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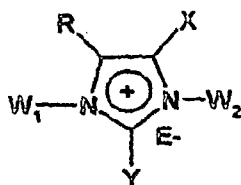
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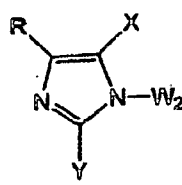
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(54) Title: 1, 3 AND 1, 3, 5 SUBSTITUTED IMIDAZOLES AS ANTIHYPERTENSIVA

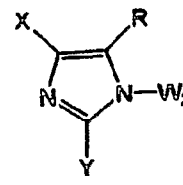


(I)



(IIa)

OR



(IIb)

(57) Abstract: The present invention provides novel 1,5 and 1,3, 5 -substituted imidazole compounds of formulas (I), (IIa), (IIb) in hydrophilic or lipophilic form, which are useful as angiotensin II AT1 receptor antagonists with sympathetic suppressant properties. In particular, the invention provides pharmaceutical compositions containing the pharmacophoric groups of Losartan and Clonidine as well compounds, processes and intermediates for preparing compounds and their use in methods of treating hypertension and cardiovascular diseases through Renin Angiotensin System (RAS) and Sympathetic System (SS). Alkylated histamine based double action Saltans are lipophilic and can act transdermally.

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2008/002796

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D403/10 C07D233/00 A61K31/4178 A61P9/12

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)  
C07D

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, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                          | Relevant to claim No. |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| A         | EP 0 427 463 A (SMITHKLINE BEECHAM CORP [US]) 15 May 1991 (1991-05-15)<br>examples 1,2,32,34-36,38,40<br>-----                                                                                                                                              | 1-56                  |
| A         | EP 0 564 356 A (FOURNIER IND & SANTE [FR])<br>6 October 1993 (1993-10-06)<br>examples<br>-----                                                                                                                                                              | 1-56                  |
| A         | NOUET ET AL: "Specific Nonpeptide<br>Photoprobes as Tools for the Structural<br>Study of the Angiotensin II AT1 Receptor"<br>J.MED.CHEM.,,<br>vol. 42, no. 22,<br>1 January 1999 (1999-01-01), pages<br>4572-4583, XP002511435<br>examples<br>-----<br>-/-- | 1-56                  |

☒ 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
- \*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

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Menegaki, Fotini

## INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                           | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| A         | <p>TUCCINARDI ET AL: "Proposal of a New Binding Orientation for Non-Peptide AT1 Antagonists: Homology Modeling, Docking and Three-Dimensional Quantitative Structure-Activity Relationship Analysis" 1 January 2006 (2006-01-01), J.MED.CHEM,, PAGE(S) 4305 - 4316 , XP002511436 example 81; table 3</p> <p>-----</p>                                                        | 1-56                  |
| A         | <p>CARINI D J ET AL: "NONPEPTIDE ANGIOTENSIN II RECEPTOR ANTAGONISTS: THE DISCOVERY OF A SERIES OF N-(BIPHENYLYLMETHYL)IMIDAZOLES AS POTENT, ORALLY ACTIVE ANTIHYPERTENSIVES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON.; US, vol. 34, no. 8, 1 August 1991 (1991-08-01), pages 2525-2547, XP000674205 ISSN: 0022-2623 examples</p> <p>-----</p> | 1-56                  |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2008/002796

### Box No. 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:  

Although claims 44, 45 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:
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 No. 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:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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 and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No  
PCT/IB2008/002796

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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