Powder embossing method for selective loading of polymeric microcontainers with drug formulation

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Powder embossing method for selective loading of polymeric microcontainers with drug formulation

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Abstract

The present study introduces powder embossing as a novel method to enhance loading of polymeric microcontainers with drug. With current loading approaches, it is not possible to handle pure powder drug in a scalable, homogenous and reproducible manner. In this work, we demonstrate simultaneous loading of 625 microcontainers with powder formulation. This is achieved in a single step by aligning a shadow mask prepared by micro-milling to an array of microcontainers in order to limit drug deposition to the container cavities with diameters of 220 µm. A pressure of 8.9 MPa is applied by a bonding press and thereby the desired powder is embossed into the container cavities. Powder in the form of pure drug, lipid-based microparticles, and pure polymer was successfully loaded with minimal residues in between the microcontainers and with 100% loaded cavities demonstrating the versatility of the method. The current work is thus contributing to the loading of powder formulations into microscale drug delivery systems such as microcontainers in a facile and reproducible manner.

Keywords: Microcontainers, shadow mask, micro-milling, drug delivery systems, microtomography, oral drug delivery

1 Introduction

In recent years, microfabricated devices have been proposed as advanced drug delivery systems [1][2][3]. Microfabrication methods allow the definition of devices with well-defined geometry and size containing a precise amount of drug in each unit and enabling controlled release. In particular, microcontainers have been presented as promising new advanced oral drug delivery systems with the potential to significantly enhance the bioavailability of drugs[4][5][6]. These microcontainers consist of walls and a bottom defining a drug reservoir with a volume in the pL to nL range. In contrast to the traditional oral drug delivery systems such as tablets, microcontainers provide a larger surface to volume ratio. This, in some cases combined with the integration of mucoadhesive features, promotes attachment of the drug delivery systems to the intestinal mucosa and a unidirectional drug release due to a cavity open only on one side [7]. Due to their small dimensions, one of the major challenges is to load drug into the microcontainers. A suitable method has to avoid damaging the drug while achieving a homogeneous and reproducible loading.

In the past, various methods for drug loading into microcontainers have been proposed. Ainslie et al. proposed UV crosslinking of hydrogel matrices with drug. However the amount of drug that can be loaded with this approach is very restricted [8][3]. Alternatively, hot punching in a spin-coated drug-polymer film or supercritical impregnation of microcontainers filled with polymer by inkjet-printing were demonstrated [9][10]. In all these methods, solubility of the drug in the polymer matrix is required. Furthermore, the polymer matrix itself will occupy a considerable part of the container volume thereby reducing the amount of drug that can be loaded.

Typically, drugs are available as powder acquired from commercial suppliers or prepared by spray drying and it is relevant to develop a technique where pure powder drug can be loaded into the microcontainers.

In the existing powder filling method for polymeric microcontainers [11], the powder is manually deposited on the microcontainers and compacted with a spatula. The residual amount of drug between the containers is blown away with pressurized air. This method is not applicable for sticky powder such as spray-dried lipid-based microparticles. Moreover, this method provides irreproducible loading and results in considerable waste of drug due to the use of pressurized air both removing powder in-between but often also from the upper part of the container reservoir.

Here, we present an improved method for loading microcontainers with powder formulation. This is achieved by clamping a shadow mask between arrays of microcontainers followed by embossing of the desired powder formulation into the cavities of the microcontainers. The overall concept is illustrated in figure 1.