2 4 SEP 2004

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 September 2001 (27.09.2001)

PCT

(10) International Publication Number
WO 01/70249 A1

(51) International Patent Classification[7]: A61K 35/78, A61P 43/00, A61K 7/48

(21) International Application Number: PCT/NL01/00240

(22) International Filing Date: 22 March 2001 (22.03.2001)

(25) Filing Language: Dutch

(26) Publication Language: English

(30) Priority Data:
1014751 24 March 2000 (24.03.2000) NL

(71) Applicants and
(72) Inventors: **VAN DE WIEL, Adriaan, Emanuel, Hendricus, Anna, Maria** [NL/NL]; Goorsteeg 90, NL-6718 TB Ede (NL). **CHRISTIAANS, Marijke** [NL/NL]; Goorsteeg 90, NL-6718 TB Ede (NL).

(74) Agent: **VISSER-LUIRINK, Gesina**; Octrooibureau LIOC, P.O. Box 13363, NL-3507 LJ Utrecht (NL).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/70249 A1

(54) Title: COSMETIC USE OF HOP AND ORNITHINE

(57) Abstract: A composition for use as cosmetic agent for enhancing breast growth and strengthening of the breast issue comprises at least hop and ornithine. Fennel or a fennel derivative such as fennel leaf or fennel seed is preferably further added thereto. The composition can also be applied as medication for suppressing and preventing benign cysts. The composition can be manufactured in convenient tablet form and be made up wholly of natural constituents. Ingestion of the composition for a period of a few months will in most cases provide the first result.

Cosmetic use of hop and ornithine

The invention relates to a composition which contains at least hop and which can be applied as cosmetic agent, in particular for enhancing growth and strengthening of breast tissue, or as medication for suppressing and preventing benign cysts, and possibly for suppressing malignant cancer cells.

Hop has for centuries been incorporated in food, including bread, by diverse peoples. This was done particularly to stimulate the production of mother's milk. Through the use of sufficient hop the volume of the mammary gland tissue increased, the breasts were enlarged, whereby the production of mother's milk increased. When the intake of hop is stopped the mammary gland tissue is reduced, whereby breast size decreases.

There is a great demand among the female part of the population for breast-enlarging means. Through the ages a prominent breast size has been for many women one of the ideal characteristics of beauty. Breast-enlargement operations are therefore very much a matter of course in plastic surgery and are even one of the most commonplace operations. For breast enlargement recourse is usually had to silicon implants, the drawbacks of which have since become known and which sometimes only manifest themselves in the medium or long term, quite apart from the discomfort of the operation itself.

The known growth agent of the type stated in the preamble does not have these drawbacks since no surgery whatever is involved and the active constituents of the agent consist, if not completely then for the major part, of wholly natural agricultural products. Hop, among other substances in the composition, is responsible for activating the mammary glands in the breast tissue, which then results in breast growth.

A substance containing hop with anti-growth action is known from J. Agric. Food Chem., 47 (1), 1999, and from the International patent application WO 00/53205. However, there continues to exist a need for other agents based on natural substances with a better action against benign cysts.

The known substance containing only hop is not ideal because the action is not strong and the result is not permanent.

Embodiments may provide a cosmetic agent and/or medication of the type stated in the preamble with an enhanced action which can thereby provide a greater and permanent result. A composition for enhancing breast growth and as medication which suppresses cysts, of the type stated in the preamble, can have the feature according to the invention and may also contain ornithine. This may involve a balanced interaction between the different components of the composition. The hop present therein can stimulate the mammary gland activity in the breast tissue, while ornithine, and in particular L-ornithine, can, as an amino acid, be a cell-building substance responsible for stronger development of the breast tissue. Ornithine can have a synergistic effect in causing benign cysts to subside and on the possible activity against cancerous growths. This composition may further improve and stabilize the condition of the female breast in the case of cysts and mammary gland infection etc. Another significant advantage compared to the action of hop alone may be that the use of the combination of hop and ornithine can have a permanent effect, particularly when used to enhance growth and strengthening of the breast tissue.

In a first aspect of the present invention, there is provided a composition at least containing hop and ornithine for use as cosmetic agent or as medication.

In a second aspect of the present invention, there is provided a use of a composition for the preparation of a cosmetic agent for the purpose of growth and/or strengthening of breast tissue, or to prevent or to aid recovery from lumps in the breast tissue.

In a third aspect of the present invention, there is provided a use of a composition for the preparation of a medication to suppress benign cysts and the growth thereof and possibly to suppress and prevent malignant cancer cells.

In a fourth aspect of the present invention, there is provided a tablet or capsule containing hop, ornithine, fennel or a derivative thereof and optional excipients.

In a fifth aspect of the present invention, there is provided a tablet or capsule containing hop, ornithine, fennel or a derivative thereof, a grain type and optional excipients.

