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Fabrication and evaluation of microgel shapes as carriers for delivery of biomacromolecules

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Hydrogels are 3D polymeric matrices that imbibe water while maintaining their structural integrity when placed in aqueous environments. They have become increasingly important for drug delivery applications due to their biocompatibility, porous matrix and high water content, making them akin to biological cells and tissue. [1] The structural and physical properties of hydrogel matrices can be adapted allowing for the controlled release of biomacromolecules. Traditionally, hydrogel based micro- and nano- carriers have been fabricated by bottom-up techniques, yielding spherical carriers. However, recent studies highlight that carrier shape and size play a significant role in carrier flow, internalization and interaction with biological membranes. [2] As a result, there has been high impetus in developing shape and size specific carriers for drug delivery, bringing top-down techniques to the forefront for their development.

Recently, we have introduced UV-assisted punching as a novel technique for the top-down fabrication of microgel shapes with varying geometries. First, the geometry of the microgel shapes is defined in a Si master, fabricated by photolithography and reactive ion-etching (RIE). This master is then used to transfer the inverse geometry into a polymeric foil by hot embossing. The wells of the stamp are loaded with the hydrogel precursor by force assisted liquid distribution (FALD) on a roll-to-plate imprinter. Thereafter, the loaded stamp was assembled with a poly-vinyl alcohol (PVA) substrate and UV-assisted punching was performed to obtain individual microgel shapes (Fig.1A). In this process, the hydrogel precursor was crosslinked by UV radiation while the stamp was pressed into the PVA substrate, penetrating it to define individual microgel shapes.

Microgel shapes in circular, elliptical, square and rod-like geometries were successfully fabricated in sizes with carrier length varying from 100 µm to 8 µm (Fig.1A, B, C). Microgel shapes could be loaded with biomacromolecules as an integral part of the fabrication process (Fig.1D). *In vitro* release of the loaded biomacromolecule in release media at pH 7 was explored to demonstrate the potential of microgel shapes as carriers for the delivery of biomacromolecules (Fig.1E). Furthermore, hemolysis assay on the microgel shapes revealed no hemolysis indicating their biocompatibility (Fig.1F).

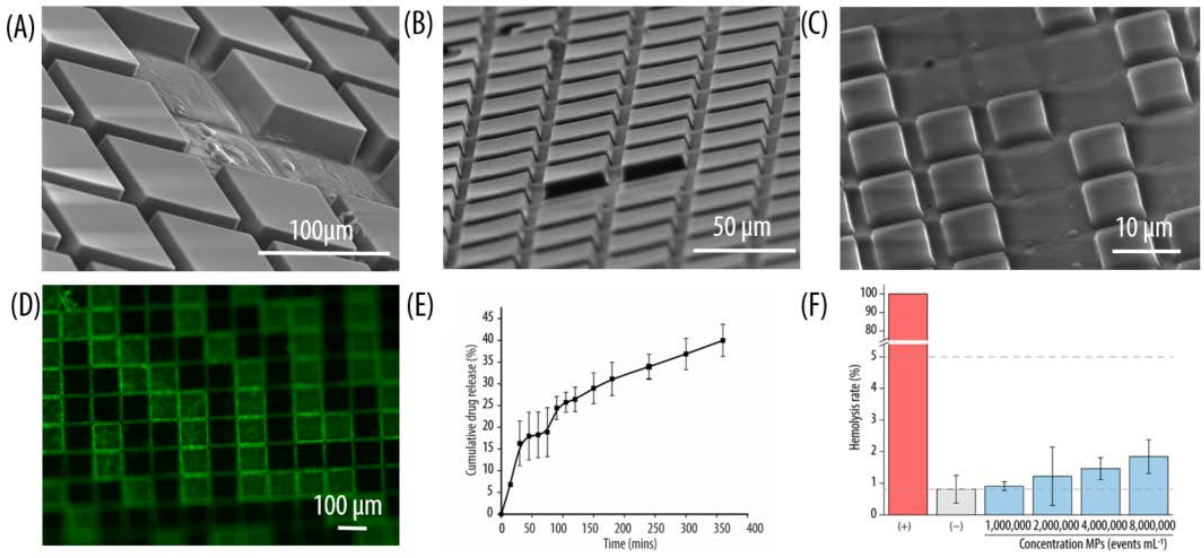

Figure 1: (a)-(c) SEM images of square microgel shapes on a PVA substrate fabricated by UV-assisted punching with dimensions - (a) 100X100X25µm, (b) 35X35X8.75µm and, (c) 8X8X2µm. (d) Fluorescent microscopy image of100X100X25µm microgel shapes loaded with BSA-FITC on the PVA substrate, (e) *in vitro* release of biomacromolecule loaded microgel shapes in release media at pH 7, (f) hemocompatibilty of the microgel shapes.

References

1. Casalini, T., & Giuseppe, P. Gels 5, no. 2 (2019): 28.
2. Shang, L., Nienhaus, K. & Nienhaus, G. U.. J. Nanobiotechnology 12 (2014): 1–11.