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(54) Title: COMPOSITIONS FOR TREATING ROSACEA COMPRISING CHITOSAN AND A DICARBOXYLIC ACID

(57) Abstract: The present invention is directed to compositions containing chitosan, a chitosan derivative or a physiologically acceptable salt thereof, and a short- medium chain dicarboxylic acid amide, or a physiologically acceptable salt thereof, forming a film after application onto the skin, useful for protecting skin of the face and of other affected areas in couperose, rosacea and teleangectasia of the legs.

DESCRIPTION

TITLE: "COMPOSITIONS FOR TREATING ROSACEA"

The present invention relates to compositions containing chitosan, a chitosan derivative or a physiologically acceptable salt thereof, and a short-medium chain dicarboxylic acid amide, or a physiologically acceptable salt thereof, for the preparation of a medicament, or a medical device, or a sanitary product, or a cosmetic, forming a film after application onto the skin of the face and of other affected areas, useful for protecting skin in rosacea, a chronic inflammatory condition of the skin, and other skin conditions characterized by teleangectasia, like couperose and leg teleangectasia.

BACKGROUND OF THE INVENTION

Rosacea is a common but often misunderstood condition that is estimated to affect over 13 million people worldwide (Plewig & Jansen in: Fitzpatrick's Dermatology in General Medicine. Freedberg et al. Eds., 6th ed., McGRAW-HILL pub., NY 2003, p. 688). It affects white-skinned people of Celtic or northern European descent, and has been named the 'curse of the Celts'. It is rarer in dark-skinned people, like American and African blacks.

It begins as erythema (flushing and redness, also called "couperose") on the central face and across the cheeks, nose, or forehead but can also less commonly affect the neck and chest. As rosacea progresses, other symptoms can develop such as semi-permanent erythema, teleangiectasia (dilation of superficial blood vessels on the face), red

domed papules (small bumps) and pustules, red gritty eyes, burning and stinging sensations, and in some advanced cases, a red lobulated nose (rhinophyma). The disorder can be confused with, and co-exist with acne vulgaris and/or seborrhoeic dermatitis. Rosacea affects both sexes, but is almost three times more common in women, is common in the third and fourth decade and peaks between the ages of 40 and 50 years. The presence of rash on the scalp or ears suggests a different or co-existing diagnosis, as rosacea is primarily a facial diagnosis.

The pathogenesis of rosacea in unknown, and various factors have been suspected to contribute to this condition. Among the various factors, the following have been claimed to play a role: degenerative changes of the perivascular/ vascular collagen, that lead to small vessel dilatation resulting in flushing, teleangiectasia, erithema; perivascular leakage of potentially inflammatory substances; abnormal tissue response to cytokines and other mediators; use of topical drugs (corticosteroids). Exposure to temperature extremes can cause the face to become flushed as well as strenuous exercise, heat from sunlight, severe sunburn, cold wind, moving from cold to hot environment. There are also some foods and drinks that can trigger flushing, these include alcohol, caffeine (hot tea and coffee), and spicy food. Microorganism also have been claimed to contribute to the development or complicate rosacea, like *Demodex folliculorum*, *Helicobacter pylori* or *Propionibacterium acnes*.

Treatment of rosacea is inconclusive. Systemic or topical treatments include antibiotics, metronidazole and antifungals; retinoids, some beta blockers,

spironolactone. No causal treatment has ever been proposed, and lifelong symptomatic treatment is often necessary, as just few cases may go into a permanent remission of the symptoms. Long term treatment of rosacea is limited by the intrinsic toxicity of drugs.

Leg teleangectasia consists in very thin varicose capillaries, with calibre within 0,1 and 1 mm, that are classified as follows:

1) Teleangectasia due to venous insufficiency, accompanied by other clinical signs of venous insufficiency. They are localized at the foot back, retromalleolar region, legs, and at the medial thigh surface.

2) Teleangectasia due to hormonal abnormalities, localized at the medial and anterolateral thigh surface. They spontaneously occur during menarche, menopause, pregnancy or under contraceptive treatment.

3) Very thin teleangectasia due to constitutional weakness of the capillary system, mainly at the distal portion of the legs. This is triggered by UV radiation, and by hot and cold temperature.

4) Matting type teleangectasia

5) Reticular varicous veins: in most cases they represent the nourishing veins for the districts that are interested by telengectasia.

No satisfactory treatment exists for leg teleangectasia and the only possible treatment is aesthetic surgery.

