DESCRIPTION

HAIR GROWTH COMPOSITION FOR CUTANEOUS APPLICATION

TECHNICAL FIELD

[0001] The present invention relates to a hair growth composition for cutaneous application which can be employed in the field of pharmaceuticals which, even after applied to the scalp of users, suppress a stiff feel of their hair to allow for continued smooth combing.

BACKGROUND ART

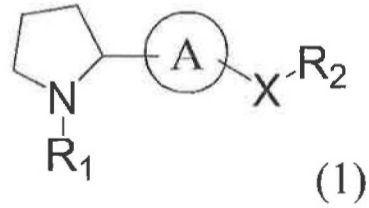
[0002] It is well known that when subjected to frequent repetition of beautification treatments as by washing, brushing, heating with a dryer, hair colors and bleaches, the hair generally undergoes considerable damage to deteriorate and as a result, it gets dry, even dried out, causing more split ends, hair breakage, etc. and leading to lower strength.

[0003] To cope with the drying-out of the hair and other problems that result from its deterioration and for the purpose of locking moisture in the hair while imparting smoothness and a moist feel to the same, it has been proposed that oils such as silicone oil or paraffinic oils, humectants such as low-molecular-weight polyols or glycerin, and a variety of raw materials extracted from natural substances should be incorporated as additives in hair care cosmetics and hair care compositions for cutaneous application (Non-Patent Document 1). Other cases known in the field of hair care cosmetics include: a composition incorporating calcium ions, etc. in combination with alcohols or ethers (Patent Document 1); a composition incorporating a magnesium compound and a cationic surfactant (Patent Document 2); a composition incorporating a polyoxyalkylene alkyl glycoside (Patent Document 3); and a composition incorporating aluminum chloride and magnesium chloride (Patent Document 4). However, a concern about hair care compositions for cutaneous application that incorporate particular compounds is that if the compounds themselves present a problem to the comfort of use, it is necessary to evaluate them individually and no study has been made to determine which additive is suitable.

[0004] It should be noted here that the compounds to be used in the present invention are

disclosed in Patent Document 5 and represented by the following formula (1):

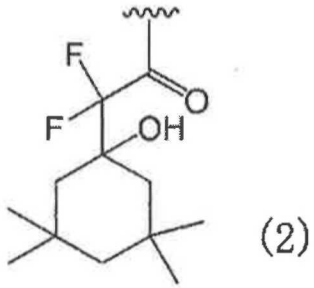
[0005] [Formula 1]



(1)

[wherein R_1 is of the following formula (2):

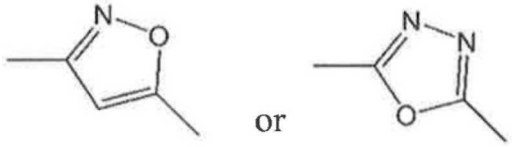
[0006] [Formula 2]



(2)

where ring A is either of the alternatives of the following formula (3):

[0007] [Formula 3]



or

(3)

where X is either $-CH_2O-$ or $-(CH_2)_2-$;

R_2 is a phenyl group or a pyridyl group (the phenyl or pyridyl group may be substituted by one to three methoxy groups)] or a pharmaceutically acceptable salt thereof.

CITATION LIST

PATENT LITERATURE

[0008] Patent Document 1: JP H7-2627 A

Patent Document 2: JP H8-53325 A

Patent Document 3: JP 2001-213734 A

Patent Document 4: JP 2010-6778 A

Patent Document 5: pamphlet of WO 2012/124750 A1

NON-PATENT LITERATURE

[0009] Non-Patent Document 1: *Shin-keshouhingaku* (New Science of Cosmetics), ed. by Takeo Mitsui, Nanzan-do (May 2006), pp. 440-462.

SUMMARY OF INVENTION

TECHNICAL PROBLEM

[0010] The conventional technology of hair care cosmetics and hair care compositions for cutaneous application proves effective to some extent in providing smoothness and a moist feel to the hair. However, if compositions containing compounds of formula (1) are simply formulated as liquids/solutions for cutaneous application or lotions, the conventional technology does not assure adequately sustained effectiveness but provides only poor smoothness and other feels of the hair during use; for these and other reasons, it has been impossible to prepare products that offer satisfactory comfort of use.

[0011] The present invention has been accomplished in view of this problem and it aims to provide a hair growth composition for cutaneous application which, when containing a compound represented by the formula (1), features good sustainability of effects such as eliminating a feel that the hair gets dried out, imparting smoothness and a moist feel to the hair, and suppressing its damage.

SOLUTION TO PROBLEM

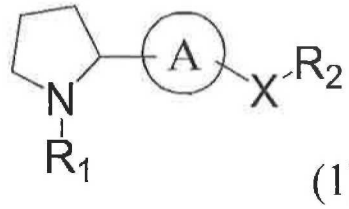
[0012] The present inventors conducted an intensive study with a view to attaining the above-stated object and found as a result that the aforementioned drawbacks of the conventional technology can be eliminated by incorporating a magnesium compound and/or a calcium compound and a specific nonionic surfactant in a compound represented by the formula (1). This finding has led to the completion of the present invention. Hereinafter, the present invention will be explained in detail. Various modes of the present invention are shown below.

