Inkjet printing as a novel drug loading technique of micro-containers

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Inkjet printing as a novel drug loading technique of micro-containers

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Purpose

We present an innovative technique to dispense precise amounts of drug solutions into large arrays of microscopic wells as an oral drug delivery device.

Introduction

Micro-containers are designed as a confinement of micro-doses of active ingredient to be delivered through the oral route [1]. Drugs of interest are those with a low solubility in the intestinal fluid, and those fragile molecules that need a protection against low pH and enzymatic degradation. Furosemide as been chosen as a test drug with a poor solubililty in water.

Ink-jet printing is a recent technology commonly used in the field of biosensing and polymer processing [2]. In this work it has been used to prepare micro doses of active pharmaceutical ingredient for the oral administration.

Materials and Methods

Micro-containers are fabricated with a cylindrical shape with an photoresist with two steps of negative photo-lithography. Cavity diameters go from 300 μm down to 50 μm. A SEM picture of a micro-well can be seen in figure 1.

A nano-plotter (NP 2.1, GeSim), designed to spot micro-arrays of water-based solutions, has been used to dispense in pico-liter quantities a solution of 5 mg/ml of furosemide in an ethanol-DMSO mixture of (50/50) into micro-containers cylindrical cavities.

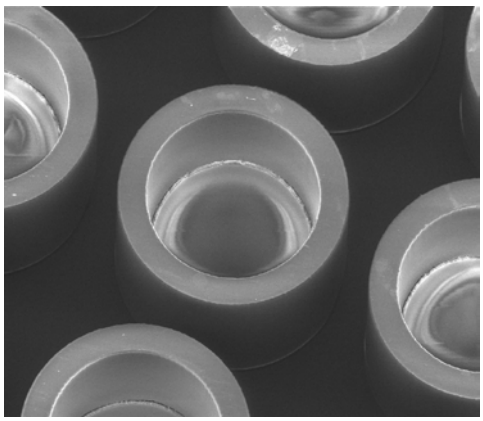

Fig. 1: Microcontainers of 300 μm in diameter

Fig., 2: Top view of an array of micro wells filled with dried furosemide solution

Results and discussion

Ink-jet printing has been shown to be a suitable technique to dispense defined volume of solution in a high reproducible way [3], which is a crucial parameter in order to control, for instance, the dose in a pharmaceutical product. The alignment of pipette and micro-containers is performed with a microscope either manually or with a structure recognition program. The pipette head can be programmed to spot large arrays and complex patterns. Regularity in the spatial distribution of spots has been optimized by tuning spotting parameters (voltage, pulse-width and frequency of the signal applied to piezo-pipette). Dispensable volume goes from 0.3 to 2 nanoliters and by means of stroboscope imaging, droplet volume and shape can be tuned. The solution is soaked in and spurted out by means of a pneumatic system using water as mean. Furosemide solution can be dispensed with high precision into arrays of micro-wells (see figure 2) with different parameters. The content of the drug can be controlled varying its original concentration in the solutions and the number of dispensed droplets.

Conclusions

In conclusion, we demonstrate a very versatile filling technique for 3D micro-structures that can be tuned for several purposes, including promising applications in the field of micro-devices for drug delivery and biomedical research.

Future Work

The solid state of the drug has to be investigated by means of Raman spectroscopy and X-ray diffraction. A further step of this loading technique, is the application to other drugs, like protein and other fragile active compound.

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