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(54) Title: HERBAL COMPOSITIONS AND METHODS FOR TREATING HEPATIC DISORDERS

(57) Abstract: Herbal compositions and their use in the prevention and/or treatment of hepatitis are provided. The herbal compositions comprise an extract of flowers, leaves, and roots from the plant genera *Cordia*, *Annona*, and *Curcuma*, respectively, wherein the specific species are *Cordia lutea*, *Annona muricata* and *Curcuma longa*.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/001764

A. CLASSIFICATION OF SUBJECT MATTER IPC: A61K 36/30 (2006.01) , A61K 36/57 (2006.01) , A61K 36/9066 (2006.01) , A61P 1/16 (2006.01) , A61P 31/12 (2006.01) , A61P 39/06 (2006.01) 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: A61K 36/30 (2006.01) , A61K 36/57 (2006.01) , A61K 36/9066 (2006.01) , A61P 1/16 (2006.01) , A61P 31/12 (2006.01) , A61P 39/06 (2006.01) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used) Canadian Patent Database, Scopus, Agricola, CAPLUS, Esp@cenet, Delpion, Biosis, Pubmed, Internet: keywords: hydroalcoholic, plant, herbs, extract, <i>Cordia</i>, <i>Ammona</i>, <i>Curcuma</i>, tumeric, liver, hepat*, free radicals, antioxidant, <i>Curcuma longa</i>, <i>Cordia lutea</i>, <i>Ammona muricata</i>																													
C. DOCUMENTS CONSIDERED TO BE RELEVANT <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</td> <td>EP 1032408 A1 (LEE J.S.) 24 July 2002 (24-07-2002) see the whole document</td> <td>1, 4, 6, 9, 17-21</td> </tr> <tr> <td>Y</td> <td></td> <td>3, 5, 8, 10-12</td> </tr> <tr> <td>X</td> <td>US 5401777 A (AMMON H.P.T. et al.) 28 March 1995 (28-03-1995) see the whole document</td> <td>1, 4, 6, 9, 17-20, 22</td> </tr> <tr> <td>Y</td> <td></td> <td>3, 5, 8, 10-12</td> </tr> <tr> <td>X</td> <td>DESHPANDE U.R. et al. Protective effect of turmeric (<i>Curcuma longa</i> L.) extract on carbon tetrachloride-induced liver damage in rats. Indian J Exp Biol. June 1998 Vol. 36, No. 6, pages 573-577, ISSN 0019-5189 see the whole document</td> <td>1, 4, 6, 9, 17, 21</td> </tr> <tr> <td>Y</td> <td></td> <td>3, 5, 8, 10-12</td> </tr> <tr> <td>X</td> <td>WO 03051380 A2 (RAY M. et al.) 26 June 2003 (26-06-2003) see the whole document.</td> <td>1, 4, 6, 9, 22</td> </tr> <tr> <td>Y</td> <td></td> <td>3, 5, 8, 10-12</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	EP 1032408 A1 (LEE J.S.) 24 July 2002 (24-07-2002) see the whole document	1, 4, 6, 9, 17-21	Y		3, 5, 8, 10-12	X	US 5401777 A (AMMON H.P.T. et al.) 28 March 1995 (28-03-1995) see the whole document	1, 4, 6, 9, 17-20, 22	Y		3, 5, 8, 10-12	X	DESHPANDE U.R. et al. Protective effect of turmeric (<i>Curcuma longa</i> L.) extract on carbon tetrachloride-induced liver damage in rats. Indian J Exp Biol. June 1998 Vol. 36, No. 6, pages 573-577, ISSN 0019-5189 see the whole document	1, 4, 6, 9, 17, 21	Y		3, 5, 8, 10-12	X	WO 03051380 A2 (RAY M. et al.) 26 June 2003 (26-06-2003) see the whole document.	1, 4, 6, 9, 22	Y		3, 5, 8, 10-12
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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex. <table border="1"> <tbody> <tr> <td>* Special categories of cited documents :</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>"A" document defining the general state of the art which is not considered to be of particular relevance</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>"E" earlier application or patent but published on or after the international filing date</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>"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>"&" document member of the same patent family</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td></td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </tbody> </table>			* Special categories of cited documents :	"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	"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent but published on or after the international filing date	"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	"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)	"&" document member of the same patent family	"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																
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Date of the actual completion of the international search 11 December 2008 (11-12-2008)		Date of mailing of the international search report 6 May 2009 (06-05-2009)																											
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 Marsha Black 819- 997-2917																											

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/001764

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. : 17-22
because they relate to subject matter not required to be searched by this Authority, namely :

Claims 17-22 are directed to a method for treatment of the human or animal body by surgery or therapy, are not required to be searched by this Authority under Rule 39.1(iv) of the PCT. Regardless, this Authority has established a search based on the alleged effect or purpose/use of the product defined in claims 17-22.
2. ☒ Claim Nos. : 1-4 and 6-9
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 :

Claims 1-4 and 6-9 define the alleged invention broadly, by the generic names *Cordia*, *Annona* and *Curcuma*. A meaningful search over the full scope of the claims could not be performed. Thus, a broad search was performed using the above generic names, and a narrow search, using the specific species *Cordia lutea*, *Annona muricata*, and *Curcuma longa*.
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 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/001764

