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Effect of temperature, pressure and depressurization rate on release profile of salicylic acid from contact lenses prepared by supercritical carbon dioxide impregnation

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ABSTRACT

Supercritical CO_2 was used for the impregnation of a contact lens with salicylic acid. The supercritical CO_2 impregnations were conducted at 308, 313 and 318 K from 9.0 to 15.0 MPa. The effects of the temperatures and pressures in the impregnation processing on the loaded amount of salicylic acid in the contact lenses were investigated. The loaded amounts of salicylic acid increase with the decrease of temperature and increase of pressures. It is found that the loaded amounts of salicylic acid in the lenses are correlated with the solubilities in supercritical CO_2. The release profile of the salicylic acid from the contact lenses into the aqueous solution at 310 K for 8 h was studied by the released amounts measured using ultraviolet-visible spectroscopy. The higher temperature and lower pressure in the impregnation processing lead to the slow release rate of salicylic acid from the contact lenses. The release profiles were investigated by changing the depressurization rate from 0.06 to 0.18 MPa min^{-1}. The lower depressurization rate results in the higher release rate of the salicylic acid from the lenses. The release profile of salicylic acid from the lenses into the aqueous solution is modeled by using kinetic constant and release exponent parameter. The modeled results suggest that the release from the lenses occurred by the superimpositions of Fickian controlled and swelling controlled releases.

1. Introduction

Polymer composite with drug have been developed and attracted much attention as a potential drug delivery system in order to sustain drug releasing and reduce the drug dosage required for the therapeutic effect. The drug delivery system based on polymer-drug composite is prepared by the incorporation of drug into the matrix of polymer using organic solvent (Pingnatello et al., 2002; Nair et al., 2012). Drying is required for the removal of solvent from the polymer in preparation of the polymer-drug composite. The limitations of the preparation of the polymer-drug composite are the residual solvent and drying that may decompose the thermolabile drugs.

Some research groups of (Braga et al., 2008, 2011; Costa et al., 2010a,b) has applied supercritical CO_2 as solvent for the impregnation of the polymer with drugs due to the unique properties, such as the low surface tension, high diffusivity and non-toxic to human body. In supercritical CO_2 process, CO_2 is separated from the prepared polymer-drug composite easily by only the depressurization without heating. The impregnations of the chitosan derivatives with flurbiprofen and timolol maleate have been conducted by supercritical

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solvent impregnation using CO_2 and CO_2 + ethanol mixture (Braga et al., 2008). The several species of the commercial contact lenses were used in the supercritical solvent impregnation (Costa et al., 2010a). The effects of the operation conditions of the impregnation on the release profile of the ophthalmic drugs were investigated. The silicone-based contact lenses were used for the impregnation in the supercritical solvent impregnation using CO_2 + ethanol and CO_2 + water mixtures (Costa et al., 2010b; Braga et al., 2011). Masmoudi et al. (2011) also studied the impregnation of the commercially available lenses with cefuroxime sodium in CO_2 + ethanol mixture. These studies concluded that the supercritical solvent impregnation would be a tunable process for the preparation of the contact lenses with drug. The loaded drug amount in the lenses can be controlled easily by changing the operation conditions during the supercritical solvent impregnation. It is very important for the process design of the supercritical solvent impregnation to understand the mechanism of the impregnation with drug in supercritical CO_2. The relationship between the impregnation condition and the drug release mechanism from the contact lenses prepared by the supercritical solvent impregnation can be a fundamental and potential knowledge to achieve the controlled release of the ophthalmic drugs.

In this work, we investigated the effects of the temperatures, pressures and depressurization rates in the supercritical solvent impregnation on the loaded amount of salicylic acid in Hilafilcon B, a commercial contact lens and the release profile of salicylic acid from the lenses. Salicylic acid in Fig. 1 was used as a model substance in this work due to inexpensive compound compared with anti-inflammatory and ophthalmic drugs. Also, salicylic acid molecule has the aromatic ring and carboxy group that are contained in the molecular structure of anti-inflammatory drug, such as flurbiprofen (Pingnatello et al., 2002) and dexamethasone (Kim et al., 2010) and ophthalmic drugs, such as ofloxacin (Yamazaki et al., 2013) and norfloxacin (González-Chomón et al., 2012). Hilafilcon B used in this work contains the monomer units of 2-hydroxyethyl methacrylate and methacrylic acid, cross-linker ethyleneglycol dimethacrylate and *N*-vinylpyrrolidone (Yañez et al., 2011). It is thought that the carboxy groups in salicylic acid makes the interaction with the monomer units, 2-hydroxyethyl methacrylate, methacrylic acid and the cross-linker, ethyleneglycol dimethacrylate in Hilafilcon B as well anti-inflammatory and ophthalmic drug molecules. The loading amount of salicylic acid in Hilafilcon B was discussed using the solubility of salicylic acid in supercritical CO_2. The release profile of salicylic acid from Hilafilcon B prepared in supercritical CO_2 into the aqueous solution is also studied. The effects of temperature, pressure and depressurization rate on the release profile were discussed by using a theoretical model with kinetic constant and release exponent parameter.

