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Hot punching of individual biopolymer microcontainers for oral drug delivery

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In this work, we present the fabrication of large arrays of polymer microcontainers for oral drug delivery. This is done in a two-step process where first hot embossing of individual polymer microstructures (hot punching) is performed and then the separated microstructures are transferred on a water soluble polymer release layer by thermal bonding.

Advances in microtechnology and pharmaceutical engineering led to the proposition of microcontainers as carriers for oral drug delivery [1]. Microcontainers can be used for oral administration and are able to protect drug from degradation during transit of the gastro-intestinal tract. Furthermore, they will enable one-directional drug release at the site of absorption and can thereby enhance the bioavailability of drugs. The microcontainers are preferentially fabricated with biocompatible or biodegradable polymers. It was shown that hot embossing is a viable method for three-dimensional structuring of these polymers [2]. However, hot embossing leads to the formation of a residual layer that connects the structures defined in the polymer. The residual layer can be removed by reactive ion etching but this is a slow and expensive process. In this abstract, we propose hot punching as a method to fabricate individual biopolymer microcontainers for oral drug delivery.

The process of hot punching is illustrated in fig. 1. First, the substrate is prepared by spin coating a PDMS layer of 500 μm on a Si wafer. Then a 30-40 μm thick layer of poly(L-lactic acid) (PLLA) is spin coated on the PDMS (fig. 1(a)). After that the sample is embossed with a Ni stamp for 1 h at a temperature of 120°C and a pressure of 1.9 MPa [2]. In total, there are 6400 containers per stamp. An individual unit consists of two parts, an inner disc and an outer ring structure. The total width of the containers is 300 µm. The wall and the outer ring thicknesses are 40 µm and 30 µm, respectively. The stamp is fabricated by electroplating Ni on a Si mold and then coated by teflon (fig. 2). The height of the outer ring is 80 μm and the inner disc is 65 μm.

The viscoelastic under layer of PDMS deforms against the stamp and pushes the polymer into the cavities of the stamp [3]. Due to this enhanced deformation, the residual layer is broken and the microcontainers are punched out of the PLA film (fig. 1(b)). Next, the stamp and the sample are demolded. At this stage, a polymer film with through holes is left on the Si wafer while the microcontainers remain in the stamp (fig. 1(c), fig. 3). In the final step, the stamp with the microcontainers is thermally bonded to a 20 μm thick film of poly(acrylic acid) (PAA) coated on a Si wafer (fig. 1(d)).The bonding is done for 1 h at a temperature of 120 °C and a pressure of 1.9 MPa. The stamp is removed and the containers remain on the PAA coated wafer (fig. 1(e), fig. 4). Free-floating microcontainers are obtained by dissolution of the PAA layer in water (fig. 1(f)).

In conclusion, we have shown how to fabricate discrete biopolymer microcontainers. As a next step, the process needs to be optimized further, to get higher yield of microcontainers per wafer and better replication of the stamp features. Once the optimization is complete, the containers will be filled with an active pharmaceutical ingredient and the drug release will be characterized.

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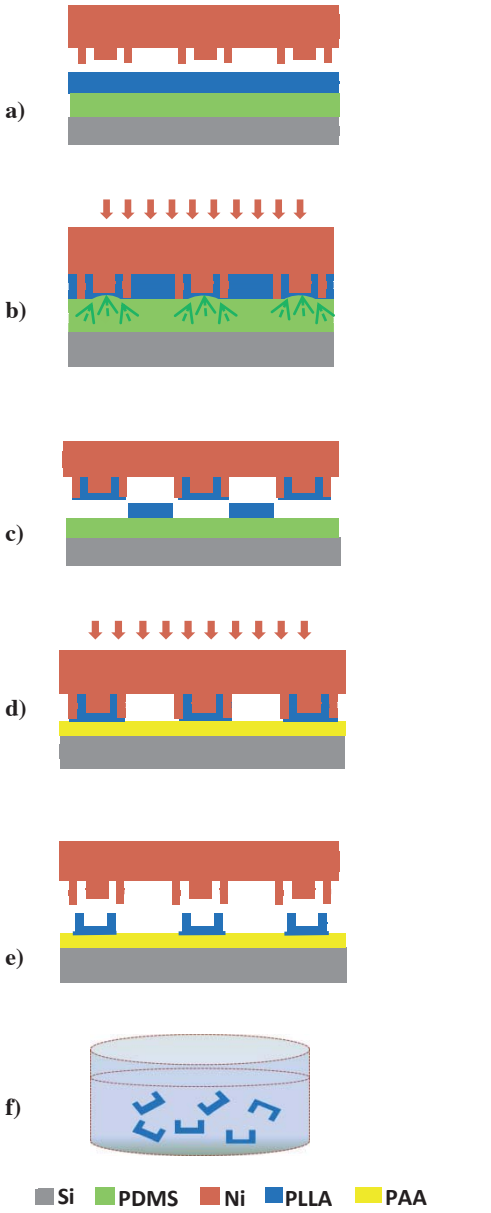

Fig 1. Hot punching of individual polymer micro-containers a),b) embossing PLLA spin coated on PDMS layer c) demolding d),e)thermal bonding f)dissolution of PAA

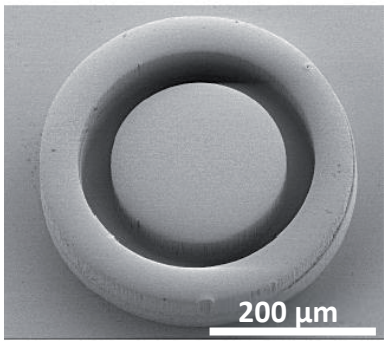

Fig.2. Ni stamp before embossing

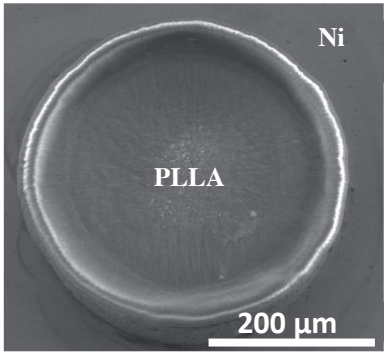

Fig.3. PLLA micro-container attached to Ni stamp after embossing

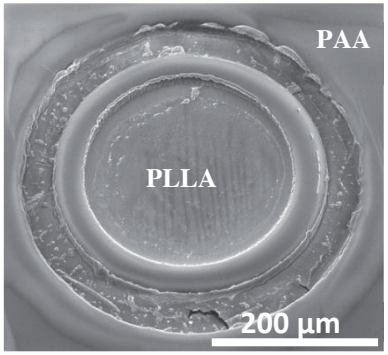

Fig.4. PLLA micro container on PAA release layer after thermal bonding