[0013] [1]

A hair growth composition for cutaneous application characterized by containing the following (a) to (d):

[0014] (a) a compound represented by formula (1):

[Formula 4]



(1)

[wherein R_1 is of the following formula (2):

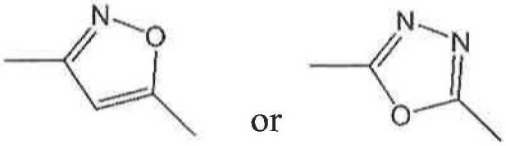
[0015] [Formula 5]



(2)

where ring A is either of the alternatives of the following formula (3):

[0016] [Formula 6]



or

(3)

where X is either $-CH_2O-$ or $-(CH_2)_2-$;

R_2 is a phenyl group or a pyridyl group (the phenyl or pyridyl group may be substituted by one to three methoxy groups)] or a pharmaceutically acceptable salt thereof;

(b) a nonionic surfactant included in either of groups (b-1) to (b-3):

(b-1) one having a polyoxyethylene structure and an HLB value of 9 or more;

(b-2) one having no polyoxyethylene structure but having an HLB value of 10 or more;

(b-3) a soybean phospholipid which is either hydrogenated or not;

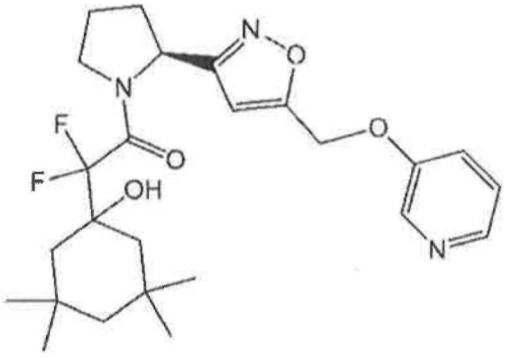
(c) at least one member selected from the group consisting of a magnesium compound and a calcium compound;

(d) water.

[2]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((pyridin-3-yloxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone represented by the following formula:

[0017] [Formula 7]

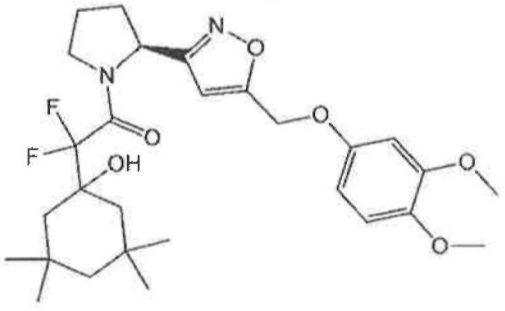


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[3]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-1-(2-(5-((3,4-dimethoxyphenoxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)ethanone represented by the following formula:

[0018] [Formula 8]



.

[4]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-1-(2-(5-((3,4-

dimethoxyphenoxy)methyl)-1,3,4-oxadiazol-2-yl)pyrrolidin-1-yl)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)ethanone.

[5]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((3,4,5-trimethoxyphenoxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone.

[6]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-(phenoxymethyl)-1,3,4-oxadiazol-2-yl)pyrrolidin-1-yl)ethanone.

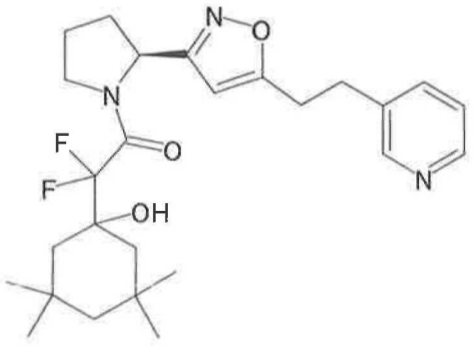
[7]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro2-(1-hydroxy3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((pyridin-4-yloxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone.

[8]

A hair growth composition for cutaneous application as recited in [1], wherein the compound represented by formula (1) in (a) above is a compound represented by the following formula:

[0019] [Formula 9]



[9]

A hair growth composition for cutaneous application as recited in any one of [1] to [8], which is characterized in that the nonionic surfactant in (b) above is one or more members selected from the group consisting of polysorbate 80, a hydrogenated soybean phospholipid, polyethylene glycol monostearate, polyoxyethylene stearyl ether, polyoxyethylene cetyl ether, and polyoxyethylene (20) polyoxypropylene (8) cetyl ether.

[10]

A hair growth composition for cutaneous application as recited in any one of [1] to [9], which is characterized in that the magnesium compound and the calcium compound in (c) above are magnesium chloride and/or calcium chloride.

[11]

A hair growth composition for cutaneous application as recited in any one of [1] to [10], which is characterized in that the dosage form of the hair growth composition for cutaneous application is a liquid for cutaneous application.

[12]

A hair growth composition for cutaneous application as recited in any one of [1] to [11], wherein the amount of incorporation of at least one member selected from the group consisting of a magnesium compound and a calcium compound in (c) above is 0.001 to 10 (w/v%) in the total amount of the hair growth composition for cutaneous application.

[13]

A hair growth composition for cutaneous application as recited in [12], wherein the amount of incorporation of at least one member selected from the group consisting of a magnesium compound and a calcium compound in (c) above is 0.01 to 5 (w/v%) in the total amount of the hair growth composition for cutaneous application.

[14]

A hair growth composition for cutaneous application as recited in any one of [1] to [13], wherein the amount of incorporation of the nonionic surfactant in (b) above is 0.01 to

10 (w/v%) in the total amount of the hair growth composition for cutaneous application.

[15]

A hair growth composition for cutaneous application as recited in [14], wherein the amount of the nonionic surfactant in (b) above is 0.1 to 5 (w/v%) in the total amount of the hair growth composition for cutaneous application.

[16]

A hair growth composition for cutaneous application as recited in any one of [1] to [15], wherein the amount of the compound represented by formula (1) is 0.0001 to 20 (w/v%) in the total amount of the hair growth composition for cutaneous application.

[17]

A hair growth composition for cutaneous application as recited in [16], wherein the amount of incorporation of the compound represented by formula (1) is 0.1 to 10 (w/v%) in the total amount of the hair growth composition for cutaneous application.

