US009408915B2

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

(10) **Patent No.: US 9,408,915 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **TOLVAPTAN SOLID DISPERSION AND ITS PREPARATION METHOD**

(75) Inventors: **Yuxia Wu**, Jiangsu (CN); **Shujun Mao**, Jiangsu (CN); **Hao Chen**, Jiangsu (CN)

(73) Assignee: **Jiangsu Hengrui Medicine Co., Ltd.**, Lianyungang, Jiangsu (CN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 95 days.

(21) Appl. No.: **13/806,173**

(22) PCT Filed: **Jun. 2, 2011**

(86) PCT No.: **PCT/CN2011/075131**

§ 371 (c)(1), (2), (4) Date: **Dec. 21, 2012**

(87) PCT Pub. No.: **WO2011/160541**

PCT Pub. Date: **Dec. 29, 2011**

(65) **Prior Publication Data**

US 2013/0102588 A1 Apr. 25, 2013

(30) **Foreign Application Priority Data**

Jun. 25, 2010 (CN) 2010 1 0224884

(51) **Int. Cl.**

A61K 47/32	(2006.01)
A61K 9/10	(2006.01)
A61K 31/55	(2006.01)
A61K 9/14	(2006.01)
A61K 9/20	(2006.01)
A61K 9/16	(2006.01)

(52) **U.S. Cl.**

CPC . ***A61K 47/32*** (2013.01); ***A61K 9/10*** (2013.01); ***A61K 9/146*** (2013.01); ***A61K 9/1623*** (2013.01); ***A61K 9/2018*** (2013.01); ***A61K 31/55*** (2013.01); *A61K 9/1652* (2013.01); *A61K 9/2054* (2013.01); *A61K 9/2077* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0051422	A1*	3/2006	Colombo et al.	424/486
2007/0218012	A1*	9/2007	Bittorf et al.	424/45
2008/0221047	A1*	9/2008	Yoshida et al.	514/29
2010/0233265	A1*	9/2010	Suzuki	424/487

FOREIGN PATENT DOCUMENTS

JP	11-021241	A	1/1999
WO	2008156217	A2	12/2008

OTHER PUBLICATIONS

Tiwari et al., "Solid Dispersions: An Overview to Modify Bioavailability of Poorly Water Soluble Drugs", 2009, vol. 1, No. 4, pp. 1338-1349.*

Kumar et al., "Enhancement of Solubility and Dissolution Rate of Irbesartan by Solid Dispersion Technique", 2011, Asian Journal of Pharmaceutical and Clinical Research, vol. 4, Issue 2, pp. 36-40.*

JP 1999-21241 English Translation.*

Int'l Search Report issued Sep. 8, 2011 in Int'l Application No. PCT/CN2011/075131.

* cited by examiner

Primary Examiner — Robert A Wax

Assistant Examiner — Randeep Singh

(74) *Attorney, Agent, or Firm* — Panitch Schwarze Belisario & Nadel LLP

(57) **ABSTRACT**

A tolvaptan solid dispersion and its preparation method are disclosed. The solid dispersion comprises tolvaptan and cross-linked polyvinylprrolidone at a weight ratio of 1:0.05-20, preferably 1:0.1-10, and more preferably 2:1. The solid dispersion can further comprise one or more water-soluble polymers, such as polyvinylprrolidone, hydroxypropyl cellulose, hydroxyethyl cellulose or methylcellulose, wherein the weight ratio of tolvaptan:the crosslinked polyvinylprrolidone:the water-soluble polymers is preferably 2:1:0.1. The solid dispersion exhibits good thermodynamic stability and solubility. The pharmaceutical composition thereof has improved release rate and bioavailability.

8 Claims, 3 Drawing Sheets