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(54) Title: SKIN CARE COSMETIC COMPOSITIONS

(57) Abstract

Cosmetic skin care methods and compositions containing branched alcohols. The inventive compositions provide control of sebum secretion from sebocytes, improved oil control and improved skin feel, prevent shine and stickiness, while also providing anti–aging benefits which results in reduced appearance of wrinkles and aged skin, improved skin color, treatment of photoaged skin, improvement in skin's radiance and clarity and finish, and an overall healthy and youthful appearance of the skin.

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SKIN CARE COSMETIC COMPOSITIONS

FIELD OF THE INVENTION

Cosmetic methods and compositions for conditioning human skin by topical application to the skin of cosmetic compositions containing branched fatty alcohols.

BACKGROUND OF THE INVENTION

Cosmetic products which improve the appearance of skin are increasingly popular with consumers. Frequently, consumers seek to alleviate or delay the signs of aged or photoaged skin, such as fine lines and wrinkles, dry and sagging skin. Consumers also seek other benefits in addition to anti-aging.

A frequent, undesirable skin condition is "oily skin," the condition which results from the excessive amount of sebum on the skin. Sebum is skin oil which is produced by sebocytes (cells of the sebaceous glands in the skin) and is then secreted to the skin surface. Oily skin is associated with a shiny, undesirable appearance and a disagreeable tactile sensation. Oily skin affects various age groups. Cosmetic products which provide both sebum control and anti-aging benefits are highly desirable.

US Patent 4,496,536 (Moller et al) discloses a cosmetic preparation for treating oily hair or seborrhea, which contains at least one long-chain alkanol and at least one anti-oxidant. The long-chain alkanol is described as having

12 to 26 carbon atoms and, preferably, one or more branches. 2-(1,3,3,-trimethylbutyl)-5,7,7-trimethyloctanol (18 carbons total length, 4 branches: 3 methyl branches and the fourth branch itself containing 3 methyl branches) is mentioned among suitable alkanols. Unfortunately, 2-(1,3,3,-trimethylbutyl)-5,7,7-trimethyloctanol is structurally complex and does not appear to be commercially available. Even more importantly, experimental data provided in the patent demonstrates that an alcohol, when used alone, does not provide any sebum suppression. Furthermore, when used in combination with anti-oxidants, branched and non-branched alcohols are shown by Moller to be equally effective.

The compositions according to the present invention include alcohols that differ from the Moller alcohols at least in the minimum chain length and the minimum number and length of the branches. Contrary to the experimental showing in the Moller patent, the alcohols included in the present invention suppress sebum excretion, even when used alone.

Furthermore, the present invention is based, at least in part, on the discovery that the alcohols within the scope of the invention provide sebum suppression, but not immediately upon application. Thus, compositions according to the invention employ a combination of the alcohol with an oil-absorbing powder, e.g. silica, which provides an immediate relief from sebum accumulation on the skin. If silica alone is employed, high amounts are needed to provide effective oil control. Unfortunately, the use of high levels of silica is not practical since it results in whitening of the skin. By virtue of including a branched alcohol as herein defined, the

inventive compositions can contain an oil-absorbing powder in an amount which does not result in whitening of the skin, yet compositions are effective for sebum suppression.

US Patent 5,093,112 (Birtwistle et al.) discloses topical cleansing (detergent) compositions containing an alcohol and an alkyl or alkenyl phosphate salt. 6,6-dimethylheptan-1-ol is mentioned among suitable alcohols. Powders such as chalk, fullers earth, kaolin, starch, fumed silica, magnesium aluminum silicate, hydrated aluminum silicate, are listed as optional ingredients. Birtwistle does not teach or suggest either a problem of excessive sebum on the skin or any compositions for skin sebum control, or any compositions containing an oil-absorbing powder which are effective for sebum control, yet are non-whitening.

US Patent 5,344,850 (Hata et al.) discloses topical compositions for treating or preventing acne, the compositions containing C18 saturated or unsaturated alcohol with four methyl branches. In this regard, it is important to note that although increased sebum production may be one of the many factors that lead to the formation of acne, an anti-acne agent does not necessarily possess antisebum activity. For instance, benzoyl peroxide and salicylic acid are well-established anti-acne agents, but they do not decrease sebum output. See Cunliffe, et al., "Topical Benzoyl Peroxide Increases The Sebum Excretion Rate In Patients With Acne", British Journal of Dermatology (1983) 109, 577-579; William J. Cunliffe, "Acne", p. 256, Martin Dunitz Ltd. (1989). See also Comparative Example 3 below.

Hata et al. do not teach compositions containing an oil-absorbing powder or any compositions for sebum control.

US Patent 4,536,399 (Flynn et al.) and US Patent 4,000,317 (Menda et al.) disclose the use of silica for sebum adsorption (a total of 1-10% and 0.5-25%, respectively). The higher the level of silica, the better the oil removal ability. However, as mentioned above, a practical limit exists on the amount of silica that can be used without resulting in an unacceptable level of skin whitening due to deposits of high levels of silica powder. Unfortunately, the reduction in silica level results in a reduction in oil-removing efficacy.

SUMMARY OF THE INVENTION

The present invention includes a skin care cosmetic composition comprising:

(i) from 0.001% to 50% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches; and

(ii) an oil-absorbing powder in an amount of not greater than 1%; and

(iii) a cosmetically acceptable vehicle.