ADVANTAGEOUS EFFECTS OF INVENTION

[0020] By means of the present invention, even in the case where a compound represented by formula (1) is contained, it becomes possible to provide a hair growth composition for cutaneous application which features good sustainability of effects such as eliminating a feel that the hair gets dried out, imparting smoothness and a moist feel to the hair, and suppressing its damage.

DESCRIPTION OF EMBODIMENTS

[0021] Hereinafter, the constitution of the present invention is described in detail.

[0022] The present invention is characterized by containing a compound represented by formula (1), a magnesium compound and/or a calcium compound, and a nonionic surfactant specified above.

[0023] The amount of incorporation of the nonionic surfactant specified above is preferably 0.01 to 10 (w/v%) in the total amount of the hair growth composition for cutaneous application, and the amount of incorporation of the magnesium compound and/or the calcium compound is preferably 0.001 to 10 (w/v%) in the total amount of the hair growth

composition for cutaneous application.

[0024] The compound represented by formula (1) can be produced by the production method described in the pamphlet of WO 2012/124750 A1.

[0025] The amount of incorporation of the compound represented by formula (1) is 0.0001 to 20 (w/v%), preferably 0.1 to 10 (w/v%), more preferably 1 to 10 (w/v%), in the total amount of the hair growth composition for cutaneous application.

[0026] The nonionic surfactant in (b) above which can be used in the present invention may be a nonionic surfactant having a polyoxyethylene structure and an HLB value of 9 or more, a nonionic surfactant having no polyoxyethylene structure but having an HLB value of 10 or more, or even a soybean phospholipid, hydrogenated or not, for which HLB cannot be clearly specified.

[0027] It should be noted that HLB, standing for hydrophile-lipophile balance, refers to the balance between lipophilicity and hydrophilicity. The HLB values as mentioned in the present invention are obtained by actual measurement based on the emulsification technique (see Handbook – Cosmetics/Preparations Raw Materials – Revised Edition, "20. Cosmetics and Pharmaceuticals", pp. 854-855 (revised edition published on February 1, 1977 by Nikko Chemicals Co., Ltd. and NIPPON SURFACTANT INDUSTRIES CO., LTD.))

[0028] Among others, polysorbate 80 (polyoxyethylene sorbitan oleate), hydrogenated soybean phospholipid, polyethylene glycol monostearate, polyoxyethylene stearyl ether, polyoxyethylene cetyl ether, and polyoxyethylene (20) polyoxypropylene (8) cetyl ether are preferred. Among these materials, polysorbate 80 (polyoxyethylene sorbitan oleate) is particularly preferred.

[0029] Polysorbate 80 may be exemplified by the trade name "NIKKOL TO-10M" manufactured by NIPPON SURFACTANT INDUSTRIES CO., LTD.; the hydrogenated soybean phospholipid may be exemplified by the trade name "NIKKOL Resinol S-10M" manufactured by Nikko Chemicals Co.; the polyethylene glycol monostearate may be exemplified by the trade name "NIKKOL MYS-10V" manufactured by Nikko Chemicals Co.; the polyoxyethylene stearyl ether may be exemplified by the trade name "NIKKOL BS-

4" manufactured by Nikko Chemicals Co.; the polyoxyethylene cetyl ether may be exemplified by the trade name "NIKKOL BC-5.5" manufactured by Nikko Chemicals Co.; the polyoxyethylene (20) polyoxypropylene (8) cetyl ether may be exemplified by the trade name "NIKKOL PBC-44" manufactured by Nikko Chemicals Co.; glyceryl monostearate may be exemplified by the trade name "NIKKOL MGS-AMV" manufactured by Nikko Chemicals Co.; sorbitan sesquioleate may be exemplified by the trade name "NIKKOL SO-10V" manufactured by Nikko Chemicals Co.; polyoxyethylene oleyl ether may be exemplified by the trade name "NIKKOL BO-2V" manufactured by Nikko Chemicals Co.; lauromacrogol may be exemplified by the trade name "NIKKOL BL-2" manufactured by Nikko Chemicals Co.; and polyoxyethylene hardened castor oil may be exemplified by the trade name "NIKKOL HCO-10" manufactured by Nikko Chemicals Co.

[0030] The amount of incorporation of the nonionic surfactant in (b) above which is to be used in the present invention is 0.01 to 10 (w/v%), preferably 0.1 to 5 (w/v%), in the total amount of the hair growth composition for cutaneous application. If the amount of interest is less than 0.01 (w/v%), smoothness as an index for the comfort of use is impaired; if the amount of interest exceeds 10 (w/v%), the comfort of use as final product is impaired.

[0031] The magnesium compound and the calcium compound that are to be used in the present invention may be exemplified by halides or complex halides, oxides or associated compounds of oxides, sulfides, nitrides, carbides, oxoates, organic magnesium compounds, organic calcium compounds, and so on, including hydrates. Among others, (i) magnesium halides and (ii) magnesium oxoates are preferred as magnesium compounds. For specific illustration, preferred examples of (i) are magnesium chloride, magnesium bromide, magnesium iodide, and so on; preferred examples of (ii) are magnesium sulfate, magnesium nitrate, and magnesium carbonate. In the group consisting of (i) and (ii), magnesium chloride is particularly preferred.

[0032] As for the calcium compound, calcium chloride is preferred.

[0033] In the case where hydrates of the magnesium compound or the calcium compound are used, the amount of their incorporation will be indicated, unless otherwise noted, as

calculated for anhydride.

