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(54) Title: USE OF POLLEN EXTRACTS TO TREAT INFLECTIONS, NEOPLASMS AND TO BALANCE THE IMMUNE RESPONSE

(57) Abstract: Disclosed is the use of pollen extract to prepare medicinal products for the treatment of systemic infections and neoplastic disorders, which may be localised or at an advanced stage.
THE USE OF POLLEN EXTRACTS TO ACTIVATE/REBALANCE THE IMMUNE RESPONSE

This invention relates to the use of pollen extracts to prepare medicinal products designed to activate/rebalance the immune response.

It has been found that the pollen extract, administered by the transdermal or systemic route, cures infectious disorders which fail to respond to other treatments, eliminates flare-ups of recurrent infectious diseases (especially viral diseases), and cures hyperproliferative and oncological disorders in situ or at an advanced stage. The results obtained demonstrate that the active constituents of pollen extract induce this reactivation/rebalance of the immune response even in defenceless or immunocompromised patients.

In order to demonstrate this effect, we treated a significant number of patients suffering from infectious diseases with a wide variety of etiogeneses (bacteria, fungi, mixed flora) which were local, disseminated or generalised, chronic, recurrent or relapsing, and generally resistant to systemic antibiotic, antifungal or antiviral treatments.

PRIOR ART

Pollen has a complex chemical composition and comprises proteins and aminoacids, carbohydrates, lipids, mineral salts and trace elements, vitamins, hormones, enzymes, growth factors, water-extractable antibiotic substances and nucleic acids.

Pollen extracts, which are available on the market from a number of sources, are mainly used in the cosmetic field, as active ingredients of formulations for dry, normal and greasy skins due to their nutrient properties.

Pollen extracts, obtained by extraction of pollens of various origins with aqueous, hydroalcoholic, oily or glycolic solvents, are also used as tonics and as adjuvants in the treatment of states of mental and physical fatigue,
depression and asthenia.

EP 1077725, filed by the Applicant, discloses that the association of pollen extract with vegetable oil unsaponifiables, applied topically, is suitable to treat a number of conditions, mainly of dermatological and circulatory interest, with an inflammatory, immune, degenerative or proliferative base.

EP 1313492-6 disclose the use of pollen extracts, possibly associated with royal jelly and Vitamin E, to treat dysphoria associated with normal hormonal variations in women of childbearing, peri- and post-menopausal age.


**DESCRIPTION OF THE INVENTION**

The administration of pollen extracts, suitably formulated for oral, topical, transdermal, intramuscular or intravenous administration, has led to improvements in infectious diseases and neoplastic disorders, and often to a cure.

The pollen extracts which can be used according to the invention may be of different types and origins, such as hydroalcoholic, aqueous, oily or glycol extracts. The extracts will be administered by oral, parenteral or topical administration, depending on the site affected by the disorder to be treated, at doses which can vary within a wide range in view of the substantial absence of toxicity of the extract. Broadly speaking, 10 mg to 500 mg a day can be given in one or more administrations by the oral or parenteral route, while a formulation of 0.1 to 10% in weight of extract can be used for topical or transdermal administration.

The extracts will be suitably formulated in transdermal systems, capsules, tablets, solutions for oral or parenteral use, suspensions, creams, gels or the like, in association with conventional excipients or vehicles, and
possibly with other active ingredients with a complementary or otherwise useful activity. The transdermal formulations may contain suitable absorption promoters in conventional use.

A significant number of patients suffering from local or generalised infections and patients suffering from oncological disorders have been treated.

Examples of disorders that respond to the treatment according to the invention include:

1. **Skin**, mucosal and subcutaneous *infections* which tend to become chronic or involve frequent relapses, supported by infectious agents including those resistant to conventional treatments (bacteria, fungi, dermatophytic yeasts, mixed flora, viruses, and in particular Staphylococci, Streptococci, Candida, corynebacteria, herpes virus, papillomavirus etc.): intertrigo, acne, epididymitis, vulvovaginitis, proctitis, balanoposthitis with reparatory events of a sclerotic or scleroatrophic nature such as phimosis, paraphimosis and synechia).