The present invention also includes a cosmetic method of controlling or preventing an oily skin condition, especially in the facial area, by applying to the skin a composition from 0.001% to 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

The invention also includes a cosmetic method of reducing, preventing or controlling sebum secretion from sebocytes by applying a composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

The invention also includes a cosmetic method of stimulating collagen and glycosaminoglycan synthesis by fibroblasts in the skin, by applying a composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

The invention also includes a cosmetic method of treating or delaying chronoaged, photoaged, dry, lined or wrinkled skin, shielding the skin from harmful UVA and UVB light (sunscreening), increasing stratum corneum firmness and flexibility, and generally increasing the quality of skin by applying to the skin the inventive composition.

According to a still further aspect, the present invention also comprises the cosmetic use of the inventive skin care composition for providing a skin care benefit selected from the following; reducing or preventing oily skin conditions; reducing or preventing sebum secretion from sebocytes; stimulating collagen and glycosaminoglycan synthesis by fibroblasts in skin; and/or treating aged, photoaged, dry, lined and/or wrinkled skin.

The inventive cosmetic methods, compositions and uses provide control of sebum secretion from sebocytes, improved

oil control and improved skin feel, prevent shine and stickiness, while also providing anti-aging benefits which results in reduced appearance of wrinkles and aged skin, improved skin color, treatment of photoaged skin, improvement in skin's radiance and clarity and finish, and an overall healthy and youthful appearance of the skin.

DETAILED DESCRIPTION OF THE INVENTION

All amounts in the specification are by weight of the oil-in-water emulsion, unless otherwise specified.

The term "skin" as used herein includes amongst others the skin on the face, neck, chest, back, arms, hands and scalp.

The inventive methods and compositions include an alcohol containing a total of at least 9 carbon atoms, generally from 9 to 15 carbon atoms, and at least two branches. The preferred alcohols contain a total of at least 10 carbon atoms, in order to obtain maximum efficacy. The most preferred alcohols according to the invention contain from 2 to 5 branches, in order to maximize efficacy at minimum cost. Preferably, the branches are methyl branches, due to commercial availability. The alcohol may contain a mix of various chain lengths' alcohols. Such mixed alcohol is suitable for use in the present invention, as long as the predominant alcohol in the mix contains a total of at least 9 carbon atoms and at least two branches.

The alcohol is employed in the inventive methods in an amount of from 0.001% to about 100%, preferably from 0.001% to 50% and more preferably from 0.1% to 20%, most preferably from 0.1% to 10%.

The inventive compositions include an oil-absorbing powder, in addition to the alcohol. Consequently, alcohol is employed in an amount of from 0.001% to 50%, preferably from 0.1% to 20%, most preferably from 0.1% to 10%, in order to accommodate the oil-absorbing powder and the cosmetically acceptable vehicle.

The branched alcohols within the scope of the invention are commercially available, e.g. from Exxon or Henkel.

The inventive compositions and the preferred inventive methods also include an oil-absorbing powder. Examples of suitable oil-absorbing powder include but are not limited to silica (preferably fumed), talcum, and clay.

The preferred oil-absorbing powder is fumed silica, due to its superior oil-absorbing capacity.

The oil-absorbing powder provides an immediate sebum control, but not a long-term relief, since it cannot be used in large amounts without whitening the skin. According to the present invention, the oil-absorbing powder is present in an amount of no greater than 1%, generally from 0.01% to 1%, preferably from 0.1% to 1%, most preferably from 0.5% to 1%.

Although the alcohol employed in the inventive methods and compositions is liquid, and thus the invention is effective even in the absence of the carrier, the compositions according to the invention comprise a cosmetically acceptable vehicle to act as a diluant, dispersant or carrier for branched alcohol and for oil-absorbing powder in the composition, so as to facilitate their distribution when the composition is applied to the skin.

The vehicle may be aqueous, anhydrous or an emulsion. Preferably, the compositions are aqueous or an emulsion, especially water-in-oil or oil-in-water emulsion. Water when present will be in amounts which may range from 5 to 99%, preferably from 40 to 90%, optimally between 60 and 90% by weight.

Besides water, relatively volatile solvents may also serve as carriers within compositions of the present invention. Most preferred are monohydric C_1-C_3 alkanols. These include ethyl alcohol, methyl alcohol and isopropyl alcohol. The amount of monohydric alkanol may range from 1 to 70%, preferably from 10 to 50%, optimally between 15 and 40% by weight.

Emollient materials may also serve as cosmetically acceptable carriers. These may be in the form of silicone oils and synthetic esters. Amounts of the emollients may range anywhere from 0.1 to 50%, preferably between 1 and 20% by weight.

Silicone oils may be divided into the volatile and non-volatile variety. The term "volatile" as used herein refers to those materials which have a measurable vapor pressure at ambient temperature. Volatile silicone oils are preferably chosen from cyclic or linear polydimethylsiloxanes containing from 3 to 9, preferably from 4 to 5, silicon atoms. Linear volatile silicone materials generally have viscosities less than about 5 centistokes at 25°C while cyclic materials typically have viscosities of less than about 10 centistokes. Nonvolatile silicone oils useful as an emollient material include polyalkyl siloxanes, polyalkylaryl siloxanes and polyether siloxane copolymers. The essentially non-volatile polyalkyl siloxanes useful herein include, for example, polydimethyl siloxanes with viscosities of from about 5 to about 25 million centistokes at 25°C. Among the preferred non-volatile emollients useful in the present compositions are the polydimethyl siloxanes having viscosities from about 10 to about 400 centistokes at 25°C.

Among the ester emollients are:

(1) Alkenyl or alkyl esters of fatty acids having 10 to 20 carbon atoms. Examples thereof include isoarachidyl neopentanoate, isononyl isonanonoate, oleyl myristate, oleyl stearate, and oleyl oleate.