[0034] The amount of incorporation of the magnesium compound and/or the calcium compound which is to be used in the present invention is 0.001 to 10 (w/v%), preferably 0.01 to 5 (w/v%), in the total amount of the hair growth composition for cutaneous application. If the amount of interest is less than 0.001 (w/v%), the effect of incorporating the magnesium compound and/or the calcium compound will not be exhibited; if the amount of interest exceeds 10 (w/v%), not only the comfort of use will be impaired but also the stability will decrease, which is by no means preferable.

[0035] In addition to the above-mentioned components, the hair growth composition for cutaneous application of the present invention permits the addition of various materials, depending on the object, within those quantitative and qualitative ranges which will not be deleterious to the intended effects of the present invention and they include, for example: polyhydric alcohols; oils; nonionic surfactants other than those listed in (b) above; anionic surfactants; amphoteric surfactants; high molecular weight compounds such as cationic, anionic, nonionic, and amphoteric high molecular weight compounds; chemicals such as polysaccharides, chelatants, antioxidants, UV absorbers, antiseptics, and vitamins; and perfumes.

[0036] Polyhydric alcohols that may be used include glycerin, 1,3-butylene glycol, propylene glycol, dipropylene glycol, polyethylene glycol, and so on.

[0037] As nonionic surfactants other than those listed in (b) above, the following may be used: lipophilic nonionic surfactants including sorbitan fatty acid esters such as sorbitan monooleate, sorbitan monoisostearate, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan sesquioleate, sorbitan trioleate, diglycerol sorbitan penta-2-ethylhexanoate, and diglycerol sorbitan tetra-2-ethylhexanoate; glycerin polyglycerin fatty acids such as mono-cottonseed oil fatty acid glycerin, monoerucic acid glycerol, sesquioleic acid glycerol, glyceryl monostearate, α,α′-glyceryl oleate pyroglutamate, and glyceryl monostearate malate; propylene glycol fatty acid esters such as propylene glycol monostearate; as well as hardened castor oil derivatives and glyceryl alkyl ethers; POE

sorbitan fatty acid esters such as POE sorbitan monooleate, POE sorbitan monostearate, and POE sorbitan tetraoleate; POE sorbite fatty acid esters such as POE sorbite monolaurate, POE sorbite monooleate, POE sorbite pentaoleate, and POE sorbite monostearate; POE glyceryl fatty acid esters such as POE glyceryl monostearate, POE glyceryl monoisostearate, and POE glyceryl triisostearate; POE fatty acid esters such as POE monooleate, POE distearate, POE monodioleate, and ethylene glycol distearate; POE alkyl ethers such as POE lauryl ether, POE oleyl ether, POE stearyl ether, POE behenyl ether, POE 2-octyldodecyl ether, and POE cholestanol ether; POE alkyl phenyl ethers such as POE octyl phenyl ether, POE nonyl phenyl ether, and POE dinonyl phenyl ether; pluaronic type compounds such as Pluronic; POE·POP alkyl ethers such as POE·POP cetyl ether, POE·POP 2-decyltetradecyl ether, POE·POP monobutyl ether, POE·POP hydrogenated lanolin, POE·POP glycerin ether; tetra-POE·tetra-POP ethylenediamine condensates such as Tetronic; POE hardened castor oil hardened castor oil derivatives such as POE castor oil, POE hardened castor oil, POE hardened castor oil monoisostearate, POE hardened castor oil triisostearate, POE hardened castor oil monopyroglutamate monoisostearate diester, and POE hardened castor oil maleate; POE beeswax·lanolin derivatives such as POE sorbite beeswax; alkanolamides such as coconut oil derived diethanolamide, lauric acid monoethanolamide, and fatty acid isopropanolamide; as well as POE propylene glycol fatty acid esters, POE alkylamines, POE fatty acid amides, sucrose fatty acid esters, POE nonyl phenyl formaldehyde condensates, alkylethoxydimethylamine oxides, trioleyl phosphoric acid, and so on. The amount of the nonionic surfactant exemplified hereinabove may be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0038] As anionic surfactants, the following may be used: base materials for soap; fatty acid soaps such as sodium laurate and sodium palmitate; higher alkyl sulfate salts such as sodium lauryl sulfate and potassium lauryl sulfate; alkyl ether sulfate salts such as POE triethanolamine lauryl sulfate and sodium POE lauryl sulfate; N-acyl sarcosinates such as sodium lauroylsarcosinate; higher fatty acid amide sulfonic acid salts such as sodium N-

myristoyl-N-methytaurine, sodium coconut oil fatty acid methyltauride, and sodium lauryl methyltauride; phosphate salts such as sodium POE oleyl ether phosphate and POE stearyl ether phosphoric acid; sulfosuccinic acid salts such as sodium di-2-ethylhexylsulfosuccinate, sodium monolauroyl monoethanolamide polyoxyethylene sulfosuccinate, and sodium lauryl polypropylene glycol sulfosuccinate; alkylbenzene sulfonic acid salts such as sodium linear dodecylbenzene sulfonate, triethanolamine linear dodecylbenzene sulfonate, and linear dodecylbenzene sulfonic acid; N-acylglutamate salts such as monosodium N-lauroylglutamate, disodium N-stearoylglutamate, and monosodium N-myristoyl-L-glutamate; higher fatty acid ester sulfuric acid salts such as sodium hardened coconut oil fatty acid glycerin sulfate; sulfated oils such as Turkey red oil; as well as POE alkyl ether carboxylic acids, POE alkylallyl ether carboxylic acid salts, α-olefinsulfonic acid salts, higher fatty acid ester sulfonic acid salts, secondary alcohol sulfonate salts, higher fatty alkylolamide sulfate salts, sodium lauroyl monoethanolamide succinate, and di-triethanolamine N-palmitoylaspartate. The amount of the anionic surfactant may, for example, be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0039] As amphoteric surfactants, the following may be used: imidazoline-based amphoteric surfactants such as 2-undecyl-N,N,N-(hydroxyethylcarboxymethyl)-2-imidazoline sodium and 2-cocoyl-2-imidazolinium hydroxide-1-carboxyethyloxy-2-sodium salt; betaine-based amphoteric surfactants such as 2-heptadecyl-N-carboxymethyl-N-hydroxyethylimidazolinium betaine, lauryldimethylaminoacetic acid betaine, alkyl betaine, amido betaine, and sulfobetaine; and amino acid salts such as N-lauroyl-β-alanine and N-stearyl-β-alanine. The amount of the amphoteric surfactant may, for example, be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0040] As cationic surfactants, the following may be used: poly(dimethyldiallylammnoum halide)-type cationic polymers, dimethyldiallylammonium halide/acrylamide copolymerized cationic polymers, or quaternary nitrogen-containing cellulose ether, or the condensation

