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(54) Title: ENCAPSULATION OF NANOSUSPENSIONS IN LIPOSOMES AND MICROSPHERES

(57) Abstract: Sustained release of hydrophobic agents may be achieved by incorporation of the agents into liposomes and microspheres. This is achieved by use of a nanosuspension comprising the hydrophobic agent. The nanosuspension may be used as the aqueous solution in the formation of the liposomes and microspheres.



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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT US/02/ 17346

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/127 A61K9/51 A61K9/10 A61K9/16 A61K9/00  
A61K31/5415 A61K31/44 A61K31/64

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 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 827 533 A (NEEDHAM DAVID) 27 October 1998 (1998-10-27)  column 1, line 10-37 --- -/--	2-4,6-8, 13,15, 28-31, 33-36, 43-45, 47-49, 54-56, 58,59, 61,63, 64,66

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* 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 document 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

Date of the actual completion of the international search

6 March 2003

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19.05.03

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT US/02/ 17346

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 770 222 A (RAMASWAMI VARADARAJAN ET AL) 23 June 1998 (1998-06-23)</p> <p style="text-align: center;"><b>INTERNATIONAL SEARCH REPORT</b></p> <p>column 2, line 30-41 column 29, line 53-67 column 30, line 1-6</p> <p style="text-align: center;">---</p>	<p>2-4,6-8, 13,15, 28-31, 33-36, 43-45, 47-49, 54-56, 58,59, 61,63, 64,66</p>
P,X	<p>US 6 284 267 B1 (ANEJA RAJINDRA) 4 September 2001 (2001-09-04)</p> <p>column 12, line 11-29</p> <p style="text-align: center;">-----</p>	<p>2-4,6-8, 13,15, 28-31, 33-36, 43-45, 47-49, 54-56, 58,59, 61,63, 64,66</p>

# INTERNATIONAL SEARCH REPORT

International application No.

PCT US/02/ 17346

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 2, 6, 28, 33, 43, 47 (all in part); 1, 5, 27, 32, 42, 46  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
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 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:

see additional 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 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.:  
1-8, 13, 15, 27-36, 42-45, 46-49, 54-56, 58-59, 61, 63, 64, 66

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 2, 6, 28, 33, 43, 47 (all in part); 1, 5, 27, 32, 42, 46

Present claims 2, 6, 28, 33, 43, 47 relate to an extremely large number of possible hydrophobic agents. 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 hydrophobic agents claimed. (N.B.: From the general wording it is not even deducible that a physiologically active agent is envisaged!) 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 those parts relating to agents as defined in the description on p.6/[0036] and in particular in the examples 1,2,9 and claim 31.

Further the term "nanoparticle" used in the above mentioned claims 2, 6, 28, 33, 43, 47 is equally considered not to be precise enough as to clearly delimit the claimed subject-matter vis-à-vis the prior art. The search has consequently been restricted to the precise indications as e.g. in claim 4.

Present claims 1, 5, 27, 32, 42, 46 relate to a liposomes/MLVs/compound (hydrophobic compound) defined by reference to a desirable characteristic or property of the comprised hydrophobic compound, namely "dispersed in at least one chamber bounded by at least one membrane".

The claims cover all liposomes/MLVs having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such liposomes/MLVs. 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. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the liposomes/MLVs by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-8,13,15,27-36,42-45,46-49,54-56,58-59,61,63,64,66

liposomes or multilamellar vesicle liposomes comprising at least one hydrophobic agent dispersed in at least one chamber bounded by at least one membrane

2. Claims: 9-12, 14, 16-26, 37-41, 50-53, 57, 60, 62, 65, 67

microspheres comprising at least one hydrophobic agent dispersed in at least one internal chamber bounded by at least one membrane

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

International Application No  
**PCT US/02/ 17346**

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