(2) Ether-esters such as fatty acid esters of ethoxylated fatty alcohols.

(3) Polyhydric alcohol esters. Ethylene glycol mono and di-fatty acid esters, diethylene glycol mono- and di-fatty acid esters, polyethylene glycol (200-6000) mono- and di-fatty acid esters, propylene glycol mono- and di-fatty acid esters, polypropylene glycol 2000 monooleate, polypropylene glycol 2000 monostearate, ethoxylated propylene glycol monostearate, glyceryl mono- and di-fatty acid esters, polyglycerol poly-fatty esters, ethoxylated glyceryl monostearate, 1,3-butylene glycol monostearate, 1,3-butylene glycol distearate, polyoxyethylene polyol fatty acid ester, sorbitan fatty acid esters, and polyoxyethylene sorbitan fatty acid esters are satisfactory polyhydric alcohol esters.

(4) Wax esters such as beeswax, spermaceti, myristyl myristate, stearyl stearate and arachidyl behenate.

(5) Sterols esters, of which cholesterol fatty acid esters are examples thereof.

Fatty acids having from 10 to 30 carbon atoms may also be included as cosmetically acceptable carriers for compositions of this invention. Illustrative of this category are pelargonic, lauric, myristic, palmitic, stearic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, arachidic, behenic and erucic acids.

Humectants of the polyhydric alcohol type may also be employed as cosmetically acceptable carriers in compositions

of this invention. The humectant aids in increasing the effectiveness of the emollient, reduces scaling, stimulates removal of built-up scale and improves skin feel. Typical polyhydric alcohols include glycerol, polyalkylene glycols and more preferably alkylene polyols and their derivatives, including propylene glycol, dipropylene glycol, polypropylene glycol, polyethylene glycol and derivatives thereof, sorbitol, hydroxypropyl sorbitol, hexylene glycol, 1,3-butylene glycol, 1,2,6-hexanetriol, ethoxylated glycerol, propoxylated glycerol and mixtures thereof. For best results the humectant is preferably propylene glycol or sodium hyaluronate. The amount of humectant may range anywhere from 0.5 to 30%, preferably between 1 and 15% by weight of the composition.

Thickeners may also be utilized as part of the cosmetically acceptable carrier of compositions according to the present invention. Typical thickeners include crosslinked acrylates (e.g. Carbopol 982), hydrophobically-modified acrylates (e.g. Carbopol 1382), cellulosic derivatives and natural gums. Among useful cellulosic derivatives are sodium carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, ethyl cellulose and hydroxymethyl cellulose. Natural gums suitable for the present invention include guar, xanthan, sclerotium, carrageenan, pectin and combinations of these gums. Amounts of the thickener may range from 0.0001 to 5%, usually from 0.001 to 1%, optimally from 0.01 to 0.5% by weight.

Collectively, the water, solvents, silicones, esters, fatty acids, humectants and/or thickeners will constitute the

cosmetically acceptable carrier in amounts from 1 to 99.9%, preferably from 80 to 99% by weight.

An oil or oily material may be present, together with an emulsifier to provide either a water-in-oil emulsion or an oil-in-water emulsion, depending largely on the average hydrophilic-lipophilic balance (HLB) of the emulsifier employed.

Surfactants may also be present in cosmetic compositions of the present invention. Total concentration of the surfactant will range from 0.1 to 40%, preferably from 1 to 20%, optimally from 1 to 5% by weight of the composition. The surfactant may be selected from the group consisting of anionic, nonionic, cationic and amphoteric actives. Particularly preferred nonionic surfactants are those with a C_{10}-C_{20} fatty alcohol or acid hydrophobe condensed with from 2 to 100 moles of ethylene oxide or propylene oxide per mole of hydrophobe; C_2-C_{10} alkyl phenols condensed with from 2 to 20 moles of alkylene oxide; mono- and di- fatty acid esters of ethylene glycol; fatty acid monoglyceride; sorbitan, mono- and di- C_8-C_{20} fatty acids; block copolymers (ethylene oxide/propylene oxide); and polyoxyethylene sorbitan as well as combinations thereof. Alkyl polyglycosides and saccharide fatty amides (e.g. methyl gluconamides) are also suitable nonionic surfactants.

Preferred anionic surfactants include soap, alkyl ether sulfate and sulfonates, alkyl sulfates and sulfonates, alkylbenzene sulfonates, alkyl and dialkyl sulfosuccinates,

C_8-C_{20} acyl isethionates, acyl glutamates, C_8-C_{20} alkyl ether phosphates and combinations thereof.

Various types of additional active ingredients may be present in cosmetic compositions of the present invention. Actives are defined as skin benefit agents other than emollients and other than ingredients that merely improve the physical characteristics of the composition. Although not limited to this category, general examples include additional anti-sebum ingredients and sunscreens.

Sunscreens include those materials commonly employed to block ultraviolet light. Illustrative compounds are the derivatives of PABA, cinnamate and salicylate. For example, avobenzophenone (Parsol 1789®) octyl methoxycinnamate and 2-hydroxy-4-methoxy benzophenone (also known as oxybenzone) can be used. Octyl methoxycinnamate and 2-hydroxy-4-methoxy benzophenone are commercially available under the trademarks, Parsol MCX and Benzophenone-3, respectively. The exact amount of sunscreen employed in the compositions can vary depending upon the degree of protection desired from the sun's UV radiation.

Many cosmetic compositions, especially those containing water, must be protected against the growth of potentially harmful microorganisms. Preservatives are, therefore, necessary. Suitable preservatives include alkyl esters of p-hydroxybenzoic acid, hydantoin derivatives, propionate salts, and a variety of quaternary ammonium compounds. Particularly preferred preservatives of this invention are methyl paraben, propyl paraben, phenoxyethanol and benzyl

alcohol. Preservatives will usually be employed in amounts ranging from about 0.1% to 2% by weight of the composition.