The hop in the composition may comprise numerous substances and trace elements which contribute toward breast growth, of which phytohormones such as genistein and daidzein are important examples. It can be further assumed that the constituents of hop, genistein and daidzein, which belong to the phyto-oestrogenic substances or isoflavonoids, can have tumour-inhibiting action. Just as the body's own oestrogens, genistein can bond to the oestrogen receptor of the damaged cell, whereby further division is inhibited. Tumours which depend for their development on oestrogen such as that in breast tissue, the prostate and the intestines, would thus be inhibited in their growth. This theory is supported by a low death rate from breast cancer among women in Asia, which is generally attributed to the phyto-oestrogenic activity of isoflavonoids such as genistein and daidzein from soya, much more of which is consumed than in the western world.

In a preferred embodiment of the composition, grain may be added to hop and ornithine. Fibres from grain can provide a better intestinal activity, whereby the components of the composition can be more readily absorbed by the body. The grain may

preferably be the full, unhusked grain, including skin. A significant enhancement of the action of the composition can thus be obtained. A particular embodiment of the composition can have a feature that the grain type may comprise at least one grain type from a group comprising buckwheat, rye, maize, wheat and barley, and more particularly barley. These grain types all may contain to greater or lesser degree the substances which stimulate the intestines into increased activity, so that a more efficient metabolism can be achieved.

An important preferred embodiment can have a feature that fennel or a derivative thereof may also be present therein. A derivative of fennel can be understood to mean (dried) fennel leaves, an extract of fennel leaves and in particular fennel seed. The inclusion hereof in the composition may bring about a significantly improved action thereof. Fennel seed, like hop, contains phytohormones. These phytohormones complement the phytohormones of the hop. A further preferred embodiment of the composition therefore can have a feature that the fennel derivative comprises fennel seed.

Good results can be achieved with a particular embodiment of the composition which can be characterized in that at least an active composition therein comprises 25-40% by weight hop, 1-10% by weight fennel, 5-15% by weight buckwheat, 1-10% by weight rye, 20-35% by weight barley, 5-15% by weight malt and 5-15% by weight L-ornithine.

The composition can be prepared in different forms, in liquid form as well as in dry form. A particularly practical embodiment of the composition can have a feature that the composition may be embodied in capsule or tablet form, wherein one or more excipients can normally be used, such as for instance silicon oxide, calcium phosphate, magnesium stearate, oats or starch. This composition can optionally also be ingested in solution or as suspension.

The preferable point of departure in respect of the composition may be purely natural products and components obtained from natural products. This can however have the drawback that the concentrations of active substances are sometimes low and that a large amount of the composition therefore has to be ingested to ensure sufficient effect. A particular embodiment of the composition can in this respect have a feature that the

composition in dry form may be processed into tablets with a minimum of 80% by weight of active substance, and for the rest an excipient, wherein the tablets may preferably have a weight which does not exceed 850 milligrams. It can be established that a tablet under 850 milligrams can still be easily ingested, while a heavier tablet could on occasion result in indigestion problems. A maximum quantity of the composition can thus still be administered per tablet in acceptable manner.

In a sixth aspect of the present invention, there is provided a method of preparing a solution or suspension for the purpose of preventing or aiding recovery from lumps in the breast tissue, or for the purpose of growth or strengthening of breast tissue, or to suppress and prevent benign cysts and the growth thereof or possibly to suppress and prevent malignant cancer cells, wherein a tablet or capsule as described above is mixed with water to form such a solution or suspension.

The invention will now be further elucidated with reference to a number of embodiments:

Example I

Per 1000 grams of active substance to be prepared, about 350 grams hop, 100 grams buckwheat, 60 grams rye, 270 grams barley and 150 grams malt are placed together in a container and ground to an homogeneous mixture. About 70 grams of L-ornithine is added hereto per 1000 grams of active substance to be prepared. This is the natural levorotatory variant of ornithine which can be extracted from sugar beets. The whole is then well mixed and mixed in a ratio of 700:120 with an excipient consisting of silicon oxide, calcium phosphate and magnesium stearate. Tablets of 820 mg each are then formed from this mixture.

Example II

Per 1000 grams of active substance to be prepared, about 330 grams hop, 100 grams buckwheat, 60 grams rye, 270 grams barley, 150 grams malt and 40 grams fennel are finely ground in a container and supplemented with 50 grams of L-ornithine. This composition is mixed in a ratio of 700 : 120 with a suitable excipient and processed into tablets of 800 mg each.

Example III

Per 1000 grams of active substance to be prepared, about 465 grams hop, 50 grams buckwheat, 50 grams rye, 200 grams barley, 85 grams malt and 50 grams fennel are finely ground in a container and supplemented with 100 grams of L-ornithine. This composition is mixed in a ratio of 700:120 with a suitable excipient and processed into tablets of 500 milligrams each. The concentrations of hop, ornithine and fennel in these tablets are significantly higher than in the foregoing embodiments, thereby enabling a smaller tablet size. This facilitates ingestion thereof. Preferably natural flavourings can optionally be added to conceal the strong hop taste in these tablets.

