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CA 2314170 C 2008/01/29

(11)(21) **2 314 170**

(12) **BREVET CANADIEN
CANADIAN PATENT**

(13) **C**

(86) Date de dépôt PCT/PCT Filing Date: 1998/12/10
(87) Date publication PCT/PCT Publication Date: 1999/06/24
(45) Date de délivrance/Issue Date: 2008/01/29
(85) Entrée phase nationale/National Entry: 2000/06/13
(86) N° demande PCT/PCT Application No.: SE 1998/002279
(87) N° publication PCT/PCT Publication No.: 1999/030701
(30) Priorité/Priority: 1997/12/16 (SE9704693-2)

(51) Cl.Int./Int.Cl. *A61K 31/122* (2006.01),
A23K 1/00 (2006.01), *A61P 29/00* (2006.01)
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(54) Titre : PROCEDE DE TRAITEMENT PROPHYLACTIQUE DE LA MASTITE
(54) Title: METHOD OF THE PROPHYLACTIC TREATMENT OF MASTITIS

(57) Abrégé/Abstract:

A method of prophylactic treatment of mastitis in mammalian, including human, mothers, is described. The method comprises administration of a prophylactically effective dosage of a human or veterinary medicament containing at least one type of xanthophylls, such as astaxanthin, to said mothers. Preferably, the astaxanthin exists in a form esterified with fatty acids, e.g. in the form of algae meal produced by culturing of the alga *Haematococcus* sp. Further, use of at least one type of xanthophylls, such as astaxanthin, for the preparation of a human or veterinary medicament for the prophylactic treatment of mastitis in mammalian, including human, mothers is disclosed.



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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 31/12, 31/07	A1	(11) International Publication Number: WO 99/30701 (43) International Publication Date: 24 June 1999 (24.06.99)
(21) International Application Number: PCT/SE98/02279 (22) International Filing Date: 10 December 1998 (10.12.98) (30) Priority Data: 9704693-2 16 December 1997 (16.12.97) SE (71) Applicant (for all designated States except US): ASTAC- AROTENE AB [SE/SE]; Idrottsvägen 4, S-134 40 Gustavs- berg (SE). (72) Inventors; and (75) Inventors/Applicants (for US only): LIGNELL, Åke [SE/SE]; Klippstigen 5, S-139 40 Värmdö (SE). INBORR, Johan [SE/SE]; Bäckvägen 27, S-531 55 Lidköping (SE). (74) Agents: NILSSON, Brita et al.; AB Stockholms Patentbyrå AB, Zacco & Bruhn (publ), P.O. Box 23101, S-104 35 Stockholm (SE).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: METHOD OF THE PROPHYLACTIC TREATMENT OF MASTITIS (57) Abstract <p>A method of prophylactic treatment of mastitis in mammalian, including human, mothers, is described. The method comprises administration of a prophylactically effective dosage of a human or veterinary medicament containing at least one type of xanthophylls, such as astaxanthin, to said mothers. Preferably, the astaxanthin exists in a form esterified with fatty acids, e.g. in the form of algae meal produced by culturing of the alga <i>Haematococcus</i> sp. Further, use of at least one type of xanthophylls, such as astaxanthin, for the preparation of a human or veterinary medicament for the prophylactic treatment of mastitis in mammalian, including human, mothers is disclosed.</p>		

METHOD OF THE PROPHYLACTIC TREATMENT OF MASTITIS

5 The present invention relates to a method of the prophylactic treatment of mastitis of mammalian, including human, mothers. The method comprises administration of a prophylactically effective dosage of a human or veterinary medicament containing at least one type of xanthophylls, such as astaxanthin, to the mothers. The invention also relates to the use of at least one type of
10 xanthophylls, such as astaxanthin, for the preparation of a human or veterinary medicament for the prophylactic treatment of mastitis.

Background

15 Mastitis (inflammation of the mammary gland) is a commonly appearing and often painful disease in both human and animal mothers during the breast feeding/suckling period as well as during the lactation period. The primary cause is usually a bacterial infection. Physical damage to the breasts, udder or the teats may predispose the individual to such infections. Further, mastitis can
20 dramatically reduce milk production, which results in reduced nutrient and immunoglobulin intake by the offspring and/or reduced income for the dairy farmer. Therapeutic treatment usually involves medication, and consultation of a doctor/veterinarian, which is expensive.

25 Ingestion of mother's milk is of crucial importance for the growth and health status of the new born mammal. The milk is the primary source of energy, proteins, fat and other essential nutrients during the breast feeding/suckling period. In addition, in dairy farming, the level of milk production and yields are of great importance for the profitability of the farmer. In summary, any reduction in
30 milk production will have serious economic and health consequences.

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Our published International patent application WO 97/35491 relates to an agent for increasing the production of/in breeding and production mammals, and discloses experiments wherein sows were given feed supplemented with astaxanthin
5 during a period prior to parturition and during lactation resulting in e.g. more piglets born alive.

Astaxanthin, and other xanthophylls, are known to exhibit antioxidative properties, and hence possess the ability to scavenge so-called free radicals. However, in biological
10 tests astaxanthin has been shown to possess clearly the best antioxidative properties compared to other carotenoids (Miki W., 1991, Pure and Appl Chem 63 (1): 141-146).

