Journal of Crystallization Process and Technology
Journal Editorial Board

Editor-in-Chief
Prof. Alicia Esther Ares  National University of Misiones, Argentina

Editorial Board
Prof. Salah Aida  University of Constantine, Algeria
Prof. Arul C. Arjunan  Sinmat Inc., USA
Dr. Margarida Fardilha  University of Aveiro, Portugal
Dr. Majid Ghashang  Islamic Azad University, Iran
Prof. R. Gopalakrishnan  Anna University, India
Prof. Wen Lei  The University of Western Australia, Australia
Prof. Shu-Shen Lu  Sun Yat-sen University, China
Prof. Krishna C. Mandal  University of South Carolina, USA
Prof. Bouzid Menaa  Fluorotronics Inc., USA
Dr. Radoljub J. Ristic  University of Sheffield, UK
Prof. Camillo Rosano  National Institute for Cancer Research, Italy
Prof. Garth Simpson  Purdue University, USA
Prof. Vitalyi Igorevich Talanin  Zaporozhye Institute of Economics and Information Technologies, Ukraine
Prof. Rina Tannenbaum  University of Alabama at Birmingham, UK
Dr. Ramaiyer Venkatraman  Jackson State University, USA
Prof. Sunil Verma  Raja Ramanna Centre for Advanced Technology, India
Table of Contents

Volume 6  Number 1  January 2016

Crystal Type I of Azilsartan Polymorphs: Preparation and Analysis

Y. H. Ge, T. T. Li, J. J. Cheng

1
Journal of Crystallization Process and Technology (JCPT)

Journal Information

SUBSCRIPTIONS


Subscription rates:
Print: $69 per issue.
To subscribe, please contact Journals Subscriptions Department, E-mail: sub@scirp.org

SERVICES

Advertisements
Advertisement Sales Department, E-mail: service@scirp.org

Reprints (minimum quantity 100 copies)
E-mail: sub@scirp.org

COPYRIGHT

COPYRIGHT AND REUSE RIGHTS FOR THE FRONT MATTER OF THE JOURNAL:
Copyright © 2016 by Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY).
http://creativecommons.org/licenses/by/4.0/

COPYRIGHT FOR INDIVIDUAL PAPERS OF THE JOURNAL:
Copyright © 2016 by author(s) and Scientific Research Publishing Inc.

REUSE RIGHTS FOR INDIVIDUAL PAPERS:
Note: At SCIRP authors can choose between CC BY and CC BY-NC. Please consult each paper for its reuse rights.

DISCLAIMER OF LIABILITY

Statements and opinions expressed in the articles and communications are those of the individual contributors and not the statements and opinion of Scientific Research Publishing, Inc. We assume no responsibility or liability for any damage or injury to persons or property arising out of the use of any materials, instructions, methods or ideas contained herein. We expressly disclaim any implied warranties of merchantability or fitness for a particular purpose. If expert assistance is required, the services of a competent professional person should be sought.

PRODUCTION INFORMATION

For manuscripts that have been accepted for publication, please contact:
E-mail: jcpt@scirp.org
Its mechanism is the selective block of the binding of angiotensin II with receptor AT₁ and thus the resulting. It can be prescribed as a treatment for hypertension by itself or in combination with other anti-hypertension drugs, blood vessel constriction [1]. It does not function through the biosynthetic pathway of angiotensin II, thus avoids affecting the concentration of bradykinin as ACE inhibitors. Azilsartan has no common side effects such as dry cough [2].

Different types of crystals from the same drug can have different solubility and absorbility in our body and thus impact on its clinical efficacy and safety. Therefore, crystal types may directly affect the quality and efficacy of drugs. The study of the polymorphic crystal types of Azilsartan will facilitate the improvement of its stability during preparation and storage. The research will also help to improve the bioavailability and efficacy and to reduce toxicity [3].

Azilsartan is a white powder. Four types of crystalline powder have been reported with respective melting points (mp) of 122 - 123 (type III), 163 - 164 (type II), 180 - 181 (type IV), and 198°C - 206°C (type I) [4]-[6]. The preparation of type II and III crystals has been reported [4] [6]. Type II crystal is obtained from DMF and acetone; whereas type III crystal is from DMF and isopropanol. The preparation of type IV crystal from THF has also been reported [5]. However, only powder diffraction data for these crystal types have been reported and no single crystal diffraction data are available. Furthermore, the stability and solubility of these crystal types have not been carefully investigated.

We have obtained type I crystal of Azilsartan from methanol. The crystals melt at 198°C - 201°C and are not hydroscopic. The advantage of this method is the low toxicity of methanol solvent and thus the suitability for pharmaceutical application. We analyze the single crystal diffraction, measure the solubility of type I and II crystals in methanol with HPLC, determine their GT values under different temperatures, and compare their stability.

2. Experimental
2.1. Reagents and Instruments
All reagents were analytical pure grade and were used without further purification. Melting points were determined using microscopic melting point apparatus. Single crystal diffraction data were obtained with Enraf-Nonius CAD4 X-ray diffractometer. Powder diffraction data were obtained with Bruker D8-Discover X-ray diffractometer. DSC data were obtained with Mettler-Toledo differential scanning calorimeter (the rate of heating is 10°C/min).

