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(54) Title: BUCCAL, POLAR AND NON-POLAR SPRAY OR CAPSULE CONTAINING DRUGS FOR TREATING DISORDERS OF THE GASTROINTESTINAL TRACT OR URINARY TRACT

(57) Abstract: Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biologically active compounds for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compositions of the invention comprise formulation I: aqueous polar solvent, active compound, and optional flavoring agent; formulation II: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation III: non-polar solvent, active compound, and optional flavoring agent; and formulation IV: non-polar solvent, active compound, optional flavoring agent, and propellant.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/12 A61K9/72 A61K48/00 A61P31/00 A61P33/00 A61P35/00 A61K31/00 A61K47/00				
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) IPC 7 A61K A61P				
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, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE, CHEM ABS Data				
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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
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X	WO 99/16417 A (DUGGER HARRY A III ;FLEMINGTON PHARMACEUTICAL CORP (US)) 8 April 1999 (1999-04-08) the whole document claims 1,8 page 2, lines 18-27 page 6, lines 5-15 example 2 page 9, lines 7-15	1-8, 19-21		
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.				
<input checked="" type="checkbox"/> Patent family members are listed in annex.				
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> "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 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td style="width: 50%; border: none; vertical-align: top;"> "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 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family </td> </tr> </table>			"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 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"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 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
"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 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"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 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family			
Date of the actual completion of the international search <p style="text-align: center; font-size: 1.2em;">19 January 2004</p>	Date of mailing of the international search report <p style="text-align: center; font-size: 1.5em;">02.06.2004</p>			
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center; font-size: 1.2em;">Luangkhot, N</p>			

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/26854

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 00/27359 A (PILKIEWICZ FRANK G) 18 May 2000 (2000-05-18) the whole document page 14, lines 14-16 page 17, lines 9,10 page 18, lines 17,18 claims 1,79,81,87</p>	1-8, 19-21
X	<p>WO 98/29097 A (QUADRANT HOLDINGS CAMBRIDGE ;COLACO CAMILO (GB); SANDERSON IAN (GB) 9 July 1998 (1998-07-09) the whole document page 1, paragraph 1 table 1 page 10, paragraph 5 - page 11, paragraph 1 claims 1,7,9</p>	1-8, 19-21
X	<p>ZERVAKIS J ET AL: "Taste effects of lingual application of cardiovascular medications" PHYSIOLOGY AND BEHAVIOR, ELSEVIER SCIENCE LTD., OXFORD, GB, vol. 68, no. 3, January 2000 (2000-01), pages 405-413, XP002264153 ISSN: 0031-9384 abstract page 405, column 1, line 9 - column 3, paragraph 1 page 406, column 1, paragraph 4</p>	1-8, 19-21
X	<p>MOCHIZUKI H ET AL: "Inhaled diuretics attenuate acid-induced cough in children with asthma." CHEST. UNITED STATES FEB 1995, vol. 107, no. 2, February 1995 (1995-02), pages 413-417; XP002267208 ISSN: 0012-3692 the whole document abstract page 414, column 1, paragraph 3</p>	1-8, 19-21
X	<p>KARLSSON J A ET AL: "A comparison of the effect of inhaled diuretics on airway reflexes in humans and guinea pigs." JOURNAL OF APPLIED PHYSIOLOGY (BETHESDA, MD.: 1985) UNITED STATES FEB 1992, vol. 72, no. 2, February 1992 (1992-02), pages 434-438, XP009024093 ISSN: 8750-7587 abstract</p>	1-8, 19-21

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/26854

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 386 700 A (HOECHST AG) 12 September 1990 (1990-09-12) page 2, lines 18-22 page 3, lines 5-7	1-8, 19-21
X	----- US 5 908 611 A (BABIOR BERNARD M ET AL) 1 June 1999 (1999-06-01) the whole document column 7, lines 42-63 column 8, lines 31-48 column 11, lines 36-65 claims 1,5,10 -----	1-8, 19-21

INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:

Although claims 20-21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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:

see FURTHER INFORMATION sheet. PCT/ISA/210
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 II Observations where unity of invention is lacking (Continuation of item 2 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.:

1-7, 8, 19-21 (all in part)

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 20-21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: -

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: -

Applicant's attention is drawn with the fact that the notion "buccal" in independent claims encompasses lingual as well as pulmonary administration. In fact when a pulmonary administration occurs, some aerosol will impact to the mouth, tongue and throat, larynx, pharynx (....), the rest can reach the lungs. Therefore buccal administration will be not limited to lingual administration.