The composition according to the invention is intended primarily as a product for topical application to human skin, especially as an agent for controlling or preventing excessive sebum secretion.

In use, a quantity of the composition, for example from 1 to 100 ml, is applied to exposed areas of the skin, from a suitable container or applicator and, if necessary, it is then spread over and/or rubbed into the skin using the hand or fingers or a suitable device.

Product Form and Packaging:

The cosmetic skin composition of the invention can be in any form, e.g. formulated as a toner, gel, lotion, a fluid cream, or a cream. The composition can be packaged in a suitable container to suit its viscosity and intended use by the consumer. For example, a lotion or fluid cream can be packaged in a bottle or a roll-ball applicator or a propellant-driven aerosol device or a container fitted with a pump suitable for finger operation. When the composition is a cream, it can simply be stored in a non-deformable bottle or squeeze container, such as a tube or a lidded jar. The invention accordingly also provides a closed container containing a cosmetically acceptable composition as herein defined.

The composition may also be included in capsules such as those described in U.S. Patent No. 5,063,057, incorporated by reference herein.

The following specific examples further illustrate the invention, but the invention is not limited thereto.

The following alcohols used in the Examples were obtained from Exxon:

Trade Name	Branching
Exxal® 7	Mixture of branched and straight chain isomers, about 40% dimethyl pentanols.
Exxal® 8	Methyl branching only, at least about 38% dimethyl hexanols.
Exxal® 9	Dimethyl heptanols (41% - 57%)
Exxal® 10	Trimethyl heptanols and dimethyl octanols
Exxal® 12	Trimethyl nonanols
Exxal® 13	Tetramethyl nonanols and trimethyl decanols

EXAMPLE 1

This example measured production of procollagen I by fibroblasts in response to treatment with various alcohols.

Collagen is a predominant skin protein. Its synthesis decreases with aging or photodamage. The degradation or destruction of collagen increases the tensile strength of the skin causing wrinkles and laxity. Many studies involving human subjects have shown that collagen type I is decreased with increasing severity of photodamage (See Kligman, A., JAMA, (1969), 210, pp. 2377-2380; Lavker, R., J. Inv Derm., (1979), 73, 79-66; Smith J. et al., J. Inv. Derm., (1962), 39, pp. 347-350; and Shuster, S. et al., Br. J. Dermatol., (1975), 93, pp. 639-643); and some correlation in the histology of wrinkles and reduction in collagen levels in the sun-exposed skin has been reported. See Chen, S.; Kiss, I., J. Inv. Derm., (1992), 98. pp. 248-254. Voorhees and colleagues have supported these findings by showing the restoration of collagen type I in photo-damaged human skin by a topical treatment with tretinoin. See Christopher, E., et al., The New Eng. Jou. of Medicine (1993), 329, pp. 530-535. Procollagen I is a precursor of collagen. Increased production of procollagen I in response to a test compound application is a marker of an increased collagen level.

Procollagen I Staining Protocol for Slot Blot

Neonatal human dermal fibroblasts were purchased from Clonetics Corp., San Diego, CA. All materials for cell culture were purchased from Life Technologies, NY (and used in passages 5-10). Cells were seeded at a density of approximately 10,000/well in the inner 48 wells of a 96-well plate in a medium containing DMEM (Dulbecco's Modified Eagle's Medium), high-glucose supplemented with 2 mM L-

glutamine, 10% fetal bovine serum, and antibiotic and antimycotic solutions. Cells were then grown to confluence for 2 days. At confluence, the medium was removed and cells were washed with serum-free DMEM, and each well dosed with 200µl of a solution of a test compound in serum-free DMEM. Each dosing was replicated in a total of six wells. Test compounds were used at concentrations indicated in Table 1 below. Control did not contain a test compound. After 24 hours, the test compound solution or the control solution was removed and cells redosed with 100µl of a solution of a test compound in serum-free DMEM. Test compounds were used at concentrations indicated in Table 1 below. After 24 hours, the test compound solution or the control solution was removed and stored over the weekend at 4°C with protease inhibitor (Aprotinin from Sigma) in a ratio of aprotinin to media of 1:200. The test compound solution was then diluted in DMEM (approximately 20µl sample in 200µl DMEM).

Nitrocellulose membrane and 3 sheets of filter paper were soaked in TRIS buffered saline (TBS, pH 7.3.). BioRad slot blot apparatus (BioRad Labs, CA) was set up with 3 sheets filter paper on bottom, membrane on top, and tightened tightened. 100ml TBS was added per well. Vacuum was used to suck TBS through membrane. The test compound solution or control was vortexed, then 100 µl was loaded per well and gravity filtered. Procollagen from the test solution was bound to the membrane at this point in the procedure. Membrane was removed from the apparatus, excess cut off, and bottom right corner notched for orientation. The membrane was placed in blocking solution (5% milk powder

in Dulbecco's phosphate buffered saline) overnight at 4°C, with shaking. The membrane was then incubated for 1.5 hrs at room temperature with 1.5mL Rat Anti-Human Procollagen Amino-Terminal Ab (Chemicon MAB1912) in TBS with 0.1% BSA (ratio of antibody to buffer/BSA was 1:100) in a sealed bag with shaking. The membrane was then removed; washed 3 times for 5 minutes in TBS/0.1% Tween. The membrane was then incubated for 1 hour at room temperature in 2 mL of Biotinylated Anti-Rat Peroxidase-Conjugated Ab (Vector Labs) in TBS with 0.1% BSA (ratio of antibody to buffer/BSA was 1:1000) in a sealed bag with shaking.

