung, soweit erforderlich unter Angabe der maßgeblichen Teile	Betr. Anspruch Nr.
Y	WO,A,9 100 110 (LONG) 10. Januar 1991 siehe das ganze Dokument siehe Seite 13, Zeile 2 - Zeile 33	1-15

ANHANG ZUM INTERNATIONALEN RECHERCHENBERICHT ÜBER DIE INTERNATIONALE PATENTANMELDUNG NR.

DE 9300575
SA 76786

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentdokumente angegeben.
Die Angaben über die Familienmitglieder entsprechen dem Stand der Datei des Europäischen Patentamts am 18/10/93
Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

Im Recherchenbericht angeführtes Patentdokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie		Datum der Veröffentlichung
DE-A-4127442	18-02-93	Keine		
WO-A-9206676	30-04-92	US-A-	5160669	03-11-92
		AU-A-	8947691	20-05-92
		CA-A-	2093526	17-04-92
		EP-A-	0558571	08-09-93
WO-A-8903459	21-09-89	EP-A-	0417104	20-03-91
		JP-A-	2258050	18-10-90
		US-A-	5061484	29-10-91
WO-A-9100110	10-01-91	EP-A-	0480925	22-04-92

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