Thus, there is an unsatisfied need of safe and active medical tools to protect a skin that is unusually vulnerable to chemical and physical insults.

Chitosan and its derivatives are amino-polysaccharides, derived from the chitin extracted from the exoskeleton of

the crustaceans, known in the art for their use in different preparations. KR20020084672 discloses chitosan as an ingredient of microspheres, useful as a carrier for separation of proteins or peptides; KR20020048534 reports chitosan as an ingredient of a pack composition for skin massage, including paraffin wax as an effective component; JP2005306746 is teaching the use of chitosan to obtain a wrinkle therapeutic agent as an ingredient of gel-like or spongy preparations of botulinus toxin. WO2005055924 reports chitosan derivatives as ingredients of hydrogels useful for cavity-filling wound dressings. JP2004231604 teaches compositions of chitosans having a high deacetylation degree, as an ingredient of a carrier sheet with a porous spongy texture. WO03042251 discloses compositions comprising chitosan in the form of a network of nano-sized fibres. WO02057983 discloses a multi-layered, air gap sheet of chitosan with a regular lamellar structure which retains drugs for a prolonged period of time; JP11060605 teaches an amphiphilic chitosan derivative which can be used as dispersion stabilizer or emulsifier in a drug for application to skin. Finally, EP1303249, discloses a nail varnish composition containing at least one antimycotic agent and an hydroxyalkyl or a carboxyalkyl chitosan, whereas WO2004/112814 discloses a nail restructuring composition based on one herb extract from the genus Equisetum in combination with hydroxypropyl chitosan.

SUMMARY OF THE INVENTION

It has now surprisingly been found that preparations comprising chitosan or its derivatives, and at least the amide of a short-medium chain (from 6 to 12 carbon atoms) aliphatic dicarboxylic acid may form an elastic film onto the skin, after application and drying, suitable to

protect the skin from chemical or physical insults. The two components of the film, saccharidic and lipidic, act in a synergistic way and have a protective activity superior to that of the two components alone.

Accordingly, a first aspect of the invention provides a composition comprising:

(A)at least chitosan, a hydroxyalkyl chitosan and/or a physiologically acceptable salt thereof, and;

(B)at least a linear and/or alkyl C_6-C_{12}-dicarboxylic acid amide of the following formula:

$$ROC-(CH_2)_n-COR$$

wherein:

- n is between 4 and 10, preferably between 6 and 8 and, more preferably, it is 7;
- R is a -N(R')(R'') group, wherein:
- R' is H or a C_1-C_4-alkyl group, and
- R'' is H, a C_1-C_4-alkyl group or a C_1-C_4-carboxy group

and/or a physiologically acceptable salt thereof.

A second aspect of the present invention provides the composition for the treatment and/or prevention of rosacea, for the treatment and/or prevention of teleangectasia, including leg teleangectasia, or for the treatment and/or prevention of couperose.

A third aspect of the present invention provides a method for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose, which comprises administering a therapetucially effective amount of the composition to a subject in need thereof.

A fourth aspect of the present invention provides use of the composition in the manufacture of a medicament for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose.

A fifth aspect of the present invention provides a use of the composition for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose.

DESCRIPTION OF THE INVENTION

The present invention provides a composition comprising:

(A) at least chitosan, a hydroxyalkyl chitosan and/or a physiologically acceptable salt thereof, and;

(B) at least a linear and/or alkyl C_6-C_{12}-dicarboxylic acid amide of the following formula:

$$ROC-(CH_2)_n-COR$$

wherein:

- n is between 4 and 10, and;
- R is a -N(R')(R'') group, wherein:
- R' is H or a C_1-C_4-alkyl group, and
- R'' is H, a C_1-C_4-alkyl group or a C_1-C_4-carboxy group

and/or a physiologically acceptable salt thereof.

Also described herein are preparations comprising chitosan, hydroxyalkyl chitosan and/or C_6-C_{12}-dicarboxylic acid amide is a sodium and/or potassium salt.

The film forming compositions according to the present invention may easily be sprayed onto the skin surface, by allowing quick drying and easy formation of an elastic

film, that avoids bothersome sensation of oily skin. The film forming compositions according to the present invention may also be applied on the skin by gently massage. The film formed after drying protects the skin from the insult of both hot and cold temperature, decreases the inflammation due to ultraviolet radiation and prevents the growth of microorganisms by coating them and inhibiting their vital functions.