product of polyethylene glycol, epichlorohydrin, propyleneamine and talloylamine obtained from tallow fatty acids, or cationized vinylpyrrolidone/dimethylaminoethyl methacrylate copolymers. The poly(dimethyldiallylammnoum halide)-type cationic high molecular weight compounds may include the product commercially available from Merck & Co., Inc., USA under the trade name Merquat 100. The dimethyldiallylammonium halide/acrylamide copolymer-type cationic polymers may include Merquat 550 (Merck & Co., Inc. USA). Examples of the condensation product of polyethylene glycol, epichlorohydrin, propyleneamine and talloylamine or cocoylamine may include the product commercially available from Henkel International Co., West Germany under the trade name Polyquat H. Examples of the quaternary nitrogen-containing cellulose include the products commercially available from Union Carbide Corp., USA under the trade names Polymer JR-400, Polymer JR-125, and Polymer JR-30M. Examples of the cationized vinylpyrrolidone/dimethylaminoethyl methacrylate copolymer include the products commercially available from GAF Corp., USA under the trade names Gafquat 755 and Gafquat 734. The amount of the cationic high molecular weight compound may, for example, be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0041] Examples of the anionic high molecular weight compound include xanthan gum, carrageenan, sodium alginate, gum arabic, pectin, carboxyvinyl polymers, and so on. The amount of the anionic high molecular weight compound may, for example, be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0042] Examples of the nonionic high molecular weight compound include polyvinyl pyrrolidone, copolymers of vinyl pyrrolidone and vinyl acetate, copolymers of vinyl pyrrolidone, vinyl acetate and acrylamino acrylate, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, methyl cellulose, dextrin, galactan, pullulan, and so on. The amount of the nonionic high molecular weight compound may, for example, be

less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0043] The amphoteric high molecular weight compound may be obtained by copolymerizing dialkyl amino ethyl acrylates, dialkyl amino ethyl methacrylates, diacetone acrylamides, etc. with acrylic acid, alkyl acrylates, methacrylic acid, alkyl methacrylates, etc. and then rendering the resulting copolymer amphoteric with acetic halides; examples include the product commercially available from Mtsubishi Petrochemical Co., Ltd. under the trade name YUKA FOAMER AM-75. The amount of the amphoteric high molecular weight compound may, for example, be less than 0.5 wt%, specifically less than 0.1 wt%, more specifically less than 0.01 wt%, relative to the total amount of the hair growth composition for cutaneous application.

[0044] Examples of the mucopolysaccharide include hyaluronic acid, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparan sulfate, and salts thereof, etc.

[0045] As the UV absorber, the following may be used: benzoic acid based compounds such as para-aminobenzoic acid (hereinafter abbreviated as PABA), glycerin PABA, and ethyldihydroxypropyl PABA; cinnamate-based compounds such as octyl methoxycinnamate and 2-ethoxyethyl-p-methoxycinnamate; benzophenone-based compounds such as 2,4-dihydroxybenzophenone, 2-hydroxy-4-methoxybenzophenone, 2-hydroxy-4-methoxy-4-methylbenzophenone; and others such as ethyl urocanate, 2-phenyl-5-methylbenzoxazole, 4-methoxy-4-t-butyl-dibenzoylmethane, and so on.

[0046] Usable as the antiseptic are alkyl esters of paraoxybenzoic acid, sodium benzoate, potassium sorbate, and other antiseptics that are commonly used in cosmetics.

[0047] Other chemicals that may be used are drug components that are also commonly used in cosmetics, as exemplified by vitamins such as of the vitamin C family and vitamin E family, placenta extract, a variety of amino acids, crude drugs, and anti-inflammatories.

[0048] The composition of the present invention may be formulated as any system selected from among a solubilized system, an emulsified system, a powder dispersed system, an oil-water dual phase system, an oil-water-powder tri-phase system, and so on.

[0049] For cutaneous application, the composition of the present invention may assume any dosage form and can be used as a gel, spray, foam, cream or liquid (e.g. lotion) product.

[0050] The solvent in liquids may be exemplified by ethanol, water, and 1,3-butylene glycol. A lotion, for example, can be prepared by using absolute ethanol in an amount in the range of 60 to 80 (w/v%), specifically 62 to 74 (w/v%), relative to the total amount of the hair growth composition for cutaneous application, with the remainder being water to make a total volume of 100 (mL).

EXAMPLES

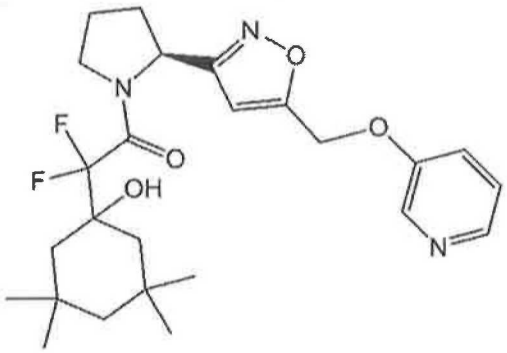
[0051] Hereinafter, the present invention is described in further detail by means of Examples, which are by no means intended to limit the scope of the present invention.

