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Nimesulide adsorbed on silica aerogel using supercritical carbon dioxide

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ABSTRACT

Silica aerogel (SA) was loaded with nimesulide, a drug model compound, to demonstrate the potentiality of adsorption processes based on the usage of supercritical carbon dioxide to treat poorly water-soluble drugs, forming new kinds of drug delivery systems. Adsorption isotherms and kinetics were measured and described by models. The effect of pressure, temperature and solution concentration on loaded SA were also studied. Modelling of kinetic data showed that the sorption process was best described by a pseudo-second-order model. The adsorption isotherm data were best fitted by the Freundlich isotherm. The drug/SA composites were characterized using scanning electron microscopy, X-ray microanalysis, and FT-IR. Release kinetics of the adsorbed drug were also evaluated by in vitro dissolution tests. Results showed that nimesulide can be uniformly dispersed into the aerogel and that the release rate of nimesulide from the composite, constituted by drug and silica aerogel, is much faster than that of the crystalline drug.

Keywords: Silica aerogel; Adsorption; Nimesulide; Drug delivery systems; Adsorption mechanisms

1. Introduction

The poor water solubility of some drugs limited their bioavailability. To improve the dissolution rate of drugs, different techniques have been developed (Pinnamaneni et al., 2002). The most common approach is based on particle size reduction that can be achieved by processes based on micronization or nanosuspension. Each technique utilizes different equipments for the reduction of the particle size (Chaumeil, 1998; Patravale et al., 2004). An alternative way to improve the availability of a drug is its dispersion on a biocompatible substrate (Hillery et al., 2001). Silica based materials used as substrate are widely employed as additives, free flow agents and drug carriers also in commercial products. A special class of silica materials are silica aerogels (SA). They are low density nanoporous solids with a fine open-pore structure that exhibit unique properties, such as high porosity (90–99%), high surface area (400–1000 m^2/g), extremely low density (0.003–0.15 g/cm^3). These properties allow them to be used as host matrix for drug delivery. Silica aerogels were recently shown to be a potential candidate for oral drug delivery systems (Smirnova et al., 2004, 2005; Guenther et al., 2008).

A promising method to adsorb a drug into porous substrates is supercritical (SC) deposition or adsorption (Smirnova et al., 2003, 2004, 2005; Caputo et al., 2010). Essentially, the process involves the dissolution of the active molecules in a supercritical fluid (SCF) and the impregnation of the substrate by its exposure to this solution. Supercritical carbon dioxide (SC-CO_2) is commonly used due to its relatively good solvent power for various drugs, mild critical temperature (31 °C), low critical pressure (74 bar) and inertness. After the removal of the SCF by expansion, a drug-loaded matrix free of solvent residues is obtained. This method takes advantage of the unique properties of SCFs. A SCF possesses a unique combination of gas-like and liquid-like properties, that can be adjusted by small changes in temperature or pressure.

Its low viscosity and high diffusivity allow a rapid equilibration and micropore penetration of the fluid phase within the matrix. SCFs also have zero surface tension that not only facilitates the rapid permeation and diffusion into porous substrates, but also avoids the pore collapse of SA that occurs using organic liquids, due to capillary stresses caused by the liquid–vapour menisci within pores.

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