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3 November 2011

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(54) Title: DIAZENIUMDIOLATED PHOSPHORYLCHOLINE POLYMERS FOR NITRIC OXIDE RELEASE

(57) Abstract: The present disclosure in a broad aspect provides for diazeniumdiolated phosphorylcholine polymers and associated methods for achieving nitric oxide release. The present polymers have superior biocompatibility and are useful for coating or fabricating medical devices such as a vascular stent.

# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/026867

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/48 A61K31/80
ADD. A61P35/00

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)
A61K A61L

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, BIOSIS, EMBASE, DISSERTATION ABS, PASCAL, 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 | WO 2007/024492 A2 (MEDTRONIC VASCULAR INC [US]; CHEN PEIWEN [US]; CHENG MINGFEI [US]; UDI) 1 March 2007 (2007-03-01) paragraph [0035] examples claims | 1-11, 15-19 |
| X | US 2007/014828 A1 (FITZHUGH ANTHONY L [US] ET AL) 18 January 2007 (2007-01-18) paragraph [0058] claims 22,26,27 | 1-11, 15-19 |

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[X] Further documents are listed in the continuation of Box C.

[X] 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 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)

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"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.

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 21 April 2011 | 18/07/2011 |

| Name and mailing address of the ISA/ | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Dullaart, Anwyn |

# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/026867

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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| X | EP 1 623 728 A1 (MEDTRONIC VASCULAR INC [US]) 8 February 2006 (2006-02-08) examples 7-9 | 1-11, 15-19 |
| Y | WO 2005/089855 A1 (ABBOTT LAB [US]; TONER JOHN L [US]; BURKE SANDRA E [US]; CROMACK KEITH) 29 September 2005 (2005-09-29) example 1 claims | 1-11, 15-19 |
| X | WO 2007/046935 A2 (ABBOTT LAB [US]; BURKE SANDRA E [US]; CROMACK KEITH R [US]; MACK MATTH) 26 April 2007 (2007-04-26) example 9 claims | 1-11, 15-19 |
| Y | MALIK N ET AL: "Phosphorylcholine-coated stents in porcine coronary arteries: in vivo assessment of biocompatibility.", THE JOURNAL OF INVASIVE CARDIOLOGY, vol. 13, no. 3, March 2001 (2001-03), pages 193-201, XP8135681, ISSN: 1042-3931 abstract page 194, right-hand column page 197, left-hand column, paragraph results - page 198, right-hand column | 1-11, 15-19 |
| Y | KUIPER K K J ET AL: "Phosphorylcholine-coated metallic stents in rabbit iliac and porcine coronary arteries", SCANDINAVIAN CARDIOVASCULAR JOURNAL, vol. 32, no. 5, 1998, pages 261-268, XP8135682, ISSN: 1401-7431 abstract page 263, right-hand column, paragraph results - page 265, left-hand column, paragraph 1 | 1-11, 15-19 |

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# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/026867

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | WO 2008/112391 A2 (MEDTRONIC VASCULAR INC [US]; CHENG PEIWEN [US]; CHEN MINGFEI [US]; UDI) 18 September 2008 (2008-09-18) examples 3,4 claims | 1-11, 15-19 |
| Y | WO 2009/014829 A2 (MEDTRONIC VASCULAR INC [US]; CHEN MINGFEI [US]; CHENG PEIWEN [US]; UDI) 29 January 2009 (2009-01-29) examples claims | 1-11, 15-19 |
| Y,P | WO 2009/117183 A1 (MEDTRONIC VASCULAR INC [US]; CHENG PEIWEN [US]; CHEN MINGFEI [US]) 24 September 2009 (2009-09-24) examples claims | 1-11, 15-19 |

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Information on patent family members

International application No
PCT/US2010/026867

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| | | US 2009232868 A1 | 17-09-2009 |

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/** 210

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

1. claims: 4, 5, 9, 15, 19(completely); 1-3, 6-8, 10, 11, 16-18(partially)

The nitric oxide donating polymer, the medical device comprising it, and the method of making the nitric oxide donating polymer as defined in these claims, where the precursor polymer capable of containing a phosphorylcholine functional group is a methacrylate, more specifically of formula I or II

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2-44. claims: 1-3, 6-8, 10, 11, 16-18(all partially)

The nitric oxide donating polymer, the medical device comprising it, and the method of making the nitric oxide donating polymer as defined in these claims, where the precursor polymer capable of containing a phosphorylcholine functional group is

2. polyester
3. polycarbonate
4. poly(ortho ester)
5. polyamide
6. polyurethane
7. polyurea
8. poly(ester amide)
9. polysulfone
10. polyketone
11. silicone
12. polyphosphazene
13. poly(amino acid)
14. polyether
15. polyimide
16. vinyl polymer
17. polyacrylate
18. polymethacrylate
19. polystyrene
20. poly(vinyl acetate)
21. poly(vinyl chloride)
22. poly(vinyl ester)
23. poly(vinyl ether)
24. polyacrylonitrile
25. poly(vinyl ketone)
26. poly(vinyl pyrolidinone)
27. fluorinated polymer
28. natural biopolymer
29. modified biopolymer
30. collagen
31. alginate
32. elastin
33. chitosan
34. fibrin
35. fibrinogen

36. cellulose
37. starch
38. collagen
39. dextran
40. dextrin
41. hyaluronic acid
42. heparin
43. glycosamino glycan
44. a different, not previously mentioned polysaccharide

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45. claims: 12-14

The medical device comprising nitric oxide donating polymer as defined in these claims, i.e., further comprising at least one bioactive agent.

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2010/026867

**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.:
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 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 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.:

see annex

**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.