[0052] [Method of preparation]

A lotion was prepared as an example of the hair growth composition for cutaneous application. The lotion is obtained from suitable amounts of a compound of formula (4), a magnesium compound and/or calcium compound, a nonionic surfactant of (b) above, ethanol and water by mixing them under agitation.

[0053] The compound represented by formula (4) is identified below:

[0054] [Formula 10]



(4)

[0055] [Testing methods]

The test and evaluation methods adopted in the respective Examples are described below.

[0056] Evaluating the stiff feel and resistance to combing after application: Using hair models for the training of beauticians, about 1 mL of the preparation was applied to 25 cm^2

of hair and after letting the hair dry by itself for 8 hours at room temperature, "stiff feel" was evaluated by a sensory test checking how the directly applied area felt on touch whereas "resistance to combing" was evaluated by a sensory test checking for the resistance that developed upon combing the hair in the applied area with a plastic comb.

[0057] Evaluation was carried out based on the following four-score rating.

[0058] 4: None; 3: Some; 2: Moderate; 1: Positive

Lotions were prepared from the recipes shown in Tables 1 to 5, which also show the results of evaluation of stiff feel and resistance to combing.

[0059] [Table 1]

	Comparative Example					
Component name	1	2	3	4	5	6
Compound of formula (4)	5	5	5	5	5	5
Aluminum chloride	-	3	-	-	-	-
Lithium chloride	-	-	3	-	-	-
Magnesium bromide	-	-	-	3	-	-
Sodium chloride	-	-	-	-	3	-
Potassium chloride	-	-	-	-	-	3
Absolute ethanol	74	74	74	74	74	74
Water	bal.	bal.	bal.	bal.	bal.	bal.
Total amount	100mL	100mL	100mL	100mL	100mL	100mL
Sensory evaluation (numerals refer to evaluation scores)						
Stiff feel	1	2	2	2	N.T.	N.T.
Resistance to combing	1	1	2	2	N.T.	N.T.

Unless otherwise noted, the unit of the numerals for the respective components in each recipe is w/v%.

The amount of incorporation of each metal salt compound is calculated for anhydride.

The samples of Comparative Examples 5 and 6 are labeled N.T. because they did not dissolve to form applicable preparations.

The number of tests for stiff feel and resistance to combing was n = 7 in Comparative Examples 1, 3 and 4, and n = 8 in Comparative Example 2.

[0060]

[Table 2]

Component name	Product name NIKKOL	HLB	Comparative Example											
			7	8	9	10	11	12	13	14	15	16	17	18
Compound of formula (4)			5	5	5	5	5	5	5	5	5	5	5	5
Polysorbate 80	TO-10M	15	-	2	-	-	-	-	-	-	-	-	-	-
Hydrogenated soybean phospholipid	S-10M	-	-	-	1	-	-	-	-	-	-	-	-	-
Glycerin monostearate	MGS-AMV	4	-	-	-	2	-	-	-	-	-	-	-	-
Polyethylene glycol monostearate	MYS-10V	11	-	-	-	-	2	-	-	-	-	-	-	-
Sorbitan sesquioleate	SO-15MV	3.7	-	-	-	-	-	2	-	-	-	-	-	-
Polyoxyethylene stearyl ether	BS-4V	9	-	-	-	-	-	-	1	-	-	-	-	-
Polyoxyethylene oleyl ether	BO-2V	7.5	-	-	-	-	-	-	-	1	-	-	-	-
Lauromacrogol	BL-2	9.5	-	-	-	-	-	-	-	-	1	-	-	-
Polyoxyethylene cetyl ether	BC-5.5	10.5	-	-	-	-	-	-	-	-	-	1	-	-
Polyoxyethylene (20) polyoxypropylene (8) cetyl ether	PBC-44	12.5	-	-	-	-	-	-	-	-	-	-	1	-
Polyoxyethylene hardened castor oil 10	HCO-10	6.5	-	-	-	-	-	-	-	-	-	-	-	1
Absolute ethanol			74	74	74	74	74	74	74	74	74	74	74	74
Water			bal.	bal.	bal.	bal.	bal.	bal.	bal.	bal.	bal.	bal.	bal.	bal.
Total amount			100mL	100mL	100mL	100mL	100mL	100mL	100mL	100mL	100mL	100mL	100mL	100mL
Sensory evaluation (numerals refer to evaluation scores)														
Stiff feel			1	1	N.T.	N.T.	1	1	1	1	1	1	1	1
Resistance to combing			2	1	N.T.	N.T.	2	2	1	1	1	1	1	2

Unless otherwise noted, the unit of the numerals for the respective components in each recipe is w/v%.

The NIKKOL series in the components refers to product names.

The indication of the hydrogenated soybean phospholipid is abbreviated from NIKKOL Resinol S-10M.

The samples of Comparative Examples 9 and 10 are labeled N.T. because they did not dissolve to form applicable preparations.

The number of tests for stiff feel and resistance to combing was n = 1.