The membrane was washed 3 times for 5 minutes in TBS/0.1%Tween. 3 mL PBS was incubated with 30µl each of solutions A and B from Vectastain Kit for 30 minutes. The membrane was placed in the resulting solution for 30 minutes in a sealed bag with shaking. The membrane was then removed and washed twice for 5 minutes in TBS/ 0.1%Tween. The membrane was then stained using the following solution:

12.5 mg 3-amino 9-ethyl carbazole (Sigma)
3.125 (approximately) mL DMF (N,N- dimethylformamide, from Sigma)
21.5 mL 0.2M NaOAc buffer, pH 5.2
12.5 µl H_2O_2

The membrane was stained until color developed and the reaction stopped with 2 washes for 10 minutes in tap water. The blot was scanned on a Bio-Rad GS700 Image Analysis densitometer. Percent change from control was calculated

from densitometer readings as follows: [(Reading for test compound-Reading for control)/Reading for control] * 100. Control has a reading of 100%. Statistical significance (p value) was calculated using student's t-test.

The results that were obtained are summarized in Table 1. TGF-B is a positive control, ensuring the integrity of the assay: transforming growth factor beta is known to increase procollagen I in fibroblasts.

TABLE 1

Sample	% Increase (+) or % decrease (--) over control	p value
Experiment 1		
TGF-B	+50*	.0027
0.01% Exxal® 7	-10*	.026
0.01% Exxal® 8	-30*	.001493
Experiment 2		
TGF-B	+140*	.001227
0.01% Exxal® 10	+50*	.0025
0.01% Exxal® 12	+40*	.040
0.01% Exxal® 13	+30*	.042

*Statistically significant at $p<0.05$

It can be seen from the results in Table 1, that Exxal 7 and Exxal 8, which are not within the scope of the invention, did not increase collagen synthesis by fibroblasts. By contrast, the alcohols within the scope of the invention (Exxal® 10, Exxal® 12, and Exxal® 13) all increased collagen synthesis.

EXAMPLE 2

This example measures production of glycosaminoglycans by fibroblasts in response to treatment with various test compounds. Glycosaminoglycans (GAGs) are a family of polysaccharides which (with the exception of hyaluronic acid (HA)) can be linked to a protein core, forming a proteoglycan. The main GAGs in the dermis are HA and dermatan sulfate, with chondroitin-4-sulfate and chondroitin-6-sulfate present in small amounts. Made by both keratinocytes and dermal fibroblasts, GAGs are essential components of the extracellular matrix, although they make up only 0.2% of the dry weight of skin. GAGs hydrate in the skin (HA can hold up to 1000x its mass in water) and maintain basement membrane integrity, regulate cellular interactions and nutrient transport, and are involved in collagen and possibly elastic fiber formation. The proportion of GAGs (especially HA) in the dermis has been shown to be diminished with aging. See Perlish et al, "The Role of Glycosaminoglycans in Aging of the Skin." Retinoic acid, the benchmark anti-aging active, has been shown to increase GAG content of the spinous and granular layers of the epidermis and the papillary dermis of aged skin in vivo. See Kligman et al., "Effects of topical tretinoin on non-sun-exposed protected skin of the elderly," J. Am Acad Dermatol 1993;29:25-33.

Protocol for measuring GAGs

Neonatal human dermal fibroblasts were purchased from Clonetics Corp., San Diego, CA and used in passages 5-10. All materials for cell culture were purchased from Life Technologies, NY. Cells were seeded at a density of approximately 50,000/well in a 12-well plate in a medium containing DMEM (Dulbecco's Modified Eagle's Medium), high-glucose supplemented with 2 mM L-glutamine, 10% fetal bovine serum, and antibiotic and antimycotic solutions. Cells were then grown to confluence for 2 days. At confluence, each well was rinsed in serum-free DMEM and the cells dosed with test compounds (in triplicate) in 750µL of serum-free DMEM. Test compounds were used at a concentration indicated in Table 2 below. Controls did not contain any test compounds. After 24 hours, this medium was aspirated and the treatment step repeated. After a second 24-hour period, this medium, containing the soluble GAGs, was collected and frozen until analysis.

A positively-charged Zeta Probe membrane was soaked in sterile water and placed into the Dot-Blot Apparatus (both Bio-Rad Labs, Hercules, CA). 100µL of water was applied to each well and pulled through using a vacuum. After thawing, 100µL of test solution samples or standards (Hyaluronic acid or Chondroitin Sulfate from bovine trachea, Sigma, St. Louis, MO) was applied to the membrane and allowed to gravity filter (about 1.5 - 2 hours). GAGs were now bound to membrane. The membrane was blocked in 3% w/v fatty acid free bovine serum albumin (Sigma) in water for one hour. A dye solution of 0.5% w/v Alcian Blue dye (ICN Biochemicals,

Cleveland, OH) in 3% acetic acid, pH approximately 2.3, was made. The membrane was washed twice in distilled water and then stained in the dye solution on a rotary shaker for 15 minutes. The dye was poured off and the membrane destained twice for 15 minutes each time in 3% acetic acid. The membrane was rinsed in water and left to dry overnight. The Bio-Rad GS 700 Image Analysis Densitometer was used to quantitate the intensity of color in each spot. Percent change from control was calculated from densitometer readings as follows: [(Reading for test compound-Reading for control)/Reading for control] * 100. Control has a reading of 100%. Statistical significance (p value) was calculated using student's t-test.

