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(54) Title: POLYAMINES AND THEIR USE AS ANTIBACTERIAL AND SENSITIZING AGENTS

(57) Abstract: Polyamines with varying chain-lengths were evaluated for antimicrobial activity in order to test the hypothesis that these *bis*-cationic amphipathic compounds may also bind to and permeabilize intact Gram negative bacterial membranes. The compounds were found to possess significant antimicrobial activity and mediated via permeabilization of bacterial membranes. Homologated spermine, *bis*-acylated with C_8 or C_9 chains was found to profoundly sensitize *E. coli* to hydrophobic antibiotics such as rifampicin.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US07/04734

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A61K 31/16**(2006.01),**31/13**(2006.01)

USPC: 514/625,674
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)
U.S. : 514/625, 674

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 practicable, search terms used)
EAST, STN-Easy

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Miller et. al., Lipopolysaccharide Sequestrants: Structural Correlates of Activty and Toxicity in a Novel Acylhomospermines, Journal of Medical Chemistry, April 07, 2005, Vol. 48, No. 7, pp. 2589-2599, entire document.	1-8, 15-21, 33, 35 and 60-62 --- 9-14, 21-34, 36-58 and 60-62
Y	David, Sunil A. Towards a rational development of anti-endotoxin agents: novel approaches to sequestration of bacterial endotoxins with samll molecules. Journal of Molecular Recognition, 2001, vol. 14, pp 370-387, whole documents.	22-31, 34, 36-40, 41-58 and 60-62
Y	David, A. et al. Lipopolyamines: Novel antiendotoxin compounds that reduce mortality in experimental sepsis caused by gram-negative bacteria, Antimicrobial Agents and Chemotherapy, April 1999, vol. 43, no. 4, pp 912-919, whole documents.	22-31, 34, 36-40, 41-58 and 60-62

☐ Further documents are listed in the continuation of Box C. ☐ See patent family 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 application or patent 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	Date of mailing of the international search report
07 November 2007 (07.11.2007)	25 JUL 2008
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. (571) 273-3201	Authorized officer Maury Audet Telephone No. 571-272-1600

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US07/04734

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.: 59
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:

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 any 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.:

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.