[0061] [Table 3]

Compound name	Product name NIKKOL	HLB	Comparative Example 19	20	21	22	23
Compound of formula (4)			5	5	5	5	5
Magnesium chloride			-	3	3	3	3
Sorbitan sesquioleate	SO-15MV	3.7	-	0.5	-	-	-
Polyoxyethylene oleyl ether	BO-2V	7.5	-	-	0.5	-	-
Lauromacrogol	BL-2	9.5	-	-	-	0.5	-
Polyoxyethylene hardened castor oil 10	HCO-10	6.5	-	-	-	-	0.5
Absolute ethanol			74	74	74	74	74
Water			bal.	bal.	bal.	bal.	bal.
Total amount			100mL	100mL	100mL	100mL	100mL
Sensory evaluation (numerals refer to evaluation scores)							
Stiff feel			1	2	2	2	2
Resistance to combing			1	2	2	2	2

Unless otherwise noted, the unit of the numerals for the respective components in each recipe is w/v%.

The amount of incorporation of each metal salt compound is calculated for anhydride.

The NIKKO L series in the components refers to product names.

The number of tests for stiff feel and resistance to combing was n = 7.

[0062]

[Table 4]

Component name	Comparative Example	
	24	25
Compound of formula (4)	5	5
α-Cyclodextrin	2	-
β-Cyclodextrin	-	2
Absolute ethanol	74	74
Water	bal.	bal.
Total amount	100mL	100mL
Sensory evaluation (numerals refer to evaluation scores)		
Stiff feel	1	1
Resistance to combing	2	2

Unless otherwise noted, the unit of the numerals for the respective components in each recipe is w/v%.

The number of tests for stiff feel and resistance to combing was n = 1.

[0063] [Table 5]

Component name	Product name NIKKOL	HLB	Example					
			1	2	3	4	5	6
Compound of formula (4)			5	5	5	5	5	5
Magnesium chloride			3	3	3	3	3	3
Polysorbate 80	TO-10M	15	0.5	-	-	-	-	-
Hydrogenated soybean phospholipid	S-10M	-	-	0.5	-	-	-	-
Polyethylene glycol monostearate	MYS-10V	11	-	-	0.5	-	-	-
Polyoxyethylene stearyl ether	BS-4V	9	-	-	-	0.5	-	-
Polyoxyethylene cetyl ether	BC-5.5	10.5	-	-	-	-	0.5	-
Polyoxyethylene (20) polyoxypropylene (8) cetyl ether	PBC-44	12.5	-	-	-	-	-	0.5
Absolute ethanol			74	74	74	74	74	74
Water			bal.	bal.	bal.	bal.	bal.	bal.
Total amount			100mL	100mL	100mL	100mL	100mL	100mL
Sensory evaluation (numerals refer to evaluation scores)								
Stiff feel			3	3	3	3	3	3
Resistance to combing			2	3	2	3	2	2

Unless otherwise noted, the unit of the numerals for the respective components in each recipe is w/v%.

The amount of incorporation of each metal salt compound is calculated for anhydride.

The NIKKO L series in the components refers to product names.

The indication of the hydrogenated soybean phospholipid is abbreviated from NIKKOL Resinol S-10M.

The number of tests for stiff feel and resistance to combing was n = 7.

[0064] [Preparation examples]

To make the preparations in accordance with the present invention, the amount of incorporation of the compound of formula (4) may be freely changed in Example 1. To be more specific, the compound of formula (4) may be incorporated in three different amounts, 2.5, 5 and 10 (w/v%) to prepare lotions at three concentrations of compound (4).

[0065] In Example 1, a lotion may be prepared by incorporating 6.4 (w/v%) of magnesium chloride in hexahydrate form.

[0066] In Example 1, the amount of incorporation of polysorbate 80 may be set at three values, 0.5, 1 and 2 (w/v%), to prepare lotions at three concentrations of polysorbate 80.

[0067] In Example 1, 1,3-butylene glycol may be further added and the amount of its incorporation may be set at three different values, 0.5, 1 and 2 (w/v%), to prepare lotions at three concentration of 1,3-butylene glycol.

[0068] In Example 1, absolute ethanol as solvent may be adjusted to fall within the range of 62 to 74 (w/v%), with the balance being water to prepare lotions each having a total volume of 100 (mL).

INDUSTRIAL APPLICABILITY

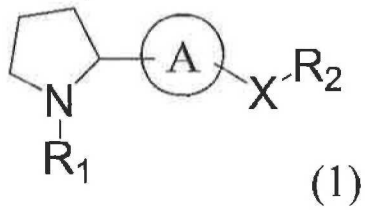
[0069] The hair growth composition for cutaneous application in accordance with the present invention contains the compound represented by formula (1) and has such an advantage that even after it is applied to the scalp of a user, the stiff feel of the user's hair is suppressed and continued smooth combing is assured.

CLAIMS

1. A hair growth composition for cutaneous application characterized by containing the following (a) to (d):

(a) a compound represented by formula (1):

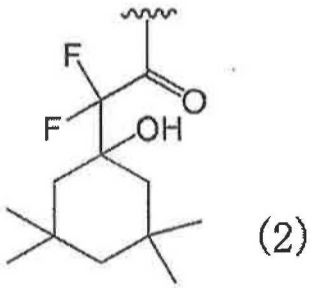
[Formula 1]



(1)

[wherein R_1 is of the following formula (2):

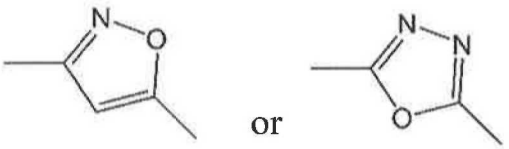
[Formula 2]



(2)

where ring A is either of the alternatives of the following formula (3):

[Formula 3]



(3)

where X is either $-CH_2O-$ or $-(CH_2)_2-$;

R_2 is a phenyl group or a pyridyl group (the phenyl or pyridyl group may be substituted by one to three methoxy groups)] or a pharmaceutically acceptable salt thereof;

(b) a nonionic surfactant included in either of groups (b-1) to (b-3):

(b-1) one having a polyoxyethylene structure and an HLB value of 9 or more;