The results that were obtained are summarized in Table 2. TGF-B is a positive control, ensuring the integrity of the assay: transforming growth factor beta is known to increase production of GAGs by fibroblasts.

TABLE 2

Sample	% Increase (+) or % decrease (--) over control	p value
TGF-B	+200*	6.2×10^{-7}
0.01% Exxal® 7	+20*	.017
0.01% Exxal® 8	0*	.096
0.01% Exxal® 10	+10*	.0050
0.01% Exxal® 12	+30*	.0006
0.01% Exxal® 13	+20*	5.6×10^{-6}

*Statistically significant at $p<0.05$

It can be seen from the results in Table 2 that all the alcohols tested, including the alcohols within the scope of the invention, significantly increased GAGs production by fibroblasts.

EXAMPLE 3

This example reports an in vitro analysis of sebum suppression by various test compounds.

In Vitro Sebocyte Lipogenesis Assay:

Human sebaceous glands were isolated from the nose of a male (age 60) and cultured using submerged tissue culture techniques (Bajor et al, J. Invest. Dermatol. 102: 1994, P. 564). These sebocytes accumulate intracellular lipid droplets characteristic of mature human sebum.

Harvested and passaged sebocytes were added to each well of a 48 well tissue culture plate and incubated at 37°C in the presence of 7.5% CO_2 for 7 days. On the day of experimentation, the growth medium was removed and the sebocytes washed three times with Dulbecco's Modified Eagle's medium (DMEM; glucose free, phenol red free). Fresh DMEM in 0.5 ml amount was added to each well and 5 μl of a test agent, at final concentrations indicated in the Tables below. Triplicate wells were utilized for each sample. Controls consisted of DMEM and ethanol (used to dilute alcohols). All cultures were incubated at 37°C/7.5% CO_2 for 30 minutes. Radioactive label was prepared by adding 100 μl of ^{14}C labeled

acetic acid (Amersham, sodium salt, specific activity of 56 mCi/mmol) to 10 ml of 25 mM sodium acetate buffer. Then, 50 μl was added to each well containing the sebocytes and test agents. The cultures were returned to the incubator for four hours. Thereafter, the sebocytes were rinsed three times with fresh phosphate buffered saline (PBS) to remove unbound active and radioactive label. Radioactive label remaining in the cultured sebocytes was counted using a Beckman scintillation counter. The results were expressed as % reduction compared to control (ethanol). The higher the number, the better the result.

The results that were obtained are summarized in Table 3 below. Statistical significance (p value) was calculated using student's t-test. Test compounds are considered to be effective at % reduction of at least 20%. Negative values indicate increase in sebum production.

TABLE 3

Sample	% Reduction	p value
0.01% Exxal® 7	-9.1%	.322
0.01% Exxal® 8	3.1%	.716
0.01% Exxal® 9	23.4%*	.026
0.01% Exxal® 10	33.9%*	.009
0.01% Exxal® 12	32.0%*	.014
0.01% Exxal® 13	33.9%*	.006

*Statistically significant at $p<0.05$

It can be seen from the results in Table 3 that Exxal® 7 and Exxal® 8 (not within the scope of the invention) did not suppress sebum secretion by sebocytes, whereas Exxal® 9, Exxal® 10, Exxal® 12, and Exxal® 13 (within the scope of the invention) all were effective at suppressing sebum secretion. The example demonstrates that the total chain length of at least 9 carbons is critical to attain sebum suppression.

COMPARATIVE EXAMPLE 4

Example 3 was repeated, using various concentrations of straight chain alcohols (no branching) which are outside the scope of the invention. The results that were obtained are summarized in Table 4.

TABLE 4

Sample	% Reduction	p value
0.01% 1-Dodecanol	-21.0%	.487
0.10% 1-Dodecanol	12.4%	.211
0.01%1-Tridecanol	-2.6%	.701
0.10% 1-Tridecanol	-7.0%	.168
0.01% 1-Hexadecanol	-5.6%	.621
0.10% 1-Hexadecanol	-27.8%	.138

It can be seen from the results in Table 4 that straight chain, non-branched alcohols which are not within the scope of the invention, do not attain sebum supression. Thus, branched alcohols are critical in order to attain sebum suppression.

COMPARATIVE EXAMPLE 5

Example 3 was repeated, using various concentrations of alcohols which contain a single branch (outside the scope of the invention). The results that were obtained are summarized in Table 5.

TABLE 5

Sample	% Reduction	p value
0.01% 1-Tridecanol	-10.5%	0.033
0.010% 2-Tridecanol	-2%	0.608
0.01% 4-Tridecanol	3%	0.503

It can be seen from the results in Table 5 that straight chain tridecanol variants of Exxal 13 were not effective sebum suppressors. By contrast, Exxal® 13 (branched alcohol within the scope of the invention) was an effective sebum suppressor (see Table 3).

COMPARATIVE EXAMPLE 6

Example 3 was repeated, with the following changes:
-PBS was used instead of DMEM during radiolabel incorporation;
-quadruplicate samples were run, instead of triplicate;
-50mM acetate buffer was used in place of 25mM to dilute the radiolabel.

The results that were obtained are summarized in Table 6.

TABLE 6

Treatment	Concentration	% Reduction	p value
Phenol Red	10μM	34.1	0.018
Phenol Red	100μM	52.4	0.0083
Dihydrotestosterone	0.00003% (1 μM)	-28.8	0.0002
Salicylic Acid	0.14% (10.0 mM)	3.6	0.205

The results in Table 6 demonstrate that the sebocyte assay is a valid and reliable test for measuring sebum suppression, because Phenol Red (phenolsulfonphthalein) provided sebum suppression, as predicted from the other sources, whereas dihydrotestosterone (androgen) actually increased sebum production, as also predicted from other sources. Salicylic acid, a known anti-acne agent did not inhibit sebum output, demonstrating that an antiacne agent does not necessarily have antisebum activity.

