The kinetic study of solidification PEGDA microparticles in flow-focusing microfluidic chip

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Abstract. Polyethylene glycol diacrylate (PEGDA) microparticles (MPs) have a great potential in a wider range of applications including cell carriers, drug delivery agents, and multiplexing assays. Among existing MP fabricating methods, only the microfluidic droplet-based methods provide both morphology complexity and substance diversity. This work is concerned with the production PEGDA-based droplets with the photoinitiator (Irgacure 2959) in a flow-focusing microfluidic generator. The kinetics of MPs solidification in mineral oil with various common surfactants (Abil EM 180, Span 80) were investigated. Also, the Young's modulus of solid PEGDA were obtained.

1. Introduction

Typically, microparticles (MPs) have been prepared through traditional emulsion polymerization using rotors/stators or high-pressure valve homogenizers. Nevertheless, these techniques have a confinement in achieving unique characteristics such as well-controlled size, various morphologies and multi-compartments. The droplet microfluidics, electrohydrodynamics-based, centrifugation-based, and template-based methods have been recently proposed to overcome this limitation [1]. However, microfluidics has shown enormous potential both in providing control over chemical, physical, mechanical, and morphological characteristics and robust approaches for the production of monodisperse geometries [2]. Meanwhile, polyethylene glycol diacrylate (PEGDA) MPs have become widely used as cell carriers, drug delivery and tissue scaffolding materials [3]. Acrylate-based polymers are preferred due to their transparency, color variation, robust mechanical properties, elasticity, chemical versatility, bioinertia and biocompatibility. Moreover, acrylates can be readily photopolymerized on industrial scales [3, 4]. A little attention is observed to study the kinetics of droplet solidification that is very important for design and optimization of drug delivery systems.

Microfluidics provides control of fluids at the microscale and generate micrometer diameter droplets with a narrow size distribution and well-tailored structures [5]. In droplet-based methods, microdroplets are generated using shear forces induced by immiscible fluids inside a pinched region of a microfluidic device and then solidified to be MPs. In cell carrying and drug delivery agents, typically used MPs diameter ranges from about 90 to 200 um are used, in some special circumstances size was up to 600 um [1].

In this work, we studied conditions of PEGDA droplet formation and solidification: solidification time from photoinitiator concentration (Irgacure 2959) and mechanical properties of solid PEGDA (Young's modulus).
2. Methods
In this work, droplet microfluidic generator, based on flow focusing principle, was used (figure 1). Its operating principle is based on the fact that the continuous phase flowing through two side channels meets the dispersed phase at a channels’ intersection, where the dispersed phase is squeezed by the continuous phase and breaks up into droplets. It allows avoiding a contact of forming droplets with channels’ walls and helps to prevent potential negative effects on sample’s components of the dispersed phase [6].

The PDMS microchips were fabricated by soft lithography method [7]. Mineral oil (330779 light, Sigma-Aldrich) with different widespread surfactants (Abil EM 180, Span 80) was used as a continuous medium. PEGDA mixed with photoinitiator (Irgacure 2959) was used as a disperse phase. The UV lamp 365 nm and 150 mW/cm² was used for droplets solidification.

![Figure 1. Flow focusing microfluidic droplet generator: (a) general view; (b) active area.](image)

To obtain Young's modulus of solid PEGDA, the atomic force microscope (AFM) Bruker Bioscope Catalyst with RTESPA probe (stiffness 42 N/m) was used. Force curves analysis was proceeded by NanoScope Analysis software. To estimate Young's modulus, the Sneddon (Conical) fit model was used.

3. Results and discussion
During a UV solidification, a PEGDA+photoinitiator compound changes color (figure 2), which was used to determine the solidification time. The last phase occurs when the color stops changing. Furthermore, the color does not change, but the compound saturate until completely solidified. In addition, droplets with different diameters have the same solidification time.

