Available online at www.sciencedirect.com
SCIENCE DIRECT®
International Journal of Pharmaceutics 291 (2005) 59–68
international journal of pharmaceutics
www.elsevier.com/locate/ijpharm

Physical characterization of pantoprazole sodium hydrates

V. Zupančič[a], N. Ograjšek[a], B. Kotar-Jordan[b], F. Vrečer[b,*]

[a] *Krka d.d., Novo mesto, Product Supply, Šmarješka cesta 6, 8501 Novo mesto, Slovenia*
[b] *Krka d.d., Novo mesto, R&D Division, Šmarješka cesta 6, 8501 Novo mesto, Slovenia*

Received 2 February 2004; received in revised form 9 June 2004; accepted 24 July 2004
Available online 29 December 2004

Abstract

Only two crystal forms of pantoprazole sodium, i.e. mono and sesquihydrate, were described in the literature. The objective of the present work was to study the polymorphisms and pseudopolymorphism of pantoprazole sodium and to characterize already known and new crystal forms.

Two additional hydrate forms; i.e. form A, form B and amorphous form were obtained and further characterized by means of thermal analyses, X-ray powder diffraction (XRPD), mid-infrared spectroscopy (IR), near infrared spectroscopy (NIR), Raman spectroscopy, dynamic vapour sorption (DVS), true density, contact angle and solubility. From the results it can be concluded, that the most physically stable form of pantoprazole sodium is form B, whereas form A is the least stable form. Monohydrate and form A are not physically stable and convert into form B from saturated solution/suspension or at high relative humidity. Amorphous form can be obtained by conventional spray drying method or by distillation of solvent under reduced pressure.
© 2004 Elsevier B.V. All rights reserved.

Keywords: Pseudopolymorphism; Thermal analysis; Infrared spectroscopy; X-ray powder diffraction; Dynamic vapour sorption; Physical characterization

1. Introduction

Many pharmaceutical substances exhibit polymorphism and pseudopolymorphism. The former is frequently defined as the ability of substance to exist in two or more crystalline phases that have different arrangement of the molecules in the crystal lattice. As a result, the polymorphic solids have different unit cells and hence display different physical properties (such as melting point, solubility, dissolution rate, physical and chemical stability, hygroscopicity, density) including those due to packing, and various thermodynamic, spectroscopic, interfacial and mechanical properties (Grant, 1999; Kristl et al., 1996).

The term pseudopolymorphism relates to the phenomenon of incorporation of solvent molecules into crystal lattice or crystal interstitial voids. When water is incorporated in the crystal lattice the term

* Corresponding author. Tel.: +386 7 33 13 790; fax: +386 7 33 13 751.
E-mail address: franc.vrecer@krka.biz (F. Vrečer).

0378-5173/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijpharm.2004.07.043

hydrate is used. The differences between polymorphs and hydrates are significant. The basis for all these differences is that polymorphs are different crystal structures of the same molecule while hydrates are crystals of drug molecule with incorporated different numbers of water molecules (Halebian, 1975). Members of both polymorphic and hydrate systems have different crystal structures and exhibit different X-ray powder diffraction patterns, thermograms (DSC, TGA), infrared spectra, dissolution rates, hygroscopicity, etc. (Morris, 1999; Brittain, 1999).

It is known that in general water solubility of hydrates is lower than that of anhydrous forms and decrease while increasing the degree of hydration (Brittain and Grant, 1999; Kristl et al., 1996). Monohydrates are the most frequent among the hydrates (Threlfall, 1995).

Hydrates can be according to mechanism of bonding of water molecules divided into three types (Morris, 1999):

1. Isolated lattice site water: water molecules are separated by drug and are not in contact with each other.
2. Lattice channel water: water molecules are in channels formed in the interior of the crystal.
3. Metal ion coordinated water: these types of hydrates are connected/linked to the metal salts of weak organic acids where metal ions are coordinated with water molecules.

On the other hand Bryn (Bryn, 1982) has divided hydrates into polymorphic and pseudopolymorphic types. In polymorphic hydrates, dehydration is associated with a change in the X-ray diffractogram (change of the crystal structure), which is not the case in the pseudopolymorphic hydrates. Another difference between the polymorphic and pseudopolymorphic hydrates is rehydration. In pseudopolymorphic hydrates, rehydration takes place immediately after contact with water, while in the polymorphic hydrates, only after a phase change (Vrbinc and Vrečer, 2002; Kristl et al., 1996; Bryn, 1982).

The behavior of hydrates has become the subject of increasing attention over the last decade, primarily due to the potential impact of hydrates in the development process and dosage form performance (Carstensen, 2001). Hydrates may hydrate/dehydrate in response to changes in environmental conditions, processing or over time if they are in a metastable thermodynamic state. In order to prevent problems associated with changes in the crystal form of drugs or excipients during the production and storage of raw materials and finished products polymorphism and pseudopolymorphism should be investigated during the predformulation phase of development (Morris, 1999).

Pantoprazole sodium, a substituted benzimidazole derivative, is an irreversible proton pump inhibitor, and was developed for the treatment of acid-related gastrointestinal disorders (Reiter et al., 1991).

Examination of the literature confirmed that only two hydrate forms (monohydrate, sesquihydrate) are known and commercially available on the market (Badwan et al., 2002).

The aim of the present study was to obtain new crystal forms of pantoprazole sodium and to perform detailed characterization of pantoprazole sodium crystal forms, i.e. already known mono- and sesquihydrate and new ones.

2. Materials and methods

2.1. Materials

Pantoprazole sodium (5-(difluoromethoxy)-2-(((3,4-dimethoxy-2-pyridinyl) methyl)sulphinyl)-1H-benzimidazole sodium) monohydrate and sesquihydrate were obtained from Aurobindo (India).

Form A was prepared by crystallization from saturated solution in water free organic solvents such as ethyl acetate.

Form B was obtained by precipitation from saturated solution of monohydrate or form A in borate buffer solution (pH 9).

Amorphous form was obtained either by lyophillization of pantoprazole sodium solution in water or by spray drying of pantoprazole sodium sesquihydrate solution in absolute ethyl alcohol on Büchi 190 Mini Spray Dryer using following parameters: air flow rate, 800 ml/min; inlet air temperature 80 °C and outlet temperature 45 °C. Amorphous form was also obtained by distillation of solvent under reduced pressure from pantoprazole sodium solution in water free organic solvents such as: acetone, ethylacetate, isopropanol, chlorophorm or ethyl alcohol.

Download English Version:

https://daneshyari.com/en/article/9918928

Download Persian Version:

https://daneshyari.com/article/9918928

Daneshyari.com