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(54) Title: CHOLINESTERASE INHIBITORS TO PREVENT INJURIES CAUSED BY CHEMICALS

(57) Abstract: The invention provides methods for treating and preventing injuries caused by chemicals by administering to a patient a therapeutically effective amount of at least one cholinesterase inhibitor. The chemicals can be, for example, agricultural compounds or chemical weapons. In one embodiment, the cholinesterase inhibitor is donepezil, a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/13575

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 31/445, 31/55, 31/40 US CL : 514/319, 212, 408 According to International Patent Classification (IPC) or to both national classification and IPC</p>														
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/319, 212, 408</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet</p>														
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X --- Y</td> <td>US 6,264,974 B1 (MADHAT) 24 July 2001 (24.07.2001), column 1, lines 6-12; column 3, lines 45-46; column 4, lines 7-18.</td> <td>3-8, 16-21, 27-32 ----- 9-11, 22-24, 33-35</td> </tr> <tr> <td>X --- Y</td> <td>US 6,114,347 A (HILLE et al) 05 September 2000 (05.09.2000), see entire documents.</td> <td>3, 16, 27 ----- 4-11, 17-24, 28-35</td> </tr> <tr> <td>X</td> <td>US 5,939,095 A (HILLE et al) 17 August 1999 (17.08.1999), see entire documents.</td> <td>3, 16, 27 ----- 4-11, 17-24, 28-35</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X --- Y	US 6,264,974 B1 (MADHAT) 24 July 2001 (24.07.2001), column 1, lines 6-12; column 3, lines 45-46; column 4, lines 7-18.	3-8, 16-21, 27-32 ----- 9-11, 22-24, 33-35	X --- Y	US 6,114,347 A (HILLE et al) 05 September 2000 (05.09.2000), see entire documents.	3, 16, 27 ----- 4-11, 17-24, 28-35	X	US 5,939,095 A (HILLE et al) 17 August 1999 (17.08.1999), see entire documents.	3, 16, 27 ----- 4-11, 17-24, 28-35
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.</p>														
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed			
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<p>Date of the actual completion of the international search 15 October 2003 (15.10.2003)</p>		<p>Date of mailing of the international search report 13 NOV 2003</p>												
<p>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. (703)305-3230</p>		<p>Authorized officer <i>Valerie Bell-Harris</i> Zohreh Fay Telephone No. 703-308-1235</p>												

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/13575

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

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

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

2. Claim Nos.: 1-2, 12-15, 25-26
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:
Please See Continuation Sheet

3. Claim 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:

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.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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Continuation of Box I Reason 2:

Claims 1-2, 12-15, 25-26 relate to an extremely large number of possible compounds having characteristics of "cholinesterase inhibitor". Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compositions claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely cholinesterase inhibitors represented by the formula I-III and recited in claims 3, 7-11, 16, 20-24, 27, 31-35.

Continuation of B. FIELDS SEARCHED Item 3:

STN ONLINE

search terms: donepezil, cholinesterase inhibitor, tacrine, physostigmine, pyridostigmine, neostigmine, rivastigmine, galantamine, citicoline, velnacrine, buperzine, metrifonate, heptastigmine, edrophonium, phenserine, tolsarine, phenethylnorcymserine, ganstigmine, epastigmine, upreazine, organophosphorus, nerve gases, soman, tabun, sarin, cyclohexyl methyophosphono-fluoridate, O-ethyl S-diisopropylaminomethyl methylphosphonothilate