It was found that the surfactant Span 80 influence on solidification because color changing does not appear in contradistinction to pure solution or with Abil EM 180.

![Figure 2. Solidification process of PEGDA droplets with different diameters at 1% w/w photoinitiator.](image)

We suggest the next qualitative scheme of the PEGDA solidification (figure 3a). When the UV is switched on, the first instantaneous solidification takes place (flash point). The flash point value depends on photoinitiator concentrations. In some cases, the value can even tending to zero. Further,
there is a gradual change of color PEGDA or maturation. Based on the color changes this process can be divided into three stages. At the first stage, the color changes smoothly from dark blue to light brown. Then, at the second stage, the color changes from light brown to blue. Finally, at the third stage, there is no color shift. Importantly, there are three dominant colors, so three stages. The colors themselves may depend on the experimental conditions. The beginning of the third stage is called $t_s$. The last stage is called the saturation stage. Since the color does not change at the third stage, it is impossible to estimate accurately the value $t_{100\%}$ (figure 3a).

![Figure 3. (a) Qualitative solidification scheme; (b) Dependences of solidification time $t_s$ on photoinitiator concentration for the droplet diameter 200 µm.](image)

The dependences of $t_s$ on photoinitiator concentration is shown in figure 4a. Four cases were considered. First, it was the bulk solution of PEGDA with photoinitiator. Second, it was droplets of PEGDA with photoinitiator in oil phase with 3.5% w/w surfactant Abil EM 180. Third, it was the bulk solution of 50% w/w water and 50% w/w PEGDA with photoinitiator. And, fourth, it was droplets of 50% w/w water and 50% w/w PEGDA with photoinitiator in oil phase with 3.5% w/w surfactant Abil EM 180. In all cases, the photoinitiator concentration was 0.25, 0.5, 1, 2, 3 % w/w (to the whole volume). The points of time values on the graph (figure 3b) are averaged value of five experiments. To better capture the color changing during the UV solidification, large drops with the diameter 200 µm were used.

From experiments, it can be concluded that solidification time $t_s$ does not depend on droplet size. The higher concentration, the faster solidification. The data was approximated by exponential fitting:

$$t_s = A e^{-\frac{C}{C_0}} + t_0$$

Values $C_0 = 1.3$, $A = 55$ s, $t_0 = 4$ s were obtain from approximation fitting. The optimal concentration is about 1%.

To estimate the Young's modulus behavior, PEGDA solutions in DI water with concentration of PEGDA 10-100% at 1% w/w photoinitiator were used. Young's modulus of PEGDA droplets is shown in figure 4. According to the shape of obtained force curves, it can be indicated if the droplet contains a solid core and a soft shell or only a solid core (figures 4b, 4c). It was found that ratio 50% w/w PEGDA and 50% w/w water is critical (figure 4b). If the concentration of PEGDA is less than 50% w/w, solidification occurs evenly without shell formation. Otherwise, shell appears. In addition, Young’s modulus of shell is smaller than modulus of core.
4. Conclusions

To sum up, the kinetic study of solidification PEGDA microparticles in flow-focusing microfluidic device was investigated. The data was collected by the optical microscopy and besides, kinetic data were processed statistically. The results show the behavior of droplets formation at different PEGDA concentration in solution. It was concluded that the solidification time $t_s$ depends exponentially on photoinitiator concentration. Moreover, optimal concentration is about 1%. The results indicate that $t_s$ does not depend on droplet size.

Young’s modulus was studied by the AFM force curve measurements. According to the shape of obtained force curves it can be indicated if the droplet contains a solid core and a soft shell or only a solid core. In addition, the Young’s modulus of the droplet shell is smaller than the modulus of the core. We obtained that the maximum Young’s modulus is 83 MPa on condition 50% w/w PEGDA and 50% w/w water. Young’s modulus changes in range from 5 to 83 MPa for core, and from 0.4 to 2 MPa for shell.

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