2.2. Preparation of Azilsartan Type I and II Crystals
Type I crystal: Methanol (100 mL) was added to an Erlenmeyer flask containing Azilsartan (2 g) and the mixture was stirred for 30 minutes. Another 100 mL of methanol was added to obtain a clear solution. To another flask was added 30 mL of the above clear solution, added 0.1 g valine, 6 mL water, and 5 mL methanol. The mixture was stirred for 30 minutes to obtain a clear solution. After two weeks, colorless crystals (0.13 g, mp 198°C - 201°C) were obtained.

Type II crystal: Type II crystals were prepared as white powder (mp 164 - 166) according to reported.

2.3. Structural Determination of Azilsartan Type I Crystals
All data were obtained at 20°C under MoKa ray (λ = 0.71073 Å) and ω-scanning method. Structure was solved and refined with SHELXL-97. Single crystal diffraction data were summarized in Table 1.

2.4. Determination of the Solubilities of Azilsartan Type I and II Crystals in Methanol
Sample Preparation: The powdered crystals (0.5 g) were each added to a flask with 15 mL methanol. The mixture was heated to 55°C and the temperature was maintained for 1 hour. An aliquot (10 μL) of the solution was taken and mixed with 10 mL of the HPLC eluent (discussed below). This solution was further diluted with the same eluent (1 mL solution with 3 mL eluent) and filtered. The original sample solution in methanol was cooled to 50°C, 45°C, 40°C, 35°C and 30°C. Samples at each temperature were prepared in the same manner.

Measurement: Measurement was done at 253 nm using WUFENGLC100 HPLC with reverse phase C18 column, eluent acetonitrile: water: acetic acid (57:43:1 by volume), temperature 30°C, flow rate 1.0 mL/min [7].
Call for Papers

Journal of Crystallization Process and Technology (JCPT)

ISSN 2161-7678 (Print)  ISSN 2161-7686 (Online)
http://www.scirp.org/journal/jcpt

Journal of Crystallization Process and Technology (JCPT) is an Open Access journal accessible for free on the Internet. At Scientific Research Publishing (SCIRP), we guarantee that no university library or individual reader will ever have to buy a subscription or pay any pay-per-view fees to access articles in the electronic version of the journal.

Journal of Crystallization Process and Technology (JCPT) is an international, specialized, English-language journal devoted to publication of original contributions concerning with the crystallization process, studies and properties of the crystalline materials. It covers the basic sciences, engineering aspects and applied technology of crystals and crystallization processes, both the experimental and theoretical aspects including physical, chemical, and biological phenomena and processes related to the design, growth, and application of crystalline materials. The journal publishes original papers including but not limited to the following fields:

- Apparatus, Instrumentation and Techniques for Crystal Growth, and Purification Methods
- Biological Substances Crystallization
- Biomineralization
- Characterization by Physical and Chemical Methods
- Characterization of Single Crystals
- Crystal Growth of Metals
- Crystal Growth of Minerals
- Crystal Growth of Semiconductors
- Crystal Growth of Superconductors
- Crystallization as Bulk or Thin Films
- Crystallization in Glasses
- Crystallization in Polymers, Liquid Crystals Crystallization in Sol-Gel Glasses and Viscous Media
- Crystallization Processes Including among Others Chemical Vapor Deposition, Hydrothermal, Organic, Solvent and Solvent-Free Processes
- Crystals Growth, Design and Properties for Applications in Medical Sciences with Organic
- Directional Growing
- Intermolecular Interactions in the Solid State
- Modeling of Crystal Growth Processes
- Nucleation Theory
- Opto-Electronics with Semiconductors, Superconductors, Magnetics, Inorganic Inorganic-Orgnic Hybrid Materials Crystallization
- Purification Methods
- Transport Phenomena in Crystal Growth

Notes for Intending Authors

Submitted papers should not have been previously published nor be currently under consideration for publication elsewhere. Paper submission will be handled electronically through the website. All papers are refereed through a peer review process. For more details about the submissions, please access the website.

Website and E-Mail
http://www.scirp.org/journal/jcpt   E-mail: jcpt@scirp.org
What is SCIRP?
Scientific Research Publishing (SCIRP) is one of the largest Open Access journal publishers. It is currently publishing more than 200 open access, online, peer-reviewed journals covering a wide range of academic disciplines. SCIRP serves the worldwide academic communities and contributes to the progress and application of science with its publication.

What is Open Access?
All original research papers published by SCIRP are made freely and permanently accessible online immediately upon publication. To be able to provide open access journals, SCIRP defrays operation costs from authors and subscription charges only for its printed version. Open access publishing allows an immediate, worldwide, barrier-free, open access to the full text of research papers, which is in the best interests of the scientific community.

- High visibility for maximum global exposure with open access publishing model
- Rigorous peer review of research papers
- Prompt faster publication with less cost
- Guaranteed targeted, multidisciplinary audience

Website: http://www.scirp.org
Subscription: sub@scirp.org
Advertisement: service@scirp.org