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(54) Title: BITOPIC MUSCARINIC AGONISTS AND ANTAGONISTS AND METHODS OF SYNTHESIS AND USE THERE-
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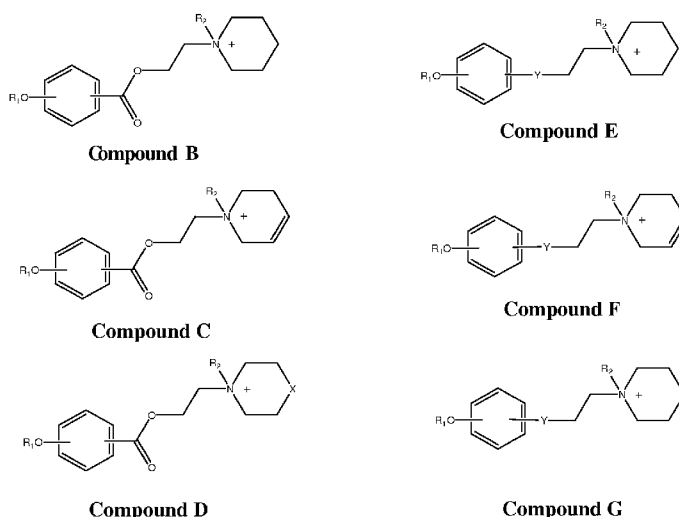


FIG. 1A

(57) Abstract: Compositions for treating a condition associated with activity of a muscarinic receptor (e.g., one or more of M₁, M₂, M₃, M₄, M₅) and for anesthetizing a subject include a bitopic muscarinic antagonist or agonist. A bitopic muscarinic antagonist named JB-D4 was discovered. This bitopic ligand and its structural analogs, as well as bitopic muscarinic agonists, may be used as neuromuscular blocking agents (e.g., for use in compositions for anesthetizing a subject) and for the treatment of central nervous system disorders (e.g., Parkinson's disease, Schizophrenia, etc.), Overactive Bladder Syndrome, Chronic Obstructive Pulmonary Disease, asthma, and many other diseases associated with the activation or inhibition of M₁-M₅ acetylcholine receptors.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2013/049634

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:

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:

See Extra 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 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 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, 2, 5-10, 12-15

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

PCT/US2013/049634
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A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C07D 295/037 (2014.01) USPC - 546/237 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(8) - A61K 31/452; C07D 295/037, 295/04, 295/104 (2014.01) USPC - 514/317, 422; 546/237; 548/578		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched CPC - A61K 31/452; C07D 295/037, 295/04, 295/104 (2013.01)		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Google Patents, STN, Google Scholar, PubMed, PubChem		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 7,947,730 B2 (COLLINGWOOD et al) 24 May 2011 (24.05.2011) entire document	1, 2, 5-10, 12-15
A	US 5,006,626 A (HOFER et al) 09 April 1991 (09.04.1991) entire document	1, 2, 5-10, 12-15
A	US 7,192,978 B2 (QUINONES et al) 20 March 2007 (20.03.2007) entire document	1, 2, 5-10, 12-15
A	US 2006/0233843 A1 (CONN et al) 19 October 2006 (19.10.2006) entire document	1, 2, 5-10, 12-15
A	US 2005/0267078 A1 (GRAS ESCARDO et al) 01 December 2005 (01.12.2005) entire document	1, 2, 5-10, 12-15
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
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Date of the actual completion of the international search 04 March 2014		Date of mailing of the international search report 21 MAR 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774