It is therefore advantageous for the present invention to provide a pharmaceutical and/or cosmetic composition containing:

(A) at least chitosan, a chitosan derivative and/or a physiologically acceptable salt thereof, and;

(B) at least a linear and/or alkyl C_6-C_{12}-dicarboxylic acid amide of the following formula:

$$ROC-(CH_2)_n-COR$$

wherein:

- n is between 4 and 10, and;
- R is a -N(R')(R'') group, wherein:
- R' is H or a C_1-C_4-alkyl group, and
- R'' is H, a C_1-C_4-alkyl group or a C_1-C_4-carboxy group

and/or a physiologically acceptable salt thereof.

Said composition is useful to form a film after application onto the skin and drying, that protects the skin of the face and the other areas affected byrosacea as well as by other skin conditions characterized by teleangectasia.

Among chitosan derivatives, water soluble chitosans are preferred; hydroxyalkyl chitosans, such as hydroxypropyl chitosan, being the most preferred water soluble chitosans derivatives.

Among the C_6-C_{12}-dicarboxylic acids, C_8-C_{10}-dicarboxylic acids are particularly preferred, C_9-dicarboxylic acids being the most preferred; such dicarboxylic acids are linear and/or alkyl acids.

The C_6-C_{12}-dicarboxylic acid amide which is used for the purposes of the present invention is represented by the following formula:

$$ROC-(CH_2)_n-COR$$

wherein:

"n" is comprised between 4 and 10, preferably between 6 and 8 and, more preferably, it is 7;

R is a -N(R')(R'') group, wherein:

R' is H or a C_1-C_4-alkyl group, and

R'' is H, a C_1-C_4-alkyl group or a C_1-C_4-carboxy group.

According to preferred embodiments, said C_1-C_4-alkyl groups are methyl or ethyl whereas said C_1-C_4-carboxy group is carboxy methyl.

The preferred C_6-C_{12}-dicarboxylic acid is azelaic acid .

Among C_6-C_{12}-dicarboxylic acid amides, azelaic acid amides, such as azeloyl diglycine, are thus preferred, and may be in form of a salt, preferably a sodium or potassium salt, such as potassium azeloyl diglycinate.

The composition according to the present invention may be applied by a gently massage on the skin, or may be sprayed by allowing the formation of an elastic film after drying.

The composition according to the present invention allows a long lasting intimate contact and continuous protection of the skin for many hours after the application.

Compositions according to the present invention are in the form are in the form of liquid, semiliquid or semisolid preparations, including solutions, suspensions, lotions, emulsions, colloids, creams, gels, with a content in component A from 0.1 to 10 wt.% (percentages by weight are given with respect to the whole preparation), preferably from 0.2 to 5 wt.%, more preferably from 0.25 to 2.0 wt.% and with a content in component B from 0.1 to 30 wt.% (percentages by weight are given with respect to the whole preparation), preferably from 0.25 to 25 wt.%, more preferably from 0.5 to 20 wt.%.

Compositions according to the present invention are superior to the conventional formulations, in that they leave an uniform and invisible film. Moreover, compositions according to the present invention do not dirty, do not dry like gels and lotions do, and do not give bothersome sensation when applied, like other rigid film preparations do.

Pharmaceutical compositions are prepared according to conventional technique, using compatible excipients, adjuvants and/or pharmaceutically or cosmetically acceptable carriers, and may contain, in combination, other active principles with complementary or, in any case, useful activity.

Examples of these compositions prepared according to the present invention include: solutions, emulsions, suspensions, colloids, creams, gels, for application to affected skin.

The compositions according to the present invention may contain one or more additional ingredients selected from solvents, sunscreens, skin-conditioning agents,

emollients, moisturizers, emulsifying agents, viscosity-increasing agents, UV-A filters, plant extracts, antioxidants.

The pharmaceutical compositions and the uses of the present invention will now be more fully described by the following examples. It should, however, be noted that such examples are given by way of illustration and not of limitation.

Example 1

An oil in water cream having the following w/w % composition was prepared:

1. POTASSIUM PALMITOYL HYDROLYZED WHEAT PROTEIN	1.00%
2. GLYCERYL STEARATE	2.00%
3. CETEARYL ALCOHOL	2.00%
4. GLYCERYL STEARATE SE	1.00%
5. DICAPRYLYL ETHER	4.00%
6. ETHYLHEXYL METHOXYCINNAMATE	4.00%
7. BUTYL METHOXYDIBENZOYLMETHANE	1.00%
8. LECITHIN	0.02%
9. TOCOPHEROL	0.001%
10. ASCORBYL PALMITATE	0.001%
11. CITRIC ACID	0.001%
12. TOCOPHERYL ACETATE	0.50%
13. PURIFIED WATER	81.00%
14. HYDROXYPROPYL CHITOSAN	0.50%
15. XANTHAN GUM	0.50%
16. DENATURATED ETHYL ALCOHOL	1.00%
17. PHENETHYL ALCOHOL	0.50%
18. CAPRYLYL GLYCOL	0.50%
19. POTASSIUM AZELOYL DIGLYCINATE	0.50%

