



US009408917B2

(12) **United States Patent**
Lu et al.

(10) **Patent No.:** **US 9,408,917 B2**
(45) **Date of Patent:** **Aug. 9, 2016**

(54) **PHARMACEUTICAL COMPOSITION**

514/785

(71) Applicant: **Industrial Technology Research Institute, Hsinchu (TW)**

2009/0118480 A1 5/2009 Holappa et al.
2010/0203163 A1 8/2010 Allen
2012/0065614 A1 3/2012 Omary et al.

(72) Inventors: **Maggie J. M. Lu**, Jhudong Township, Hsinchu County (TW); **Yu-Wen Lo**, Shueishang Township, Chiayi County (TW); **Chih-Peng Liu**, Hsinchu (TW); **Chia-Wen Huang**, Hukou Township, Hsinchu County (TW); **Shuen-Hsiang Chou**, Zhunan Township, Miaoli County (TW); **Po-Hung Lai**, New Taipei (TW); **Tsan-Lin Hu**, Jhubei (TW); **Min-Ying Lin**, Hsinchu (TW); **Chia-Mu Tu**, Taipei (TW)

FOREIGN PATENT DOCUMENTS

EP 2 294 126 A1 3/2011
TW 201016223 A1 5/2010
WO WO 2009/150651 A1 12/2009
WO WO-2013-063263 * 5/2013

(73) Assignee: **INDUSTRIAL TECHNOLOGY RESEARCH INSTITUTE, Hsinchu (TW)**

OTHER PUBLICATIONS

Kumbar S, synthesis and characterization of modified chitosan microspheres: effect of the grafting ratio on the controlled release of nifedipine through microspheres, journal of applied polymer science, 89, 2940-2949, 2003.*
Khan, I, Assessment of palmitoyl and sulphate conjugated glycol chitosan for development of polymeric micelles, 2013, 3(2), 97-100.*
Chiu et al., "pH-triggered injectable hydrogels prepared from aqueous N-palmitoyl chitosan: In vitro characteristics and in vivo biocompatibility," Biomaterials, vol. 30, pp. 4877-4888 (2009).
Bhattarai et al., "PEG-grafted chitosan as an injectable thermosensitive hydrogel for sustained protein release," J. of Controlled Release, vol. 103, pp. 609-624 (2005).
Li et al., "A Novel Composite Hydrogel Based on Chitosan and Inorganic Phosphate for Local Drug Delivery of Camptothecin Nanocolloids," J. of Pharmaceutical Sciences, vol. 100, No. 1, pp. 232-241 (Jan. 2011).
Wu et al., "A thermo- and pH-sensitive hydrogen composed of quaternized chitosan/glycerophosphate," Int'l J. of Pharma., vol. 315, pp. 1-11 (2006).
Ruel-Gariépy et al., "A thermosensitive chitosan-based hydrogel for the local delivery of paclitaxel," Eur. J. of Pharma. & Biopharma., vol. 57, pp. 53-63 (2004).
Fujita et al., "Vascularization in vivo caused by the controlled release of fibroblast growth factor-2 from an injectable chitosan/non-anticoagulant heparin hydrogel," Biomaterials, vol. 25, pp. 699-706 (2004).
Yang et al., "Chitosan/Gelatin Hydrogel Prolonged the Function of Insulinoma/Agarose Microspheres In Vivo During Xenogenic Transplantation," Transplantation Proc., vol. 40, pp. 3623-3626 (2008).
Cheng et al., "Thermosensitive chitosan-gelatin-glycerol phosphate hydrogel as a controlled release system of ferulic acid for nucleus pulposus regeneration," Biomaterials, vol. 32, pp. 6953-6961 (2011).
Chiu et al., "Controlled release of thymosin β 4 using collagen-chitosan composite hydrogels promotes epicardial cell migration and angiogenesis," J. of Controlled Release, vol. 155, pp. 376-385 (2011).

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **13/926,363**

(22) Filed: **Jun. 25, 2013**

Prior Publication Data

US 2014/0199369 A1 Jul. 17, 2014

Foreign Application Priority Data

Jan. 17, 2013 (TW) 102101736 A

(51) **Int. Cl.**
A61K 47/36 (2006.01)
A61K 9/00 (2006.01)
A61K 9/127 (2006.01)

(52) **U.S. Cl.**
CPC **A61K 47/36** (2013.01); **A61K 9/0024** (2013.01); **A61K 9/0085** (2013.01); **A61K 9/127** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(Continued)

References Cited

U.S. PATENT DOCUMENTS

7,098,194 B2 8/2006 Chenite et al.
8,119,102 B1* 2/2012 Sung et al. 424/1.69
8,187,571 B1* 5/2012 Sung et al. 424/1.73
8,257,740 B1 9/2012 Sung et al.
8,263,130 B2 9/2012 Chen et al.
8,283,317 B1 10/2012 Sung et al.
8,287,905 B1 10/2012 Sung et al.
8,354,094 B1* 1/2013 Sung et al. 424/1.73
2004/0225077 A1* 11/2004 Gravett et al. 525/418
2005/0019404 A1 1/2005 Sung et al.
2005/0208122 A1 9/2005 Allen et al.
2008/0008755 A1 1/2008 Kwon et al.
2008/0248991 A1* 10/2008 Dyer et al. 514/2
2009/0076177 A1* 3/2009 Bausch A61K 9/146

Primary Examiner — Frederick Krass
Assistant Examiner — Celeste A Roney
(74) *Attorney, Agent, or Firm* — Muncy, Geissler, Olds & Lowe, P.C.

(57) **ABSTRACT**

The disclosure provides a pharmaceutical composition. The pharmaceutical composition includes a chitosan with palmitoyl groups and an active agent. According to another embodiment, the pharmaceutical composition can further include a gelling accelerating agent. According to an embodiment of the disclosure, the active agent of the disclosure can be administered in the form of a nano-drug, liposome, micelle, or microparticle.