The notion of "oral mucosa" in claim 20 is unclear in the sense of Art. 6 PCT because it could mean buccal, lingual, throat, larynx, respiratory, as well as gastro-intestinal mucosa (delivery to gastro-intestinal mucosa via oral administration). Therefore oral mucosa administration will be not limited to lingual or sublingual administration.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising acetazolamide and a polar solvent

2. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising benzthiazide and a polar solvent

3. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising bendroflumethazide and a polar solvent

4. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising bumetamide and a polar solvent

5. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising a chlorthalidone and a polar solvent

6. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising chlorothiazide and a polar solvent

7. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising ethacrynic acid and a polar solvent

8. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising furosemide and a polar solvent

9. claims: 1-7, 8, 19-21 (all in part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Propellant-free buccal spray composition comprising hydrochlorothiazide and a polar solvent

10. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising hydroflumethiazide and a polar solvent

11. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising methyclothiazide and a polar solvent

12. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising polythiazide and a polar solvent

13. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising quinethazone and a polar solvent

14. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising spironolactone and a polar solvent

15. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising triamterene and a polar solvent

16. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising torsemide and a polar solvent

17. claims: 1-7, 8, 19-21 (all in part)

Propellant-free buccal spray composition comprising trichlormethazide and a polar solvent

18. claims: 1-7 (in part), 9, 19-21 (in part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Propellant-free buccal spray composition comprising an anti-spasmodic as described in claim 9 and a polar solvent

19. claims: 1-7 (in part), 10, 19-21 (in part)

Propellant-free buccal spray composition comprising an agent for treating urinary incontinence as described in claim 10 and a polar solvent

20. claims: 1-7 (in part), 11, 19-21 (in part)

Propellant-free buccal spray composition comprising an anti-diarrheal as described in claim 11 and a polar solvent

21. claims: 1-7 (in part), 12, 19-21 (in part)

Propellant-free buccal spray composition comprising an agent for treating nausea or vomiting as described in claim 12 and a polar solvent

22. claims: 1-7 (in part), 13, 19-21 (in part)

Propellant-free buccal spray composition comprising hyoscine and a polar solvent

23. claims: 1-7 (in part), 14, 19-21 (in part)

Propellant-free buccal spray composition comprising an anti-secretary agent as described in claim 14 and a polar solvent

24. claims: 1-7 (in part), 15, 19-21 (in part)

Propellant-free buccal spray composition comprising an enzyme as described in claim 15 and a polar solvent

25. claims: 1-7 (in part), 16, 19-21 (in part)

Propellant-free buccal spray composition comprising an anti-diuretic as described in claim 16 and a polar solvent

26. claims: 1-7 (in part), 17, 19-21 (in part)

Propellant-free buccal spray composition comprising an anti-ulcerant as described in claim 17 and a polar solvent

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

27. claims: 1-7 (in part), 18, 19-21 (in part)

Propellant-free buccal spray composition comprising the bile acid replacment and/or gallstone solubilizing agent as described in claim 18 and a polar solvent

28. claims: 22-43

Buccal spray composition comprising an active compound as described in claim 22, a polar solvent and a propellant

29. claims: 44-31

Propellant-free buccal spray composition an active compound as described in claim 44 and a non-polar solvent

30. claims: 62-83

Buccal spray composition comprising an active composition as described in calims 62 or 65, a non-polar solvent and a propellant

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/26854

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International Application No

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