EXAMPLE 7

This example reports an in-vivo assessment of skin whiteness following application of creams containing various levels of fumed silica.

Procedure:

Thirty milligrams of sample cream was applied on a 15 cm^2 circular area on the forearm of the subject. Two sites per forearm were used in the study. The creams were applied and

rubbed in using a latex finger cot to prevent loss during rubbing. The sites were measured before application and 10 minutes after application to allow for drying.

A chromameter (Minolta CR 10) was used to quantify the increase in skin whiteness. The L, a, and b values were recorded and an E value was calculated using the following formula: E = square root of $[(L-40)2 + a^2 + b^2]$, where L, the luminescence, is measured on a scale from 0 to 100, a (the red-green axis) is measured from -60 (green) to +60 (red), and b (the yellow-blue axis) is measured from -60 (blue) to +60 (yellow). As can be seen from Table 8 below, the decrease in E value corresponds to an increase in skin whiteness. The percent change in E value after application of the samples was calculated. The samples containing silica were compared to the base formulation to evaluate the statistical significance of the increased whiteness due to addition of silica by calculating the p value using student's t-test.

The whiteness level was assessed visually and graded according to the following scale: (1) not white, (2) very slightly white, (3) slightly white, (4) white, (5) very white.

Samples:

A simple cream (base formula) was prepared according to Table 7 below by heating phase A and phase B separately to 75C. Phase A was then added to phase B at 75C while mixing at 1000 rpm for 5 minutes. The sample was then homogenized

for 10 minutes while cooling using an L4R Silverson homogenizer at half power, and transferred to a jar where it was allowed to cool to room temperature overnight. 200 g samples were prepared. The samples containing silica were prepared according to same procedure and following the same recipe as the base formula except that some water was removed from phase B to accommodate the fumed silica.

TABLE 7

Base formula

Phase	Ingredient	CTFA or Chemical Name	Wt. %
A	Pristerene 4911	stearic acid	15
A	Lanette 16 NF	cetyl alcohol	1
A	propyl paraben	same	0.1
B	Aerosil 200	fumed silica	0
B	methyl paraben	same	0.1
B	potassium hydroxide (25%)	same	1.5
B	water	same	to 100

Results:

TABLE 8

Sample	E value before application	E value after application	change in E value (%)	p value (compared to base formula)	whiteness score
base formula	21.64	20.81	- 3.8%	-	2
1% silica in base formula	21.34	19.74	- 7.5%	0.099	3
2% silica in base formula	22.07	20.04	-9.2%*	0.018	4
5% silica in base formula	21.48	17.37	-19.1%*	0.013	5

* Statistically significant at $p<0.05$

It can be seen from the results in Table 8 that a level of 2% fumed silica yielded a skin whiteness score of 4, a whiteness level unacceptable for cosmetic applications. Consequently it appears that a level of 1% fumed silica is the upper limit for use in cosmetic applications corresponding to a decrease in E value of no more than 8% in our test. The addition of 1% silica did not result in a significantly different change in E value when compared to the base formula with no silica. However the addition of 2% and 5% both resulted in a significant higher decrease in E value when compared to the base formula.

EXAMPLE 8

Examples 8 illustrates topical compositions according to the present invention. The compositions can be processed in conventional manner. They are suitable for cosmetic use. In particular the compositions are suitable for application to oily, wrinkled, rough, aged and/or UV-damaged skin to improve the appearance and the feel thereof as well as for application to healthy skin to prevent or retard deterioration thereof.

OIL-IN WATER EMULSION CREAM

Ingredient	CTFA or Chemical Name	weight %
Polawax Regular	Emulsifiable Wax	5
Exxal® 12	isoalcohol	5
Myristyl myristate	same	2
Dow Corning 3225	cyclomethicone and dimethicone copolyol	2
Aerosil 200	silica	1
Sepigel 305	poyacrylamide and C13-14 isoparaffin and laureth-7	0.5
Glycerine microsponges	Methacrylate copolymer with glycerine	0.5
Brij 58	ceteth-20	0.3
methyl paraben	same	0.2
germall 115	imidazolidinyl urea	0.2
propyl paraben	same	0.15
BHT	butylated hydroxy toluene	0.05
water	same	to 100

OIL-IN-WATER EMULSION CREAM

Ingredient	CTFA or Chemical Name	weight %
Sequesterene Na2	disodium EDTA	0.05
Veegum Ultra	magnesium aluminum silicate	0.6
Methyl Paraben	methyl paraben	0.15
DC Antifoam Emulsion	simethicone	0.01
Butylene Glycol 1,3	butylene glycol 1,3	3.0
Natrosol 250HHR	hydroxyethylcellulose	0.5
Aerosil 200	fumed silica	0.5
Glycerine USP	glycerine, USP	2.0
Keltrol 1000	xanthan gum	0.2
Triethanolamine 99%	triethanolamine	1.2
Pristerene 4911	stearic acid	3.0
Propylparaben NF	propyl paraben NF	0.1
Naturechem GMHS	glyceryl hydrostearate	1.5
Lanette 18DEO	stearyl alcohol	1.5
Exxal® 13	isoalcohol	4.0
Protachem ISP	isostearyl palmitate	3.0
Hetester FAO	C12-15 alcohols octanoate	2.0
Silicone Fluid 200(50cts)	dimethicone	1.0
Cholesterol NF	cholesterol NF	0.5
Sorbitan Stearate	sorbitan stearate	1.0
Embanox BHT	butylated hydroxytoluene	0.05
Vitamine E Acetate	tocopheryl acetate	0.1
MYRJ 59	PEG-100 stearate	2.0
Pationic SSL	sodium stearoyl lactylate	0.5
Alpha-bisabolol	alpha-bisabolol	0.2
water	same	to 100