2. **Generalised systemic infections**, with or without rashes, whether or not accompanied by a septic central inflammatory response (sepsis generated by gram-positive or gram-negative bacteria or other micro-organisms), including those resistant to all other treatments.

3. **Local infections** of the tissues and/or blood vessels (venous lymphatic infections with consequent phlebitis, lymphangitis, adenitis and the like, or selectively affecting organs or limbs) in situations which fail to respond to prior treatments.

4. **Oncological disorders** such as tumours *in situ*, affecting the limbs and lymph node stations or at an advanced stage.

5. **Disorders resulting from or correlated with** an alteration in the CD4+/CD8+ ratio at district level or in the peripheral blood.

Persons who failed to respond to other treatments or are compromised
(diabetics, oncological, cachectic or immunocompromised patients or persons who cannot be given systemic treatments, such as breastfeeding women with viral infections) have been successfully treated.

For example, some specific disorders responded to transdermal treatment with a 10% gel formulation of pollen extract in weight:

- erysipelas
- diabetic gangrene of the lower limbs
- decubitus gangrene in terminal or cachectic patients
- sepsis following invasive surgery or resulting from haematic diffusion of various primary sepsigenic foci such as bedsores, diabetic sores, etc.
- herpes zoster and other herpes infections
- Mibelli’s porokeratosis
- lymphomas, in particular non-Hodgkin’s lymphoma (even at an advanced stage of the disease, such as the 3rd or 4th stage according to the TNM classification)
- breast cancer
- basalioma and spinaloma.
- carcinomatous skin metastases.

On average, the treatment of these disorders requires from 4-5 days to several months’ application of the gel or transdermal system to which the invention relates. The treatment may also be accompanied by the administration of pollen extract, especially oral administration.
CLAIMS

1. Use of pollen extract to prepare medicinal products for the treatment of systemic infections and neoplastic disorders, which may be localised or at an advanced stage.

2. Use as claimed in claim 1, wherein the medicinal product is administered by the transdermal, parenteral or oral route.

3. Use as claimed in claim 1 or 2 for the treatment of localised or diffuse skin, mucosal and subcutaneous infections supported by bacteria, viruses or fungi.

4. Use as claimed in claim 1 or 2 for the treatment of lymphoma, spinalioma, basalioma and carcinoma.

5. Use as claimed in claim 1, wherein the medicinal product is administered transdermally.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K36/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>X</td>
<td>US 2004/147459 A1 (ONEAL JOSEPH ET AL) 29 July 2004 (2004-07-29) paragraphs [0021], [0022]; claims 8, 14-17</td>
<td>1, 2</td>
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<td>X</td>
<td>WO 02/32442 A (BIOLEE CO., LTD) 25 April 2002 (2002-04-25) claims 1, 2, 5-7; examples</td>
<td>1-3, 5</td>
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:
  *A* document defining the general state of the art which is not considered to be of particular relevance
  *E* earlier document but published on or after the international filing date
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*T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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*F* document member of the same patent family

Date of the actual completion of the international search

31 May 2006

Date of mailing of the international search report

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Name and mailing address of the ISA/

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Authorized officer

Kanbier, D
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<td>US 5 712 377 A (JATON ET AL) 27 January 1998 (1998-01-27) columns 1,2,8; examples 1,8</td>
<td>1,2,4,5</td>
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INTERNATIONAL SEARCH REPORT

Box II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. □ Claims Nos.;
   because they relate to subject matter not required to be searched by this Authority, namely:

2. □ Claims Nos.;
   because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. □ Claims Nos.;
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. □ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. □ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. □ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. □ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

□ The additional search fees were accompanied by the applicant’s protest.

X No protest accompanied the payment of additional search fees.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3; partly 5

   Use of pollen extract to prepare medicaments for treating (systemic) infections

2. claim: 4; partly 5

   Use of pollen extract to prepare medicaments for treating neoplastic disorders
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