After an ingestion period of a month to several months, all compositions described in these examples displayed the first result in the form of an enhanced breast development, which continued the longer the composition is used until a maximal effect is obtained. The use of the composition can then be cut down and optionally stopped.

Example IV

A group of women in the age-group of 20 to 35 years with breasts free of cysts were investigated in a study into the effects of ingesting ERDIC®, a preparation containing hop, L-ornithine, fennel, buckwheat, rye, malt, barley and excipients, on the growth and firmness of the breast. Half of these women used ERDIC® tablets as prescribed, i.e. 10-15 tablets a day together with at least 2 litres of water. The other half used a placebo in the same way. Enlargement and firmness of the breasts were determined in both subjective and objective manner, i.e. by means of measuring the breast size and estimating the elasticity and the slackness of the breast.

The result is shown in tables 1 and 2 below.

Table 1

breast enlargement	after 2 months	after 4 months	after 6 months
ERDIC®	30%	50%	60%
Placebo	10%	10%	20%

Table 2

breast firmness	after 2 months	after 4 months	after 6 months
ERDIC®	20%	50%	80%
Placebo	0%	10%	20%

It will be apparent from this data that in most of the women the ERDIC® preparation according to the invention has a clearly positive effect on the size and particularly the firmness of the breast.

Example V

A group of women in the age-group of 38 to 52 years with benign cysts in their breast were investigated in a study into the effects of ingesting ERDIC® (described in example IV) on the development of these cysts. This development was monitored both subjectively (see table 3) and objectively using an ultrasonograph and a mammograph (see table 4). The months show the period of ingestion of ERDIC®.

Table 3

	start	1 month	3 months	6 months
cysts	100%	50%	15%	10%
less pain	0%	30%	60%	60%
disappeared	0%	20%	25%	30%

Table 4

	start	6 months
worsening		5%
stationary	100%	65%
improvement		35%

This study shows that the more subjective observations as shown in table 3 are confirmed by the objective ultrasonographic and mammographic observations as shown in table 4.

Although the invention has been further elucidated solely with reference to these five embodiments, it will be apparent that the invention is by no means limited thereto. On the contrary, many more variations are possible for a person with ordinary skill in the art within the scope of the invention. Instead of in tablet form, the composition can thus be used in other form, for instance liquid. The stated constituents and quantities thereof in the agents of the given examples can also be further added to and varied in order to further optimize the action of the composition.

Claims

1. Composition at least containing hop and ornithine for use as cosmetic agent or as medication.

2. Composition as claimed in claim 1, wherein a grain type is also present.

3. Composition as claimed in claim 1 or 2, wherein the weight ratio of hop to ornithine amounts to 1.5 to 10.

4. Composition as claimed in one or more of the foregoing claims, wherein fennel or a derivative of fennel is also present.

5. Composition as claimed in claim 4, wherein the derivative of fennel comprises fennel seed.

6. Composition as claimed in claim 4 or 5, wherein the weight ratio of hop to fennel amounts to 2 to 10.

7. Composition as claimed in one or more of the claims 2-6, wherein the grain type comprises at least one grain type from a group comprising buckwheat, rye, maize, wheat and barley.

8. Composition as claimed in claim 7, wherein the grain type comprises barley.

9. Composition as claimed in one or more of the foregoing claims, **characterized in that** at least the active composition therein comprises 25-40% by weight hop, 1-10% by weight fennel, 5-15% by weight buckwheat, 1-10% by weight rye, 20-35% by weight barley, 5-15% by weight malt and 5-15% by weight L-ornithine.

10. Composition as claimed in one or more of the foregoing claims, **characterized in that** at least the active part therein comprises only natural products and components obtained from natural products.

11. Composition as claimed in any of the foregoing claims, **characterized in that** the composition in dry form is processed into tablets with a minimum of 80% by weight of active substance and for the rest an excipient.

12. Composition as claimed in claim 11, **characterized in that** the tablets have a weight which does not exceed 850 milligrams.

13. Use of a composition as claimed in any of the foregoing claims for the preparation of a cosmetic agent for the purpose of growth and/or strengthening of breast tissue, or to prevent or to aid recovery from lumps in the breast tissue.

14. Use of a composition as claimed in any of the claims 1-12 for the preparation of a medication to suppress benign cysts and the growth thereof and possibly to suppress and prevent malignant cancer cells.

15. Use as claimed in claim 14 for the purpose of suppressing and preventing benign cysts and possibly suppressing and preventing malignant cancer cells in the female breast or in the prostate.

16. Tablet or capsule containing hop, ornithine, fennel or a derivative thereof and optional excipients.

17. Tablet or capsule containing hop, ornithine, fennel or a derivative thereof, a grain type and optional excipients.

18. Method of preparing a solution or suspension for the purpose of preventing or aiding recovery from lumps in the breast tissue or for the purpose of growth or

strengthening of breast tissue, or to suppress and prevent benign cysts and the growth thereof or possibly to suppress and prevent malignant cells, wherein a tablet or capsule as described in claim 16 or 17 is mixed with water.