COMPOSITIONS FOR THE TREATMENT OF ATOPIC DERMATITIS, SKIN ALLERGIC CONDITIONS AND ACNE

The present invention relates to compositions containing medicinal plant extracts or purified or standardized fractions thereof, useful in the treatment of atopic dermatitis, skin allergic conditions and acne.

PRIOR ART

Atopic dermatites are characterized by persistent inflammatory conditions which may cause lacerations of the skin with possible infections. Inflammation is often accompanied by intense itching; the consequent scratching by the patient may further irritate the affected area.

Dermatites, which are also frequently referred to as eczema, are superficial skin inflammations, with acute or chronic course and variable clinical and histological manifestations, which affect an unnegligible percentage of population (2-3%).

The etiology of the various forms of dermatitis is still partly unclear, although the immune component is definitely one of the factors. The pathological manifestations are often alike, and are mainly characterized by the presence of papules, erythematous spots and vesicles, which can form plaques, edema, scaling-crusting lesions and the like. The most common dermatites comprise atopic dermatitis, contact allergies, contact dermatitis, stasis dermatitis, seborrheic dermatitis, lichen simplex and acne vulgaris.

The choice treatment consists in the use of corticosteroids, which involve well-known side effects (possible secondary infections, inefficacy after prolonged use, and the like).

DISCLOSURE OF THE INVENTION

It has now been found that compositions containing:

a) an extract, fraction thereof or pure compound with inflammatory

action;

b) an extract, fraction thereof or pure compound, with antimicrobial and/or antifungal action; and

c) an extract, fraction thereof or pure compound, with anti-itching action;

exert immediate, beneficial effect to the patient and induce the fast remission of the pathological condition, even compared with known medicaments such as topical anti-inflammatories and steroids.

More precisely, the compositions of the invention comprise:

a) *Ginkgo biloba* terpenes;

b) floroglucinols, either pure or in mixture thereof, extracted from *Humulus lupulus*, *Hypericum* sp and *Mirtus* sp;

c) *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract.

According to the present invention, the *Ginkgo biloba* content can range from 0.1 to 2%; the floroglucinols content can range from 0.1 to 1%; and the *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract content can range from 0.01 to 0.5%.

According to the invention, *Ginkgo biloba* terpenes are present in the free form or preferably in the form of complex with natural or synthetic phospholipids. "*Ginkgo biloba* terpenes" herein means the terpenes, either pure or in a mixture wherein the total triterpenes content ranges from 60 to 100%, preferably 90%, the bilobalide content ranges from 20 to 70%, preferably 45%, and ginkgolides A, B, C and J total content ranges from 25 to 75%, preferably 50%.

Ginkgo biloba terpenes, in addition to the antinflammatory action, also exert antiallergic action, as observed in a number of models both in animals and humans, thereby reducing one of the symptoms involved, which keep irritation

and the continuous recidivation. This antiallergic action makes said terpenes particularly useful when an immune factor is involved in the etiology.

Floroglucinols, either pure or in a mixture thereof extracted from *Humulus lupulus*, *Hypericum* sp and *Mirtus* sp., are active against anaerobic bacteria such as *Propionibacterium acnis* and the like and on *Candida albicans* strains, at concentrations of 0.5-4 μg/mL.

In particular, *Humulus lupulus* extracts are characterized by a floroglucinols content of 20 to 80%, preferably 60%. Among the extracts of *Hypericum* sp., particularly preferred is a *Hypericum perforatum* extract with a floroglucinols (adhyperforin/hyperforin) content ranging from 20 to 80%, preferably 60%. Among the extracts of *Mirtus* sp, particularly preferred is an extract of *Mirtus communis* leaves prepared by extraction with carbon dioxide under pressure ranging from 235 to 260 bars, at a temperature ranging from 40 to 60°C, preferably a 45°C. The resulting extract usually contains about 35% of mirtocumulone.

The compositions of the invention containing a *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract enriched in isobutylamides, active as topical analgesics inhibiting the nervous conduction proved particularly effective in the treatment of localized itching. Therefore, according to a preferred aspect, the compositions of the present invention will contain, as component c), a *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract enriched in isobutylamides. The *Zanthoxylum* extract can be prepared for example as disclosed in WO 00/02570, while the *Echinacea* extract can be prepared for example as disclosed in EP 0 464 298.

The compositions of the invention further containing natural compounds with estrogenic and/or antiandrogenic action proved particularly effective in the treatment of seborrheic dermatitis and acne. Therefore, according to a preferred aspect, the compositions of the present invention will contain, in addition to

components a), b) and c) above, also natural compounds with estrogenic action, such as ferutinine and/or extracts of various *Ferula* species, and/or natural compounds with antiandrogenic action, such as lauric acid.

According to a further preferred aspect, the compositions of the present invention will contain *Oenothera biennis* oil as lipophilic excipient.

The present invention, therefore, relates to topical compositions for the treatment of atopic dermatitis, skin allergic conditions and acne, containing the combinations described above. Said compositions will be prepared according to conventional methods well known in the pharmaceutical technique, such as those described in "Remington's Pharmaceutical Handbook", Mack Publishing Co., N.Y., USA, together with suitable excipients commonly used in the art.

The examples reported hereinbelow further illustrate the invention.