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	AFZAL M. et al. Antioxidant activity of <i>Cordia myxa</i> L. and its hepatoprotective potential. Electronic Journal of Environmental, Agricultural and Food Chemistry, June 2007, Vol. 6, No. 6. pages 2109-2118, ISSN 1573-4377. see the whole document	1, 2, 6, 7, 17, 21, 22 3, 5, 8, 10-12
X Y	BUSSMANN R.W. et al., Traditional medicinal plant use in Northern Peru: tracking two thousand years of healing culture. J Ethnobiol Ethnomed. Nov 7 2006, Vol. 2:47, ISSN 1746-4269. [Retrieved December 10, 2008]. Retrieved from the internet: URL: http://www.ethnobiomed.com/content/2/1/47 See Additional file 1. Species encountered in Northern Peru, page 19 URL: http://www.ethnobiomed.com/content/supplementary/1746-4269-2-47-s1.pdf	1, 2, 4, 6, 7, 9, 17-20 3, 5, 8, 10-12
X Y	WO 04048358 A1 (MCLAUGHLIN J.L. et al.) 10 June 2004 (10-06-2004) see the whole document, especially pages 3-4, claims 1 and 7	1, 6, 17 3, 5, 8, 10-12
X Y	BASKAR, R. et al. <i>In vitro</i> antioxidant studies in leaves of <i>Annona</i> species. Indian J Exp Biol. May 2007, Vol. 45, No. 5, pages 480-485, ISSN 0019-5189. see the whole document	1, 4, 6, 9, 22 3, 5, 8, 10-12
X Y	Graviola <i>Annona muricata</i> , Raintree Nutrition Monograph, March 2004, pages 1-10 [Retrieved December 10, 2008] Retrieved from the internet. URL: http://www.rain-tree.com/Graviola-Monograph.pdf see the whole document	1, 4, 6, 9, 17-20 3, 5, 8, 10-12
X	MORA S. et al. Anxiolytic and antidepressant-like effects of the hydroalcoholic extract from <i>Aloysia polystachya</i> in rats. Pharmacol Biochem Behav. October 2005, Vol.82, No.2, pages 373-378, ISSN 0091-3057. see the whole document	15, 16

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2008/001764

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
EP 1032408A1	06-09-2000	AU 728967B2	25-01-2001
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		NZ 539141A	30-11-2007
		US 2004101584A1	27-05-2004

The claims are directed to a plurality of inventive concepts as follows:

- Group A - Claims 1, 4, 6, 9 (partly), 2, 7 (fully) and 17-22 (partly) are directed to a herbal composition for treating hepatic disorders comprising one species of *Cordia* and methods for the treatment or prevention of hepatic disorders or for neutralizing and preventing the formation of free radicals, using said composition.
- Group B - Claims 1, 4, 6, 9, and 17-22 (all partly) are directed to a herbal composition for treating hepatic disorders comprising one species of *Annona*, and methods for the treatment or prevention of hepatic disorders or for neutralizing and preventing the formation of free radicals, using said composition.
- Group C - Claims 1, 4, 6, 9 and 17-22 (partly) are directed to a herbal composition for treating hepatic disorders comprising one species of *Curcuma*, and methods for the treatment or prevention of hepatic disorders or for neutralizing and preventing the formation of free radicals, using said composition.
- Group D - Claims 1, 4, 6, 9 (partly), 3, 5, 8, 10-14 (fully) and 17-22 (partly) are directed to herbal compositions for treating hepatic disorders comprising a combination of one species of each of *Cordia*, *Annona*, and *Curcuma* and methods for the treatment or prevention of hepatic disorders or for neutralizing and preventing the formation of free radicals, using said composition.
- Group E - Claims 15 and 16 are directed to a method for obtaining hydroalcoholic extracts from a plant organ for use in preparation of a herbal composition.
- Group F - Claim 22 (partly) is directed to a method for neutralizing free radicals and for preventing the formation of free radicals by using the herbal composition of claims 1-14.

The claims must be limited to one inventive concept as set out in Rule 13 of the PCT. There is a lack of unity *a priori* between Groups A-D, because each of these groups refer to one species of the genera *Cordia*, *Annona*, or *Curcuma* (Groups A-C) or a combination of all of these (Group D) for treating hepatic disorders. Group E, directed to a method of obtaining hydroalcoholic extracts from a plant organ, cannot be linked to any one of Groups A-D. Finally, Group F, directed to a method of using the herbal composition of claims 1-14 for prevention of free radical formation, cannot be linked with Groups A-D, where the herbal composition is for the treatment of hepatic disorders.

An *a posteriori* analysis has concluded that, as herbal extracts from *Cordia*, *Annona* and *Curcuma* for the treatment of hepatic disorders or neutralizing free radicals are known [e.g. see US 5401777 (AMMON H.P.T. et al.) 28 March, 1995, AFZAL M. et al. Electronic Journal of Environmental, Agricultural and Food Chemistry, June 2007, Vol. 6, No. 6, pages 2109-2118, WO2004048358 A1 (MCLAUGHLIN J.L. et al.) 10 June 2004, and BASKAR, R. et al. Indian J Exp Biol. May 2007, Vol. 45, No. 5, pages 480-485, ISSN 0019-5189], a herbal composition for treating hepatic disorders or neutralizing free radicals containing a plant species from one of the genera *Cordia*, *Annona*, or *Curcuma* cannot be regarded as representing a special technical feature that defines a contribution over the prior art, and cannot be relied upon to provide a single general inventive concept required to establish unity of invention regarding Groups A-D.