anhydrous composition

CTFA or Chemical Name	weight %
isostearyl neopentanoate	20
peg-8 caprylic/capric glycerides	16
cetyl octanoate	17
polyglyceryl-6 dioleate	15
cyclomethicone	20
glyceryl isostearate	0.5
talcum	0.5
ceramide III	0.1
ppg-5-cetheth-20	3
trimethyl heptanol	3
ethanol	to 100

water-in-oil emulsion

CTFA or Chemical Name	weight %
squalane	5
macadamia oil	5
pentaerythritol tetraoctanoate	15
petrolatum	5
glyceryl stearate	3
tocopherol acetate	0.5
butylated hydroxytoluene	0.05
methyl paraben	0.15
propyl paraben	0.15
sodium citrate	1
butylene glycol	2
glycerol	2
bentone clay	0.5
disodium EDTA	0.05
trimethyl nonanol	10
water	to 100

oil-in-water emulsion

CTFA or Chemical Name	weight %
glycerin	1
tetrasodium EDTA	0.1
cetyl alcohol	1
stearyl alcohol	1
mineral oil	5
dimethicone	1
dimethiconol	0.2
polyquaternium 37	2
steareth-21	1
Steareth-2	0.5
Trimethyl decanols (Exxal® 13)	1
Cyclomethicone	0.5
Silica	0.6
Water	to 100

water-in-oil emulsion

CTFA or Chemical Name	weight %
light mineral oil	10
stearoxytrimethylsilane and stearyl alcohol	5
dimethicone	2
stearyl stearate	10
quaternium-15	3
peg-22 dodecyl glycol copolymer	1
Sorbitol	0.5
Methyl paraben	0.2
disodium EDTA	0.1
butylated hydroxytoluene	0.1
dimethyl heptanols (Exxal® 9)	5
silica	1
water	to 100

It should be understood that the specific forms of the invention herein illustrated and described are intended to be representative only.

CLAIMS

1. A skin care cosmetic composition comprising:

(i) from about 0.001% to about 50% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches; and

(ii) an oil-absorbing powder in an amount of not greater than about 1%; and

(iii) a cosmetically acceptable vehicle.

2. The composition of claim 1 wherein the oil-absorbing powder is selected from the group consisting of silica, talcum, and clay.

3. A cosmetic method of reducing or preventing oily skin conditions, the method comprising applying to the skin a composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

4. A cosmetic method of reducing or preventing sebum secretion from sebocytes, the method comprising applying to the skin a composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

5. A cosmetic method of stimulating collagen and glycosaminoglycan synthesis by fibroblasts in the skin,

the method comprising applying to the skin the composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

6. A cosmetic method of treating aged, photoaged, dry, lined or wrinkled skin, the method comprising applying to the skin the composition comprising from about 0.001% to about 100% of an alcohol containing a total of at least 9 carbon atoms and containing at least two branches.

7. Cosmetic use of a composition according to claim 1 for providing a skin care benefit selected from the following; reducing or preventing oily skin conditions; reducing or preventing sebum secretion from sebocytes; stimulating collagen and glycosaminoglycan synthesis by fibroblasts in skin; and/or treating aged, photoaged, dry, lined and/or wrinkled skin.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/02519

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/48

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 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 practical, 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.
X	US 4 478 853 A (CHAUSSEE JAMES G) 23 October 1984 (1984-10-23) abstract column 2, line 12 - line 27 column 6, line 30 - line 35 column 7, line 47 - line 55 ---	1,2,6,7
X	DE 196 32 043 A (HENKEL KGAA) 12 February 1998 (1998-02-12) abstract page 4, line 10 - line 67 --- -/--	1,2,6,7

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

[X] Patent family members are listed in 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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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
19 August 1999	27/08/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cielen, E

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/02519

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 371 801 A (UNILEVER PLC ;UNILEVER NV (NL)) 6 June 1990 (1990-06-06) cited in the application abstract page 2, line 3 - line 5 page 3, line 1 - line 22 page 4, line 14 - line 54 page 9, line 50 - line 54 page 10, line 55 - page 11, line 34 claims 7,11,17,23	1,2
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X	EP 0 315 912 A (HENKEL KGAA) 17 May 1989 (1989-05-17) abstract page 2, line 1-16 page 4, line 38 - line 43	3,4
X	US 4 362 715 A (STRIANSE SABBAT J ET AL) 7 December 1982 (1982-12-07)	3,6
A	column 1, line 34 - line 51 column 2, line 46 - line 68 examples 9-12	1,7
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P,X	EP 0 900 561 A (SHISEIDO CO LTD) 10 March 1999 (1999-03-10) abstract page 5, line 7 - line 10	5

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

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/02519

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 536 399 A (FLYNN ROBERT G ET AL) 20 August 1985 (1985-08-20) cited in the application abstract column 2, line 19 - line 46 claims	1-7

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 99/02519

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
See FURTHER INFORMATION SHEET PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/EP 99 02519

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-7 relate to a large number of possible compounds, methods and uses of these compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a small proportion of the compounds, methods and uses claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds, methods and use of the compounds as described in the description p. 15 lines 10-22 and branched fatty alcohols in general taking into account the definitions given on p. 6 of the description.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/02519

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