(b-2) one having no polyoxyethylene structure but having an HLB value of 10 or more;

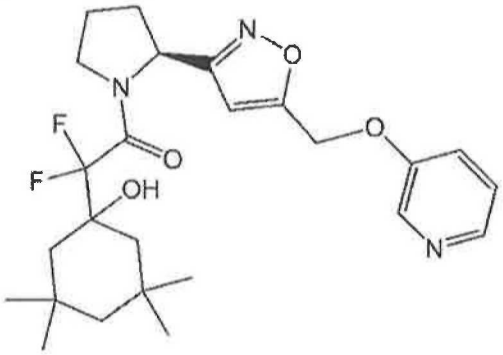
(b-3) a soybean phospholipid which is either hydrogenated or not;

(c) at least one member selected from the group consisting of a magnesium compound and a calcium compound;

(d) water.

2. A hair growth composition for cutaneous application according to claim 1, wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((pyridin-3-yloxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone represented by the following formula:

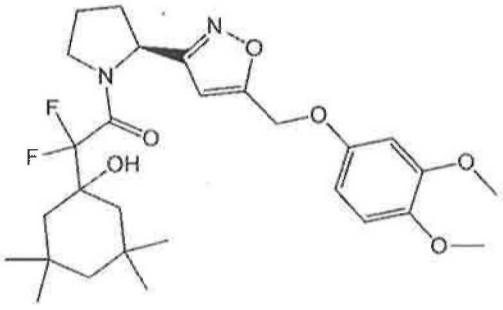
[Formula 4]



.

3. A hair growth composition for cutaneous application according to claim 1, wherein the compound represented by formula (1) in (a) above is (S)-1-(2-(5-((3,4-dimethoxyphenoxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)ethanone represented by the following formula:

[Formula 5]



.

4. A hair growth composition for cutaneous application according to claim 1, wherein

the compound represented by formula (1) in (a) above is (S)-1-(2-(5-((3,4-dimethoxyphenoxy)methyl)-1,3,4-oxadiazol-2-yl)pyrrolidin-1-yl)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)ethanone.

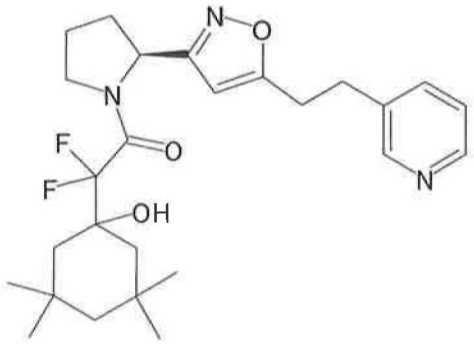
5. A hair growth composition for cutaneous application according to claim1, wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((3,4,5-trimethoxyphenoxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone.

6. A hair growth composition for cutaneous application according to claim 1, wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro-2-(1-hydroxy-3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-(phenoxymethyl)-1,3,4-oxadiazol-2-yl)pyrrolidin-1-yl)ethanone.

7. A hair growth composition for cutaneous application according to claim 1, wherein the compound represented by formula (1) in (a) above is (S)-2,2-difluoro2-(1-hydroxy3,3,5,5-tetramethylcyclohexyl)-1-(2-(5-((pyridin-4-yloxy)methyl)isoxazol-3-yl)pyrrolidin-1-yl)ethanone.

8. A hair growth composition for cutaneous application according to claim 1, wherein the compound represented by formula (1) in (a) above is a compound represented by the following formula:

[Formula 6]



.

9. A hair growth composition for cutaneous application according to any one of claims 1 to 8, which is characterized in that the nonionic surfactant in (b) above is one or more

members selected from the group consisting of polysorbate 80, a hydrogenated soybean phospholipid, polyethylene glycol monostearate, polyoxyethylene stearyl ether, polyoxyethylene cetyl ether, and polyoxyethylene (20) polyoxypropylene (8) cetyl ether.

10. A hair growth composition for cutaneous application according to any one of claims 1 to 9, which is characterized in that the magnesium compound and the calcium compound in (c) above are magnesium chloride and/or calcium chloride.

11. A hair growth composition for cutaneous application according to any one of claims 1 to 10, which is characterized in that the dosage form of the hair growth composition for cutaneous application is a liquid for cutaneous application.

12. A hair growth composition for cutaneous application according to any one of claims 1 to 11, wherein the amount of incorporation of at least one member selected from the group consisting of a magnesium compound and a calcium compound in (c) above is 0.001 to 10 (w/v%) in the total amount of the hair growth composition for cutaneous application.

13. A hair growth composition for cutaneous application according to claim 12, wherein the amount of incorporation of at least one member selected from the group consisting of a magnesium compound and a calcium compound in (c) above is 0.01 to 5 (w/v%) in the total amount of the hair growth composition for cutaneous application.

14. A hair growth composition for cutaneous application according to any one of claims 1 to 13, wherein the amount of incorporation of the nonionic surfactant in (b) above is 0.01 to 10 (w/v%) in the total amount of the hair growth composition for cutaneous application.

15. A hair growth composition for cutaneous application according to claim 14, wherein the amount of the nonionic surfactant in (b) above is 0.1 to 5 (w/v%) in the total amount of the hair growth composition for cutaneous application.

16. A hair growth composition for cutaneous application according to any one of claims 1 to 15, wherein the amount of the compound represented by formula (1) is 0.0001 to 20 (w/v%) in the total amount of the hair growth composition for cutaneous application.

17. A hair growth composition for cutaneous application according to claim 16, wherein the amount of incorporation of the compound represented by formula (1) is 0.1 to 10 (w/v%)

in the total amount of the hair growth composition for cutaneous application.