Preparation

Phase A: Hydroxypropyl chitosan was dispersed in ca. 50%wt of total water until a clear solution was obtained. The solution was heated at 65°C ± 2°C and Xanthan gum was added and stirred until a homogenous solution was obtained.

Phase B: Potassium palmitoyl, Glyceryl Stearate, Cetearyl Alcohol, Glyceryl Stearate SE, Dicaprylyl Ether, Ethylehexyl methoxycinnamate, Butyl methoxydibenzoyl-methane, Lecithin, Tocopherol, Ascorbyl Palmitate, Citric Acid and Tocopheryl Acetate were mixed together and heated at 65°C ± 2°C.

Phase B was added to Phase A under agitation (turbo) to allow the emulsification. The resulting emulsion was cooled to 35°C ± 2°C under continuous mixing.

Caprylyl Glycol dissolved into Phenethyl Alcohol, Potassium Azeloyl Diglycinate dissolved in the rest of purified water (50%wt) and Ethyl Alcohol were mixed into the emulsion at the end of preparation. The product was kept under gentle agitation until a homogenous oil in water cream was obtained.

Example 2

An oil in water cream having the following w/w % composition was prepared:

1.	POTASSIUM PALMITOYL HYDROLYZED WHEAT PROTEIN	3.00%
2.	GLYCERYL STEARATE	5.00%
3.	CETEARYL ALCOHOL	5.00%
4.	GLYCERYL STEARATE SE	3.00%
5.	DICAPRYLYL ETHER	6.00%
6.	ETHYLHEXYL METHOXYCINNAMATE	6.00%
7.	BUTYL METHOXYDIBENZOYLMETHANE	3.00%
8.	LECITHIN	0.04%
9.	TOCOPHEROL	0.01%
10.	ASCORBYL PALMITATE	0.01%
11.	CITRIC ACID	0.01%
12.	TOCOPHERYL ACETATE	1.00%
13.	PURIFIED WATER	59.93%
14.	HYDROXYPROPYL CHITOSAN	1.00%
15.	XANTHAN GUM	1.00%
16.	DENATURATED ETHYL ALCOHOL	3.00%
17.	PHENETHYL ALCOHOL	1.00%
18.	CAPRYLYL GLYCOL	1.00%
19.	POTASSIUM AZELOYL DIGLYCINATE	1.00%

Preparation

The formulation was prepared by using the same method described for Example 1.

Example 3

An oil in water cream having the following w/w % composition was prepared:

1.	POTASSIUM PALMITOYL HYDROLYZED WHEAT PROTEIN	2.00%
2.	CETEARYL ALCOHOL	5.00%
3.	GLYCERYL STEARATE SE	3.00%
4.	DICAPRYLYL ETHER	5.00%
5.	ETHYLHEXYL METHOXYCINNAMATE	4.00%
6.	LECITHIN	0.04%
7.	ASCORBYL PALMITATE	0.01%
8.	CITRIC ACID	0.01%
9.	TOCOPHERYL ACETATE	1.00%
10.	PURIFIED WATER	72.94%
11.	HYDROXYPROPYL CHITOSAN	1.00%
12.	XANTHAN GUM	1.00%
13.	DENATURATED ETHYL ALCOHOL	3.00%
14.	PHENETHYL ALCOHOL	1.00%
15.	POTASSIUM AZELOYL DIGLYCINATE	1.00%

Preparation

Phase A: Hydroxypropyl chitosan was dispersed in ca. 50%wt of total water until a clear solution was obtained. The solution was heated at 65°C ± 2°C and Xanthan gum was added and stirred until a homogenous solution was obtained.

Phase B: Potassium palmitoyl, Cetearyl Alcohol, Glyceryl Stearate SE, Dicaprylyl Ether, Ethylehexyl methoxycinnamate, Lecithin, Ascorbyl Palmitate, Citric Acid and Tocopheryl Acetate were mixed together and heated at 65°C ± 2°C.

Phase B was added to Phase A under agitation (turbo) to allow the emulsification. The resulting emulsion was cooled to 35°C ± 2°C under continuous mixing.

