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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 2006/085141 A3

(54) Title: COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING HEPADNAVIRIDAE INFECTION

(57) Abstract: The present disclosure relates generally to the use of certain castanospermine esters to treat or prevent infections caused by *Hepadnaviridae*, particularly infections caused by hepatitis B virus (HBV), and to the use of such compounds to examine the biological mechanisms of HBV infection.

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/IB2005/004028

<p>A. CLASSIFICATION OF SUBJECT MATTER                  IPC: <b>A61K 31/437</b> (2006.01) , <b>A61P 31/12</b> (2006.01)                  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)                  IPC<sup>8</sup>: A61K, A61P</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched                  structure and keyword searches across all classifications</p> <p>Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)                  STN, Delphion, SCOPUS, NCBI/PubMED, Canadian Patent Database (hepatitis, <i>Hepadnaviridae</i>, vir*, infect*, glucosid*, castanospermine)</p>																
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1" style="width:100%; border-collapse: collapse;"> <thead> <tr> <th style="width:10%;">Category*</th> <th style="width:60%;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width:30%;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td align="center">Y</td> <td>                     “<math>\alpha</math>-Glucosidase Inhibitors as Potential Broad Based Anti-Viral Agents”  <i>FEBS Letters</i>, 1998, vol. 430, pp. 17-22 (MEHTA ET AL.)  <ul style="list-style-type: none"> <li>• see the abstract, Figure 1 and page 19, right column</li> </ul> </td> <td align="center">1-52, 54-66, 67 (in part) and 68-70</td> </tr> <tr> <td align="center">Y</td> <td>                     EP 297 534 A2 (MERRELL DOW PHARMACEUTICALS INC.)                      1 January 1989  <ul style="list-style-type: none"> <li>• see page 2, line 25 to page 3, line 47 and Table 1</li> </ul> </td> <td align="center">1-52, 54-66, 67 (in part) and 68-70</td> </tr> <tr> <td align="center">Y</td> <td>                     US 5 004 746 (MERRELL DOW PHARMACEUTICALS INC.)                      2 April 1991  <ul style="list-style-type: none"> <li>• see the abstract and the claims</li> </ul> </td> <td align="center">1-52, 54-66, 67 (in part) and 68-70</td> </tr> <tr> <td align="center">A</td> <td>                     “Hepatitis B Antiviral Therapy”  <i>Today's Life Science</i>, September 1990, vol. 2, 9, pp. 32-38 and 80 (Locarnini)                      --                 </td> <td align="center">1-52, 54-66, 67 (in part) and 68-70</td> </tr> </tbody> </table>		Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	Y	“ $\alpha$ -Glucosidase Inhibitors as Potential Broad Based Anti-Viral Agents” <i>FEBS Letters</i> , 1998, vol. 430, pp. 17-22 (MEHTA ET AL.) <ul style="list-style-type: none"> <li>• see the abstract, Figure 1 and page 19, right column</li> </ul>	1-52, 54-66, 67 (in part) and 68-70	Y	EP 297 534 A2 (MERRELL DOW PHARMACEUTICALS INC.) 1 January 1989 <ul style="list-style-type: none"> <li>• see page 2, line 25 to page 3, line 47 and Table 1</li> </ul>	1-52, 54-66, 67 (in part) and 68-70	Y	US 5 004 746 (MERRELL DOW PHARMACEUTICALS INC.) 2 April 1991 <ul style="list-style-type: none"> <li>• see the abstract and the claims</li> </ul>	1-52, 54-66, 67 (in part) and 68-70	A	“Hepatitis B Antiviral Therapy” <i>Today's Life Science</i> , September 1990, vol. 2, 9, pp. 32-38 and 80 (Locarnini) --	1-52, 54-66, 67 (in part) and 68-70
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C.      <input checked="" type="checkbox"/> See patent family annex.</p> <table border="1" style="width:100%; border-collapse: collapse;"> <tbody> <tr> <td style="width:50%; vertical-align: top;">                     * 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 application or patent 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%; 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                      “&amp;” document member of the same patent family                 </td> </tr> </tbody> </table>		* 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 application or patent 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													
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Date of the actual completion of the international search 17 October 2006 (17-10-2006)	Date of mailing of the international search report 2 November 2006 (02-11-2006)															
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer <p align="center"><b>Ryan Jaecques 819-953-6570</b></p>															

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
PCT/IB2005/004028

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
EP0297534	04-01-1989	AR245128 A1	30-12-1993
		AT116318T T	15-01-1995
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**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/IB2005/004028**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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.  Claim Nos. : 1-70

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

Claims 1-70 are directed to methods for treatment of the human or animal body which the International Search Authority is not required to search. However, this Authority has carried out a search based on the alleged effects or purposes/uses of the product defined in these claims.

2.  Claim 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.  Claim Nos. :

because they are dependant 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 claim 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 claim 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.

The claims on file consist of 4 independent claims: claims 1, 17, 40 and 64. The first is the use of castanospermine esters for the treatment or prevention of *Hepadnaviridae* infection, whereas the latter three claims are directed to combinations of same with other agents useful in treating said infections. Some combinations of the castanospermine esters and other medicaments are taught in the description to produce a synergistic effect.

The technical features which is common to each of these claims is the use of the specified castanospermine esters for the treatment or prevention of *Hepadnaviridae* infection (i.e. the subject-matter of claim 1). However, this technical feature does not define a contribution over the art as required by Rule 13.2 PCT, and thus cannot be considered to unify the inventive concepts of these claims. As such, the claims are considered to be directed to a plurality of inventive concepts:

**Group A** - Claims 1-16 are directed to methods for the treatment or prevention of *Hepadnaviridae* infection using castanospermine esters of structural formula (I);

**Group B** - Claims 17-39, 64 (in part), 65, 66 and 68-70 (in part) are directed to methods for the treatment or prevention of *Hepadnaviridae* infection using castanospermine esters of structural formula (I) in combination with an agent that alters immune function;

**Group C** - Claims 40-63, 64 (in part), 67 and 68-70 (in part) are directed to methods for the treatment or prevention of *Hepadnaviridae* infection using castanospermine esters of structural formula (I) in combination with an agent that alters viral replication;

**Group D** - Claim 64 and 68-70 (in part) is directed to a method for the treatment or prevention of *Hepadnaviridae* infection using castanospermine esters of structural formula (I) in combination with a compound that inhibits infection of cells by *Hepadnaviridae* and alters the symptoms thereof; and

**Group E** - Claim 64 and 68-70 (in part) is directed to a method for the treatment or prevention of *Hepadnaviridae* infection using castanospermine esters of structural formula (I) in combination with a compound that inhibits the release of viral RNA from the viral capsid or the function of *Hepadnaviridae* gene products.

Since there are no "special technical features" common throughout the claims—that is, there are no technical features which define a contribution over the art—the subject-matter of these independent claims cannot be considered so linked as to form a unified inventive concept as required by Rule 13 PCT.

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