Uniform Microparticulate Hydrogels for Drug Delivery

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Statement of Purpose: Microfabrication techniques[1-2] were utilized to produce homogeneously-sized particles. Uniform microparticles are desired to examine the hypothesis that particle size will dictate the distribution in the body following injection with the ultimate goal of cancer-targeting. A narrow size range particle is expected to be more uniform in distribution and recognition by the body. As a preliminary study to our ultimate goal of drug delivery, we synthesized micro-sized poly(ethylene glycol) diacrylate (PEGDA, MW = 700 g/mol) hydrogels using various size templates. Following fabrication, hydrogel size was quantified by differential interference contrast (DIC) microscopy. From these results, we confirmed the feasibility of synthesizing reproducible, microparticulate PEGDA hydrogels as a mobile platform for drug delivery. In future studies, these microparticulate PEGDA hydrogels will be used as the drug delivery platform for cancer-targeting agents[3].

Methods: To make the micro-size square shaped hydrogels, specific sized templates were prepared from 400 μm to 1000 μm in 100 μm increments using a standard laser printer. Printed templates were colored using a black marker to give more limited UV penetration where printed. The template window size was quantified by light microscopy. We have recently begun studies using photolithographically-prepared masks based upon the preliminary data achieved using the laser-printed masks.

The hydrogels were synthesized using a 990 μL aliquot of 10% PEGDA and a 10 μL aliquot of 5% Irgacure 2959 solution prepared in phosphate buffered saline (PBS), pH 7.4. Immediately after combining, the homogeneous solution was poured into a masked fabrication apparatus at room temperature and exposed to long-wavelength UV irradiation (365nm) for a desired period time with mild heating. Synthesized hydrogels were washed with PBS to remove un-reacted monomer and initiator. The size of the hydrogels was examined by DIC.

Results/Discussion: Templates, Figure 1(a), were redrawn based on the regression equation since the observed lengths correlated well ($R^2 \sim 0.99$). This showed the feasibility to obtain templates with the expected window sizes for polymerization. The average observed window size was similar to the expected size and showed very low standard deviation. This study shows the feasibility of making templates with uniform, predictable windows of various sizes as long as the size was greater than 400 μm. Hydrogel size, Figure 1(b), and template window size was around 500 μm, indicating that the templates can be used to predictably make hydrogel particles.

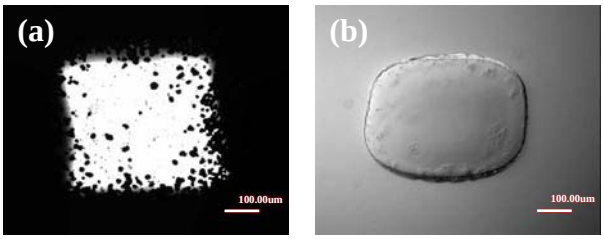

Figure 1. (a) Template window (500 μm) observed by light microscopy and (b) hydrogel observed by DIC. The scale bar is 100 μm in each image.

Table 1. Expected and average size of hydrogels.

Expected width (μm)	Average width (μm: mean±stdev)
500.0	455.6±24.0

The average observed hydrogel size presented less than 10 % size variation from the average width, and was consistent among the tests. Hydrogels had greater width due to the linear arrangement of the windows on the mask. This fault is expected to be corrected by using a photolithograph mask. This study shows the feasibility of making templates with uniform, predictable hydrogel particles of various sizes.

Conclusions: A microparticulate hydrogel microfabrication methodology using an ultra-violet polymerization system was developed. The templates to make micro-sized hydrogels were successfully predicted by the preliminary regression study. The template windows can be reproducibly manufactured in the size interval from 400 μm to 1000 μm, and they created homogeneous windows of expected size. Hydrogels fabricated using the 500 μm template suggest the feasibility of making predictable hydrogel particles.

From these results, we confirmed the feasibility of synthesizing microparticulate PEGDA hydrogels as a mobile platform of cancer treatment. In future studies, these microparticulate PEGDA hydrogels will be used as a drug delivery platform for a cancer-targeting agent.

References:

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