Available online at www.sciencedirect.com
ScienceDirect
Advanced Drug Delivery Reviews 60 (2008) 328–338
Advanced DRUG DELIVERY Reviews
www.elsevier.com/locate/addr

Supercritical carbon dioxide processing of active pharmaceutical ingredients for polymorphic control and for complex formation ☆

Kunikazu Moribe [a], Yuichi Tozuka [b], Keiji Yamamoto [a,*]

[a] Graduate School of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan
[b] Department of Pharmaceutical Engineering, Gifu Pharmaceutical University, 5-6-1 Mitahora-Higashi, Gifu 502-8585, Japan

Received 2 October 2006; accepted 27 March 2007
Available online 5 October 2007

Abstract

Supercritical fluid technique have been exploited in extraction, separation and crystallization processes. In the field of pharmaceutics, supercritical carbon dioxide ($scCO_2$) has been used for the purpose of micronization, polymorphic control, and preparation of solid dispersion and complexes. Particle design of active pharmaceutical ingredients is important to make the solid dosage forms with suitable physicochemical properties. Control of the characteristic properties of particles, such as size, shape, crystal structure and morphology is required to optimize the formulation. For solubility enhancement of poorly water-soluble drugs, preparation of the solid dispersion or the complexation with proper drugs or excipients should be a promising approach. This review focuses on aspects of polymorphic control and complexation behavior of active pharmaceutical ingredients by $scCO_2$ processing.
© 2007 Elsevier B.V. All rights reserved.

Keywords: Supercritical carbon dioxide; Active pharmaceutical ingredient (API); Polymorph; Complex

Contents

1. Introduction

A number of interesting properties are associated with the critical state. One of these is that the density of the liquid and of the vapor become identical, and for this reason the meniscus, the interface between the two phases, disappears. A second property of the critical state, which can be predicted from the kinetic

☆ This review is part of the *Advanced Drug Delivery Reviews* theme issue on "Drug Delivery Applications of Supercritical Fluid Technology".

* Corresponding author. Tel.: +81 43 290 2937; fax: +81 43 290 2939.
E-mail address: yamamotk@p.chiba-u.ac.jp (K. Yamamoto).

0169-409X/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.addr.2007.03.023

theory of gases, is that the intermolecular van der Waals forces of the liquid and the vapor must be identical. Actually the constants appearing in the van der Waals equation of state for a real gas can be evaluated from the critical constants, i.e., critical pressure, critical temperature and critical volume [1].

During the past decade, interest regarding the supercritical state has increased significantly because of its importance in a variety of fields, including synthetic chemistry, environmental chemistry, analytical chemistry, material science, food industry, and powder technology [2,3]. Particularly, its characteristics have been exploited in extraction, separation and crystallization processes [4].

It is an important mission of the pharmaceutical industry to design and produce effective, stable, uniform and safe dosage forms that contain exact quantities and qualities of active pharmaceutical ingredients. The quality of a product is strongly related to and influenced by its design in research and development. The quality depends on the inter-relationship of many factors besides the active substance in a dosage form. Without considering physicochemical characteristics of the materials and manufacturing processes for the product, it would be impossible to establish the specifications required to assure product uniformity [5].

Active pharmaceutical ingredients may exist in numerous solid forms that may feature different physical and chemical properties [6,7]. These solid forms include polymorphs, solvates, desolvates and amorphous solids. Different solid forms of a given compound have different properties such as melting point, solubility, stability and bioavailability. Byrn et al. reported a conceptual approach to the characterization of pharmaceutical solids generally encountered [8]. They developed flow charts which describe approaches to regulatory issues for polymorphs, solvates, desolvated solvates and amorphous forms. The successful utilization of a solid form may provide greater therapeutic effect. On the other hand, the existence of unrecognized, multiple modifications in a particular formulation may possibly result in unacceptable dose-to-dose variations. Distinct solid forms can be prepared by precipitation, evaporation, milling, freeze drying, spray drying, and many other unit processes including supercritical technology.

Numerous attempts have been made to improve dissolution behavior and to enhance bioavailability of poorly water-soluble drugs, including the use of solid dispersions, complex formation and inclusion compound formation, as well as micronization [9]. The approach of solid dispersion was first demonstrated by Sekiguchi and Obi, using a eutectic mixture of sulfathiazole and urea [10]. Inclusion compounds have also been developed for the modification of solubility, stability, prevention of irritative action to gastrointestinal tracts and volatility depression. It is believed that pharmaceutical technology will play an important role in preparing these high potential solid systems for future dosage forms.

In this review, an attempt is made to review the current pharmaceutical literature on supercritical technology concerning crystal modification and complex formation of active pharmaceutical ingredients.

2. Crystal modification of active pharmaceutical ingredients by supercritical carbon dioxide treatment

Particle design of active pharmaceutical ingredients (APIs) is important to make the solid dosage forms with suitable physicochemical properties. Control of the characteristic properties of particles, such as size, shape, crystal structure and morphology are required to optimize the formulation. For example, polymorphic form of solid pharmaceuticals influences the dissolution properties and stabilities of solid dosage forms. Since the bioavailability of orally applied drugs depends on the rate of dissolution and absorption, the polymorphic control is necessary to achieve significant levels of APIs in the blood [11–13].

Supercritical fluid technology is a relatively new approach to obtain micro/nanoparticles. For pharmaceutical applications, supercritical carbon dioxide ($scCO_2$) is most widely used because of its low and easily accessible critical temperature (31.2 °C) and pressure (7.4 MPa), non-flammability, non-toxicity and inexpensiveness [11,14]. Several supercritical fluid techniques have been used for micronization of drugs. Many APIs can be dissolved or liquefied in $scCO_2$ before being sprayed through a nozzle upon depressurization to produce fine drug particles. This can be achieved with solvent techniques such as the rapid expansion of supercritical solutions (RESS) and particles from gas-saturated solutions (PGSS) [14–17]. High supersaturation of drug in $scCO_2$, which contributes to the particle size reduction, is obtained by the RESS process. Alternatively, $scCO_2$ can be used as an antisolvent for the precipitation of drugs already dissolved in organic solvents. Gas or supercritical antisolvent (GAS or SAS) techniques, solution-enhanced dispersion by supercritical fluids (SEDS), and aerosol solvent extraction systems (ASES) are all variations of the antisolvent approach [11,14–16].

Since many reviews [11,14–16,18–22] have been published on micronization of active pharmaceutical ingredients using $scCO_2$, this review focused on aspects of polymorphism in APIs prepared using supercritical fluid techniques.

2.1. Polymorphism and polymorphic transformation

Active ingredients and excipients can exist as different solid phases classified as polymorphs, pseudopolymorphs (solvates and hydrates), and amorphous [23–29]. Polymorphs have the same chemical composition but differ in crystal structure. This arises from different crystal packing and/or different molecular conformations. The pseudopolymorph is a crystalline adduct containing solvent molecules (water in hydrates) within the crystal structure. Unlike polymorphs, amorphous materials have disordered arrangements of molecules. The decrease of crystallinity causes an increase in the surface energy, leading to lower stability and higher reactivity, including dissolution. Because of the different crystal lattice energy, polymorphs show different thermodynamic, spectroscopic and surface properties. Less stable form of polymorphic pairs shows higher solubility and dissolution rate in spite of the lower physical and chemical stability.

From a thermodynamic point of view, a less stable polymorph converts to the more stable one. The polymorphic transformation

Download English Version:

https://daneshyari.com/en/article/2071967

Download Persian Version:

https://daneshyari.com/article/2071967

Daneshyari.com