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(54) Title: TREATMENT OF VIRAL INFECTIONS BY MODULATION OF HOST CELL METABOLIC PATHWAYS

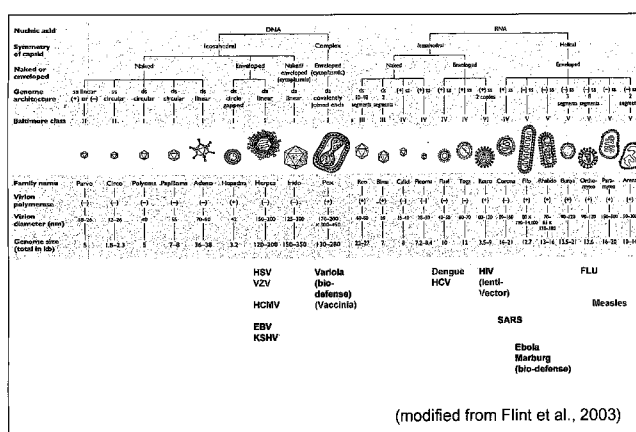


FIG. 1

(57) Abstract: Alterations of certain metabolite concentrations and fluxes that occur in response to viral infection are described. Host cell enzymes in the involved metabolic pathways are selected as targets for intervention; i.e., to restore metabolic flux to disadvantage viral replication, or to further derange metabolic flux resulting in 'suicide' of viral-infected cells (but not uninfected cells) in order to limit viral propagation. While any of the enzymes in the relevant metabolic pathway can be selected, pivotal enzymes at key control points in these metabolic pathways are preferred as candidate antiviral drug targets. Inhibitors of these enzymes are used to reverse, or redirect, the effects of the viral infection. Drug candidates are tested for antiviral activity using screening assays in vitro and host cells, as well as in animal models. Animal models are then used to test efficacy of candidate compounds in preventing and treating viral infections. The antiviral activity of enzyme inhibitors is demonstrated.

WO 2009/023059 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/06959

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A01N 43/02; A61K 31/335 (2009.01) USPC - 514/449 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) USPC - 514/449</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 435/123; 435/886; 514/909; 549/263; 549/328 (text search - see search terms below)</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST (USPT, PGPB, EPAB, JPAB) and Google Scholar Search terms: lipstatin, orlistat, tetrahydrolipstatin, viral, antiviral, hepatitis, carrier, amount, dosage, salt, prodrug, lipase, inhibitor, host cell, metabolic</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:70%;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width:20%;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td align="center">X ----- Y</td> <td>Bacon. Clinical Case: Management of Patients with Chronic Hepatitis C from the book Management of Patients with Viral Hepatitis, Marcellin, editor. January 2007, pg 144, para 4-5</td> <td align="center">1 ----- 31</td> </tr> <tr> <td align="center">Y</td> <td>US 4,598,089 A (Hadvary et al.) 01 July 1986 (01.07.1986) col 1, Formula I, ln 29; col 7, ln 11-13, 43-44</td> <td align="center">31</td> </tr> <tr> <td align="center">A</td> <td>US 6,576,636 B2 (Webb et al.) 10 June 2003 (10.06.2003) entire document</td> <td align="center">1, 31</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X ----- Y	Bacon. Clinical Case: Management of Patients with Chronic Hepatitis C from the book Management of Patients with Viral Hepatitis, Marcellin, editor. January 2007, pg 144, para 4-5	1 ----- 31	Y	US 4,598,089 A (Hadvary et al.) 01 July 1986 (01.07.1986) col 1, Formula I, ln 29; col 7, ln 11-13, 43-44	31	A	US 6,576,636 B2 (Webb et al.) 10 June 2003 (10.06.2003) entire document	1, 31
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/></p>														
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<p>Date of the actual completion of the international search</p> <p>28 April 2009 (28.04.2009)</p>		<p>Date of mailing of the international search report</p> <p align="center">07 MAY 2009</p>												
<p>Name and mailing address of the ISA/US</p> <p>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201</p>		<p>Authorized officer:</p> <p align="center">Lee W. Young</p> <p>PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774</p>												

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/06959

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.: 35-36
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 and 31, limited to a compound of formula I.

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

International application No.

PCT/US 08/06959

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1-14 and 31 directed to various methods for treating or preventing viral infections in a mammal, comprising administering to a mammalian subject in need thereof a therapeutically effective amount of one or more compound or prodrug thereof, or a pharmaceutically acceptable salt of said compound or prodrug, wherein the compound is a compound of any of Formula I-LXVII

Group II: claims 15-30 and 32-34 directed to various methods for treating or preventing viral infection in a mammal, comprising various methods of administering to a mammalian subject in need thereof a therapeutically effective amount of a compound which inhibits or reduces the activity of various enzymes, etc. and related pharmaceutical compositions.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The methods of group II do not require that any of the compounds specified in the claims of group I be applied in the various methods claimed. While compounds of group I may be used in the methods of the claims of group II, they are not required to practice said methods.

Thus, the inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature. According to PCT Rule 13.2, unity of invention exists only when the same or corresponding technical feature is shared by all claimed inventions.

In addition, the claims of groups I are directed to more than one species of the invention. For the group I, compounds I-LXVII do not share any special technical feature that is an advance over the prior art. Compounds of formula I are known in the art (see US 4,598,089 A to Hadvary et al.). Furthermore, the compounds of formula I-LXVII do not share any special technical feature and would be expected to have different physical, chemical and pharmacological properties.

In this case the first named invention and first named species that will be searched without additional fees is Group I represented by claims 1 and 31, limited to a compound of formula I.

In order for more than one species (invention) to be examined, the appropriate additional examination fees must be paid and the desired species clearly identified.

Claims 35-36 are improper multiple dependent claims because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).