Phenethyl Alcohol, Potassium Azeloyl Diglycinate dissolved in the rest of purified water (50%wt) and Ethyl Alcohol were mixed into the emulsion at the end of preparation. The product was kept under gentle agitation until a homogenous oil in water cream was obtained.

Example 4

An oil in water cream having the following w/w % composition was prepared:

1. POTASSIUM PALMITOYL HYDROLYZED WHEAT PROTEIN	2.00%
2. GLYCERYL STEARATE	4.00%
3. CETEARYL ALCOHOL	4.00%
4. GLYCERYL STEARATE SE	2.00%
5. DICAPRYLYL ETHER	5.00%
6. ETHYLHEXYL METHOXYCINNAMATE	8.00%
7. BUTYL METHOXYDIBENZOYLMETHANE	2.00%
8. BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE	3.00%
9. LECITHIN	0.040%
10. TOCOPHEROL	0.002%
11. ASCORBYL PALMITATE	0.002%
12. CITRIC ACID	0.002%
13. TOCOPHERYL ACETATE	0.20%
14. HYDROXYPROPYL CHITOSAN	1.00%
15. XANTHAN GUM	0.30%
16. DENATURATED ETHYL ALCOHOL	2.00%
17. PHENETHYL ALCOHOL	0.50%
18. CAPRYLYL GLYCOL	0.50%
19. POTASSIUM AZELOYL DIGLYCINATE	0.50%

20. PURIFIED WATER q.s to 100.00%

Preparation

The preparation was made as in Example 1. A homogenous oil in water cream was obtained.

Example 5

A comparative evaluation of the inhibition of VEGF (Vascular Endothelial Growth Factor) release on human 3D artificial skin was tested by the preparation as per the Example 4, compared to two different preparations, respectively named LPOL2899A (same as per the Example 4, but not containing POTASSIUM AZELOYL DIGLYCINATE), LPOL2899B (same as per the Example 4, but not containing HYDROXYPROPYL CHITOSAN) and LPOL2899C (same as per the Example 4, but not containing either POTASSIUM AZELOYL DIGLYCINATE or HYDROXYPROPYL CHITOSAN).

The effect of the four preparations was tested on the inhibition of Vascular Endothelial Growth Factor (VEGF) production induced by a pro-inflammatory stimulus on 3D human epidermis. VEGF is a strong angiogenic protein that significantly influences the vessels permeability and is constitutively expressed in keratinocytes, i.e. the cells of the skin. Under stressful conditions, such as exposure to soluble inflammation mediator like IL-1 alpha, epidermal keratinocytes increase the synthesis and release of VEGF.

Epidermis units have been treated with IL-1α in the cell medium to induce an increase in the VEGF synthesis, and at the same time treated applying the investigated samples undiluted on the epidermis corneous layer. Following 24 h

treatment, the cell culture medium below the epidermis units was collected and analyzed for the VEGF content through an ELISA assay.

The tested samples were the preparation as per the Example 4 and the two comparative preparations LPOL2899A and LPOL2899B. Skin units treated with IL-1α only have been used as positive controls. The experiment was carried out in three replicas.

In vitro test system employed consists of a tridimensional artificial system of human epidermis (Mattek, USA) i. e. a reconstructed artificial human skin model comprising normal human epidermal keratinocytes, growing as an integrated three-dimensional cell culture model, perfectly mimicking the human skin *in vitro*. The model exhibits normal barrier functions (presence of a differentiated stratum corneum).

About 20 mg of each undiluted sample have been applied on epidermis unit in three replicas, the exposure 30' following the products application, epidermis units, except the controls, have been treated for 2 h with 500 pg/ml of IL-1α (Prospec) in the cell medium, to improve the VEGF synthesis.

After 2 h the cel medium has been removed and changed. The incubation of the samples has been carried up to 24 hours at 37°C, 5% CO_2.

As positive control epidermis units treated with IL-1 α only have been used. At the end of the exposure period, the products were removed, the tissue gently washed with phosphate buffer (PBS) for further MTT and viability assay, and the culture medium have been collected for VEGF assay.

VEGF release assay following IL-1α treatment, 500 pg/ml, with and without treatment with the samples is reported in the following table.

