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Fabrication and application of porous silicon multilayered microparticles in sustained drug delivery

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ABSTRACT

In the present study, the ability of porous silicon (PSi) based distributed Bragg reflector (DBR) microparticles for sustained and observable delivery of the antiviral agent acyclovir (ACV) is demonstrated. DBR was fabricated by electrochemical etching of single crystal silicon wafers and ultrasonic fractured to prepare microparticles. The hydrogen-terminated native surface of DBR microparticles was modified by thermal oxidation and thermal hydrosilylation. Particles were loaded with ACV and drug release experiments were conducted in phosphate buffered saline. Drug loading and surface chemistry of particles were characterized by scanning electron microscopy and Fourier transform infrared spectroscopy. Drug release profiles from PSi DBR particles show sustained release behavior from all three studied surface chemistries. Drug release from particles was also monitored from change in color of particles.

1. Introduction

Porous silicon (PSi) based sustained drug delivery systems has shown growing interest in recent years owing to its highly tunable pore size, porosity, and thickness, high surface area to volume ratio, chemically functionalizable surface, biocompatibility, and biodegradability [1–4]. PSi single- and multilayer structures can be prepared by electrochemical etching of single crystal silicon wafers in

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hydrofluoric acid based electrolytes. Distributed Bragg reflector (DBR), microcavity, and rugate filter are PSi multilayer structures which can be easily designed by varying etching parameters such as current density and etching time [5–8]. PSi multilayer structures tender dual advantages of drug loading into porous matrix and drug release monitoring in real time using its optical properties [9]. PSi rugate filter has been prepared and its feasibility for intraocular drug delivery application has been studied [10]. These PSi multilayer rugate structure microparticles showed good biocompatibility in rabbit eye without any toxicity [10]. In addition, PSi rugate filter was fabricated and utilized for anthracycline drug daunorubicin delivery applications. Drug release was obtained for 30 days in a linear and sustained fashion in phosphate buffered saline solution and change in color of particles was observed as drug releases from particles [9]. DBR films and particles were fabricated for smart patch and drug delivery applications, respectively [11,12], and apart from these two studies, not much details on drug delivery applications using DBR are reported. Furthermore, a detailed study on effect of different surface chemistries of DBR on drug loading and release have not been carried out.

DBR is one-dimensional photonic crystal composed of a stack of alternating layers of two different refractive indices (n_1,n_2) and thicknesses (L_1,L_2). DBR exhibits high reflectivity band called photonic bandgap at Bragg wavelength λ_{Bragg}, as following:

$$\frac{\lambda_{\text{Bragg}}}{4} = n_1 L_1 = n_2 L_2 \tag{1}$$

PSi single layer micro- and nanoparticles have been prepared for the controlled delivery of acyclovir (ACV) [13]. However, multilayer PSi DBR microparticles have not been exploited yet as a possible ACV delivery carrier. ACV is one of the most effective drugs against herpes simplex virus and has also shown anti-cancer and anti-hepatitis B virus activity [14,15]. Herpetic infections including systemic, epidermal, and ocular are currently treated using capsules, tablets, suspension, and topical ointment of ACV. Unfortunately, current use of ACV is associated with many drawbacks, for example, low bioavailability (10–20%), variable and incomplete absorption in the gastrointestinal tract and short plasma half-life. Moreover, frequent drug administration is required which is associated with systemic toxicity [16,17].

PSi DBR microparticles were prepared by ultrasonic fracture of freestanding films. PSi particles with native surface were modified by thermal oxidation (TOPSi) and thermal hydrosilylation with undecylenic acid (UnPSi). ACV was loaded into microparticles by physical adsorption and covalent attachment. Surface chemistry and ACV loading of particles were characterized using Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM). *In vitro* drug release experiments were conducted in phosphate buffered saline and amount of drug released was measured by UV–VIS spectrometry. In addition, color change of the particles was monitored by optical microscope in order to develop observable drug delivery system.

2. Experimental

2.1. Fabrication of PSi DBR

PSi DBR samples were prepared by electrochemical etching of highly boron-doped p^+ type (1 0 0) silicon wafers (resistivity of 0.01–0.02 Ω cm). The etching solution consisted of a 1:2 (v/v) hydrofluoric acid (40%) and ethanol (99.9%). Silicon wafer was mounted on Teflon etch cell, and current was supplied by programmable power source. DBR was fabricated by applying periodic square wave current between 10 mA cm^{-2} for 11 s and 50 mA cm^{-2} for 5.2 s with 20 repeats. The resulting PSi DBR films were removed from the silicon substrate by electropolishing with current density of 6 mA cm^{-2} for 120 s in 1:29 solution of hydrofluoric acid based electrolytes. The etching and electropolishing procedure was repeated five times per wafer, and the resulting films were then placed in ethanol to prepare particles.

2.2. Preparation of PSi DBR microparticles

PSi DBR films in ethanol were fractured by ultrasonication (Elma Transsonic TI-H5 MF2, USA) with frequency of 45 kHz and 100 W power for 10 min to prepare PSi microparticles. Thermal oxidation of