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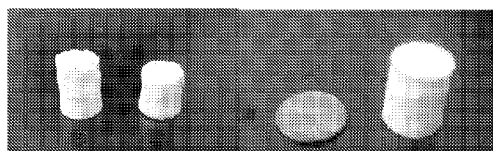
(81) Designated States (unless otherwise indicated, for every
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CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ,
EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO,
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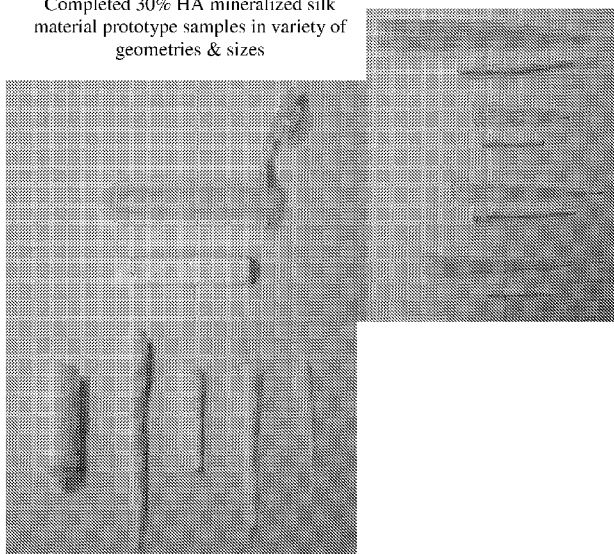
[Continued on next page]

(54) Title: 3-DIMENSIONAL SILK HYDROXYAPATITE COMPOSITIONS

Figure 7



Completed 30% HA mineralized silk
material prototype samples in variety of
geometries & sizes



(57) Abstract: Described herein are methods and compo-
sitions comprising a mixture of silk polymer and hydrox-
yapatite. The methods described herein can be used to
prepare a mixture of silk polymer and hydroxyapatite and
further provide mixtures that can be molded into a desired
shape. Also encompassed herein are compositions com-
prising a mixture of silk polymer and hydroxyapatite hav-
ing a desired shape, which can further be implanted, for
example, to facilitate bone healing or tooth structure or
support. Such compositions can also include agents, such
as therapeutic agents, or cells.



ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR),
OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))*

Published:

— *with international search report (Art. 21(3))*

(88) Date of publication of the international search report:

8 October 2009

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/033309**A. CLASSIFICATION OF SUBJECT MATTER****A61L 27/14(2006.01)i, A61L 27/12(2006.01)i, A61L 27/54(2006.01)i, A61F 2/28(2006.01)i**

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: A61L 27/14, A61L 27/12, A61L 27/54, A61L 27/00, A61F 2/02, A61F 2/06, A61F 2/28, A61K 38/48

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

Korean Utility models and applications for Utility models since 1975

Japanese Utility models and applications for Utility models since 1975

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

eKOMPASS(KIPO internal) & keywords: silk, polymer, fibroin, implant, hydroxyapatite, lyophilize, freeze dry, matrix, scaffold, insoluble

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/0099630 A1 (DIBENEDETTO, ANTHONY T. et al.) 29 May 2003 See abstract, figures 1 and 2, page 6, claims 1-10, 15-22, 29-42	1-3, 8-10, 14, 22
X	LI, CHUNMEI et al., Electrospun silk-BMP-2 scaffolds for bone tissue engineering, Biomaterials, June 2006, Vol. 27, Iss. 16, Pages 3115-3124. See abstract, table 1, page 3116	1-3, 8-10, 14, 22
A	US 2006/0159837 A1 (KAPLAN, DAVID L. and LI, CHUNMEI) 20 July 2006 See abstract, pages 2 and 3, claims 1-5, 10-16	1-3, 8-10, 14, 22
A	US 2004/0078090 A1 (BINETTE, FRANCOIS et al.) 22 April 2004 See abstract, claims 1, 2, 9-11, 14 and 15	1-3, 8-10, 14, 22
A	US 2005/0119732 A1 (FURUZONO, TSUTOMU et al.) 2 June 2005 See abstract, claims 1 and 8	1-3, 8-10, 14, 22

☐ 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 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 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

18 AUGUST 2009 (18.08.2009)

Date of mailing of the international search report

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Name and mailing address of the ISA/KR

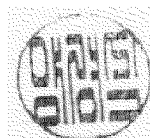
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gu, Daejeon 302-701, Republic of Korea

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/033309**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.: 25
because they relate to subject matter not required to be searched by this Authority, namely:
Claim 25 pertains to a method for treatment of the human or animal body by therapy methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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.: 4-7, 11, 13, 15-21, 23, 24, 26-29
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 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.:

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

Information on patent family members

International application No.

PCT/US2009/033309

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003-0099630 A1	29.05.2003	US 2007-0190099 A1	16.08.2007
US 2006-0159837 A1	20.07.2006	WO 2005-000483 A1	06.01.2005
US 2004-0078090 A1	22.04.2004	AU 2003-252886 A1	06.05.2004
		AU 2003-252882 B2	06.07.2006
		AU 2003-252882 A1	06.05.2004
		AU 2003-252886 B2	27.10.2005
		AU 2003-252882 A1	08.10.2003
		AU 2003-252886 B2	09.10.2003
		CA 2445356 A1	18.04.2004
		EP 1410811 B1	15.10.2008
		EP 1410811 A1	21.04.2004
		EP 1410810 B1	24.01.2007
		EP 1410810 A1	21.04.2004
		JP 2004-136096 A	13.05.2004
		JP 2004-136097 A	13.05.2004
		US 2004-0078077 A1	22.04.2004
US 2005-0119732 A1	02.06.2005	CA 2475023 A1	11.12.2003
		EP 1508586 A1	23.02.2005
		JP 3836444 B2	25.10.2006
		JP 2004-051952 A	19.02.2004
		US 07473731 B2	06.01.2009
		WO 2003-102059 A1	11.12.2003