Sample	VEGF pg/ml (DS%)	% inhibition
Preparation of Example 4 + 500pg/ml IL-1α	313,21 (26,9)	***46,4***
LPOL 2899A + 500pg/ml IL-1α	386,03 (4,6)	***33,9***
LPOL 2899B + 500pg/ml IL-1α	433,86 (6,9)	***25,7***
LPOL 2899C + IL-1α	477,25 (4,1)	***18,3***
500pg/ml IL-1α (positive control)	583,93 (7,5)	--------

The preparation containing the vehicle, but not the two ingredients potassium azeloyl diglycinate and hydroxypropyl chitosan, inhibited the IL-1 α induced VEGF release by only 18%. the effect of the preparation containing hydroxypropyl chitosan was 25.7% inhibition and that of the preparation containing potassium azeloyl diglycinate was 33.9% inhibition. The preparation as per the Example 4 had the strongest inhibitory effect (46.4% inhibition) confirming a synergistic activity of the two components on the protection of skin against the insult of IL-1 α.

In the claims which follow and in the preceding description of the invention, except where the context requires otherwise due to express language or necessary implication, the word "comprise" or variations such as "comprises" or "comprising" is used in an inclusive sense,

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i.e. to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

It is to be understood that, if any prior art publicationis referred to herein, such reference does not constitute an admission that the publication forms a part of the common general knowledge in the art, in Australia or any other country.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A composition comprising:

(A) at least chitosan, a hydroxyalkyl chitosan and/or a physiologically acceptable salt thereof, and;

(B) at least a linear and/or alkyl C_6-C_{12}-dicarboxylic acid amide of the following formula:

$$ROC-(CH_2)_n-COR$$

wherein:

- n is between 4 and 10, and;
- R is a -N(R')(R'') group, wherein:
- R' is H or a C_1-C_4-alkyl group, and
- R'' is H, a C_1-C_4-alkyl group or a C_1-C_4-carboxy group

and/or a physiologically acceptable salt thereof.

2. A composition according to claim 1, characterized in that said hydroxyalkyl chitosan is water soluble.

3. A composition according to claim 1 or 2, characterized in that said hydroxyalkyl chitosan is hydroxypropyl chitosan.

4. A composition according to any one of claims 1-3, characterized in that the physiologically acceptable salt of said chitosan, hydroxyalkyl chitosan and/or C_6-C_{12}-dicarboxylic acid amide is a sodium and/or potassium salt.

5. A composition according to any one of claims 1-4, characterized in that said C_6-C_{12}-dicarboxylic acid is a C_8-C_{10}-dicarboxylic acid, or a C_9-dicarboxylic acid.

6. A composition according to claim 1, characterized in that said dicarboxylic acid is azelaic acid.

7. A composition according to any one of claims 1 to 6, characterized in that n is between 6 and 8, or it is 7.

8. A composition according to any one of claims 1 to 7, characterized in that said C_1-C_4-alkyl group is methyl and/or ethyl and said C_1-C_4-carboxy group is carboxy methyl.

9. A composition according to claim 1, characterized in that said C_6-C_{12}-dicarboxylic acid amide is azeloyl diglycine.

10. A composition according to claim 1, characterized in that said C_6-C_{12}-dicarboxylic acid amide salt is potassium azeloyl diglycinate.

11. A composition according to any one of claims 1-10, characterized in that component (A) is present in amounts of from 0.1 to 10%, from 0.2 to 5%, or from 0.25 to 2.0%, with respect to the weight of the whole composition.

12. A composition according to any one of claims 1-11, characterized in that component (B) is present in amounts of from 0.1 to 30%, 0.25 to 25%, or from 0.5 to 20 wt%, with respect to the weight of the whole composition.

13. A composition according to any one of claims 1-12, characterized by being in liquid, semiliquid or semisolid form, including solution, suspension, lotion, emulsion, colloid, cream or gel.

14. A composition according to any one of claims 1-13, characterized by further comprising pharmaceutically and/or cosmetically acceptable active ingredients, excipients, adjuvants and/or carriers.

15. A composition according to any one of claims 1-14, for the treatment and/or prevention of rosacea, for the treatment and/or prevention of teleangectasia, including leg teleangectasia, or for the treatment and/or prevention of couperose.

16. A method for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose, which comprises administering a therapeutically effective amount of a composition according to any one of claims 1-14 to a subject in need thereof.

17. Use of a composition according to any one of claims 1-14 in the manufacture of a medicament for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose.

18. Use of a composition according to any one of claims 1-14 for the treatment and/or prevention of rosacea, teleangectasia, including leg teleangectasia, or couperose.

19. A composition as defined in claim 1, or methods or uses involving the composition, substantially as herein described with reference to any one of the Examples.