Example 1

Oil-in-water emulsion

Ginkgo biloba terpenes in form of phospholipid complexes	0.5 g
Humulus lupulus extract (60% in floroglucinols)	0.1 g
Zanthoxylum bungeanum extract	0.05 g
Oenothera biennis oil	5.0 g
Polyoxyethylene glycol-20 glyceryl stearate	10.0 g
C_{10}-C_{18} triglycerides	10.0 g
Glycerin	5.0 g
Hydroxylated lanolin	0.5 g
Hydroxyethyl cellulose	0.5 g
Methyl and propyl paraben	0.2 g
Tocopherol	0.1 g
Purified water	q.s. to 100.0 g

Example 2

Oil-in-water emulsion

Ginkgo biloba terpenes in form of phospholipid complexes	0.5 g
Mirtus communis lipophilic extract (35% in mirtocumulone)	0.1 g
Zanthoxylum bungeanum extract	0.05 g
Oenothera biennis oil	5.0 g
Stearic acid	10.0 g
Mineral oil	6.0 g
White petrolatum	6.0 g
Sorbitan monostearate	2.0 g
Polyoxyethylene sorbitan monostearate	1.0 g
Methyl and propyl paraben	0.2 g
Purified water	q.s. to 100.0 g

Example 3

Cream

Ginkgo biloba terpenes in form of phospholipid complexes	0.5 g
Humulus lupulus extract (60% in floroglucinols)	0.1 g
Echinacea angustifolia extract	0.05 g
Oenothera biennis oil	5.0 g
Stearic acid	12.0 g
Glycerin	10.0 g
Cetostearyl alcohol	2.0 g
Potassium hydroxide	0.9 g
Methyl and propyl paraben	0.2 g
Purified water	q.s. to 100.0 g

Example 4

Cream

Ginkgo biloba terpenes in form of phospholipid complexes	0.5 g
Hypericum perforatum extract (60% in floroglucinols)	0.1 g
Echinacea angustifolia extract	0.05 g
Oenothera biennis oil	5.0 g
Stearic acid	12.0 g
Glycerin	10.0 g
Cetostearyl alcohol	2.0 g
Potassium hydroxide	0.9 g
Methyl and propyl paraben	0.2 g
Purified water	q.s. to 100.0 g

Example 5

Cream

Ginkgo biloba terpenes in form of phospholipid complexes	0.5 g
Humulus lupulus extract (60% in floroglucinols)	0.1 g
Zanthoxylum bungeanum extract	0.05 g
Oenothera biennis oil	5.0 g
Ferutinine	0.3 g
Lauric acid	0.3 g
Cetostearyl alcohol	20.0 g
White petrolatum	15.0 g
Propylene glycol	10.0 g
Sodium lauryl sulfate	1.0 g
Methyl and propyl paraben	0.2 g
Purified water	q.s. to 100.0 g

CLAIMS

1. Topical compositions for the treatment of atopic dermatitis, skin allergic conditions and acne, containing:

a) *Ginkgo biloba* terpenes;

b) floroglucinols, either pure or in mixture thereof, extracted from *Humulus lupulus*, *Hypericum* sp and *Mirtus* sp;

c) *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract.

2. Compositions as claimed in claim 1, containing:

a) 0.1 to 2% *Ginkgo biloba*;

b) 0.1 to 1% floroglucinols, either pure or in a mixture thereof, extracted from *Humulus lupulus*, *Hypericum* sp and *Mirtus* sp;

c) 0.01 to 0.5% of *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract.

3. Compositions as claimed in the above claims, wherein *Ginkgo biloba* terpenes are present in the free form.

4. Compositions as claimed in the above claims, wherein *Ginkgo biloba* terpenes are present in the form of complex with natural or synthetic phospholipids.

5. Compositions as claimed in claim 4, wherein the total triterpenes content ranges from 60 to 100%.

6. Compositions as claimed in claim 5, wherein the total triterpenes content is 90%.

7. Compositions as claimed in claim 4, wherein the bilobalide content ranges from 20 to 70%.

8. Compositions as claimed in claim 7, wherein the bilobalide content is 45%.

9. Compositions as claimed in claim 4, wherein the total A, B, C and J ginkgolides content ranges from 25 to 75%.

10. Compositions as claimed in claim 9, wherein the total A, B, C and J ginkgolides content is 50%.

11. Compositions as claimed in claims 1-2, wherein the floroglucinols content of the *Humulus lupulus* extracts ranges from 20 to 80%.

12. Compositions as claimed in claim 11, wherein the floroglucinols content of the *Humulus lupulus* extracts is 60%.

13. Compositions as claimed in claims 1-2, wherein the *Hypericum* sp. extract is a *Hypericum perforatum* extract in which the floroglucinols content ranges from 20 to 80%.

14. Compositions as claimed in claim 13, wherein the floroglucinols content of the *Hypericum perforatum* extract is 60%.

15. Compositions as claimed in claims 1-2, wherein the extract of *Mirtus communis* leaves is prepared by extraction with carbon dioxide under conditions of pressure ranging from 235 to 260 bars and temperatures ranging from 40 to 60°C.

16. Compositions as claimed in claim 15, wherein the *Mirtus* sp. extract is an extract of *Mirtus communis* leaves with a mirtocumulone content of 35%.

17. Compositions as claimed in claims 1-2, wherein the *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract is enriched in isobutylamides.

18. Compositions as claimed in the above claims, further containing ferutinine.

19. Compositions as claimed in the above claims, further containing extracts of various *Ferula* species.

20. Compositions as claimed in the above claims, further containing lauric acid.

21. Compositions as claimed in the above claims, further containing *Oenothera biennis* oil as lipophilic excipient.

22. The use of a combination of:

a) *Ginkgo biloba* terpenes;

b) floroglucinols pure or in mixture thereof, extracted from *Humulus lupulus*, *Hypericum* sp and *Mirtus* sp;

c) *Zanthoxylum bungeanum* or *Echinacea angustifolia* lipophilic extract;

for the preparation of a medicament for the treatment of atopic dermatitis, skin allergic conditions and acne.