2. Experimental

2.1. Chemicals

Hilafilcon B, commercial soft contact lenses (SCLs) from Bausch & Lomb®, Medalist® One-Day Plus (Group 2 SCL, 59 wt% water content, 8.6 mm base curve, −0.25 D power, 14.2 mm diameter) was used. Hilafilcon B was in soaking solution for a commercial soft contact lens including sodium chloride and poloxamine. Salicylic acid was purchased from Wako Pure Chemical Industries, Ltd. The purity was higher than 99.5%.

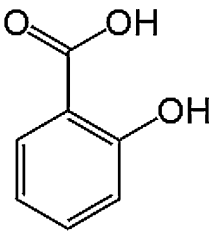

Fig. 1 – Salicylic acid.

Carbon dioxide was supplied from Fujii Bussan Co. Ltd. The purity was higher than 99.95%. Phosphate buffer solution with pH 6.86 from Wako Pure Chemical Industries, Ltd. was used as a solvent for salicylic acid release. Ultrapure water was also supplied from Wako Pure Chemical Industries, Ltd. and used as the medium for aqueous solution impregnation.

2.2. *Preparation of hilafilcon B composite with salicylic acid*

2.2.1. *Supercritical CO_2 impregnation*

A schematic diagram of the experimental apparatus is shown in Fig. 2. This apparatus is composed of a CO_2 supply part, a high-pressure cell and a trap part. The high-pressure cell was immersed in an air bath for controlling the desired temperature within ±0.1 K. The deviation of the pressure in the system during the impregnation was ±0.1 MPa. The volume of high-pressure cell was 170 ml, and the inside of the cell was partitioned into two parts by a petri dish. Three pieces of Hilafilcon B in 14.2 mm diameter wetted with the soaking solution for a commercial soft contact lens were set inside of the dish horizontally and the known amount of salicylic acid was set outside of the dish. The amount of salicylic acid introduced into the high-pressure cell was 0.088–0.700 g that was much greater than the saturated solubility in supercritical CO_2 at the experimental temperatures and pressures 0.084–0.66 g L^{-1} (Gurdial and Foster, 1991). The petri dish was covered with a stainless steel mesh (0.2 mm of mesh size) not to contact salicylic acid directly to the surface of Hilafilcon B. Carbon dioxide from a gas cylinder was liquefied through a cooling unit. The liquefied CO_2 was pressurized and supplied to the system by a feed pump. A back-pressure regulator was used for

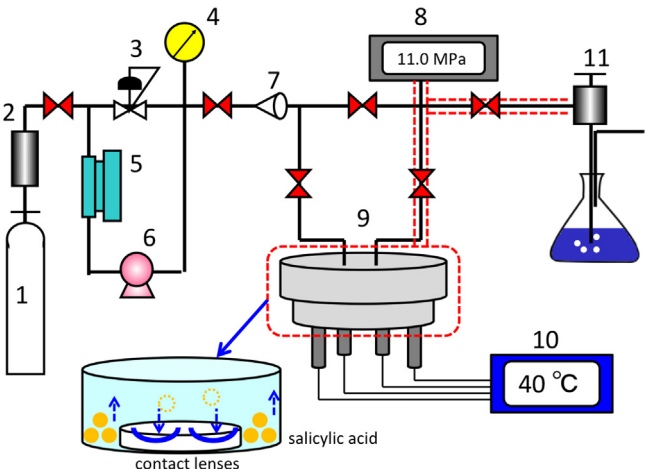

Fig. 2 – Supercritical CO_2 impregnation apparatus. (1) CO_2 bottle; (2) dryer; (3) back pressure regulator; (4) pressure gauge; (5) cooling bath; (6) feed pump; (7) check valve; (8) pressure gauge; (9) high-pressure cell; (10) temperature control unit; (11) depressurization valve.