Description of the invention

The present invention is directed to a method of
15 prophylactic treatment of mastitis in mammalian, including human, mothers, comprising administration of a prophylactically effective dosage of a human or veterinary medicament containing at least one type of xanthophylls to said mothers.

20 In a preferred embodiment the type of xanthophylls is astaxanthin. In a particularly preferred embodiment the astaxanthin exists in a form in which it is esterified with fatty acids. The last mentioned form of astaxanthin may be in the form of algal meal produced by culturing of the alga
25 Haematococcus sp.

A prophylactically effective dosage of the preparation contains e.g. 0.01 to 1 mg astaxanthin per kg body weight per day.

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The invention is also directed to the use of at least one type of xanthophyll for: (i) the preparation of a human or veterinary medicament for the prophylactic treatment of mastitis in mammalian, including human, mothers, or (ii) for
5 the prophylactic treatment of mastitis in mammalian, including human, mothers.

The invention also provides a commercial package comprising at least one type of xanthophyll and associated therewith instructions for the use thereof in the prophylactic
10 treatment of mastitis in mammalian, including human, mothers.

Here again, in a preferred embodiment the type of xanthophylls is astaxanthin. In a particularly preferred embodiment the astaxanthin exists in a form in which it is esterified with fatty acids. The last mentioned form of astaxanthin may be in the form of algal meal produced by culturing of the alga *Haematococcus* sp.

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For example, the amount astaxanthin in the medicament is 0.01 to 1 mg per body weight of the human or animal mother.

10 In the present invention the human and veterinary medicaments may comprise a mixture of different types of xanthophylls or different forms of the same xanthophyll, such as a mixture of synthetic astaxanthin and naturally produced astaxanthin.

15 The human and veterinary medicament of the invention may comprise additional ingredients which are pharmacologically acceptable inactive or active, such as flavoring agents, excipients, diluents, carriers, etc., and it may be presented in a separate unit dose or in admixture with food or feed. Examples of separate unit doses are tablets, gelatin capsules and predetermined amounts of solutions, e. g. oil solutions, or emulsions, e.g. water-in- oil or oil-in-water emulsions.

20 Examples of food in which the preparation of the invention may be incorporated is dairy products, such as yogurt, chocolate and cereals.

Description of experiments

25 The medicament used in the experiments contained the xanthophyll astaxanthin which was produced via the alga *Haematococcus* sp. by AstaCarotene AB, Gustavsberg, Sweden.

30 Naturally produced astaxanthin can be obtained also from fungi and crustaceans, in addition to from alga. Astaxanthin from other sources, and other xanthophylls as well, are expected to be similarly useful for the purposes of the invention. An advantage of using astaxanthin from alga is, however, that the

astaxanthin exists in a form esterified with fatty acids [Renström B. et al, 1981, Phytochem 20(11) :2561-2564], which esterified astaxanthin thereby is more stable during handling and storage than free astaxanthin.

5 **Experimental design and results**

10 A group of 120 dairy cows with a known record of milk production and incidence of mastitis from the previous lactation period were given algal meal (from *Haematococcus pluvialis*) to provide 100 mg natural astaxanthin per day during a period extending from parturition to 12 weeks thereafter.

During this period only one incidence of mastitis was recorded. This number should be compared to 8 cases recorded in the same cows during the previous lactation period.

15 Milk production was 6% higher in the current period (100 mg natural astaxanthin/day/cow) compared to the previous one (no natural astaxanthin).

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CLAIMS:

1. Use of at least one type of xanthophyll for the preparation of a human or veterinary medicament for the prophylactic treatment of mastitis in a mammalian mother.
- 5 2. Use of at least one type of xanthophyll for the prophylactic treatment of mastitis in a mammalian mother.
3. Use according to claim 1 or 2, wherein the type of xanthophyll is astaxanthin.
4. Use according to claim 3, wherein the astaxanthin
10 exists in a form esterified with a fatty acid.
5. Use according to claim 4, wherein the esterified astaxanthin is in the form of algal meal produced by culturing of the alga Haematococcus sp.
6. Use according to claim 3, wherein the amount of
15 astaxanthin is 0.01 to 1 mg per kg body weight.
7. Use according to any one of claims 1 to 6, wherein the mammalian mother is a human mother.
8. A xanthophyll for the preparation of a human or veterinary medicament for the prophylactic treatment of
20 mastitis in a mammalian mother.
9. A xanthophyll for the prophylactic treatment of mastitis in a mammalian mother.
10. A xanthophyll according to claim 8 or 9, which is astaxanthin.
- 25 11. A xanthophyll according to claim 10, wherein the astaxanthin exists in a form esterified with a fatty acid.

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12. A xanthophyll according to claim 11, wherein the esterified astaxanthin is in the form of algal meal produced by culturing of the alga *Haematococcus* sp.

13. A xanthophyll according to claim 10, wherein the
5 amount of astaxanthin is 0.01 to 1 mg per kg body weight.

14. A xanthophyll according to any one of claims 8 to 13, wherein the mammalian mother is a human mother.

15. A commercial package comprising a xanthophyll as
10 defined in any one of claims 8 and 10 to 12, and associated therewith instructions for the use thereof in the prophylactic treatment of mastitis in a mammalian mother.

16. A commercial package according to claim 15, wherein the mammalian mother is a human mother.

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