

Continuous Synthesis of Uniform Core-Shell Particles for Novel Biodegradable Brachytherapy Source

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1. Introduction

According to the National Cancer Center of Korea, the incidence of prostate cancer has steadily increased in the last decade. It can be cured by brachytherapy. It has a higher cure rate than surgery and has no side effects [1].

In the past, Palladium-103 (¹⁰³Pd) and Iodine-125 (¹²⁵I) were used radioactive sources for brachytherapy, but since 2004, cesium-131 (¹³¹Cs) has been intensively studied as an alternative. The half-life of ¹³¹Cs is 9.7 days and emits higher energy of 30 keV in average. Therefore, the treatment period with Cs-131 is shorter than before [2].

Cesium seeds for brachytherapy are made of metal. After the treatment the metal seeds remains in the body and cause discomfort in everyday life of patients. To solve this problem, we studied brachytherapy sources made of biodegradable polymer.

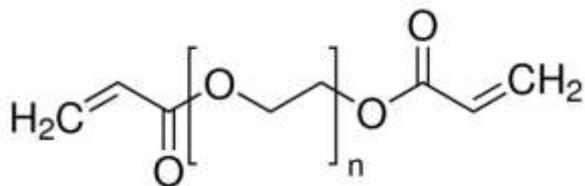


Fig. 1. Structure of poly (ethylene glycol) diacrylate-250 (PEGDA) structure.

2. Experimental

2.1. Preparation of lab-on-a-chip devices for the synthesis of core-shell particles

The core-shell manufacturing system was designed through a photolithography process on a silicon wafer as shown in Fig. 2. The microfluidic chip is mixed with a polydimethylsiloxane (PDMS) base and a curing agent in a ratio of 10:1, and mixed for a sufficient time. The PDMS mixture was then poured to the mold and air bubbles were removed with a vacuum pump. It was cured in a convection oven at 70 °C for 60 min.

After the crosslinking reaction, PDMS is treated with oxygen plasma. This reaction improves adhesion of microfluidic chip and functional groups.

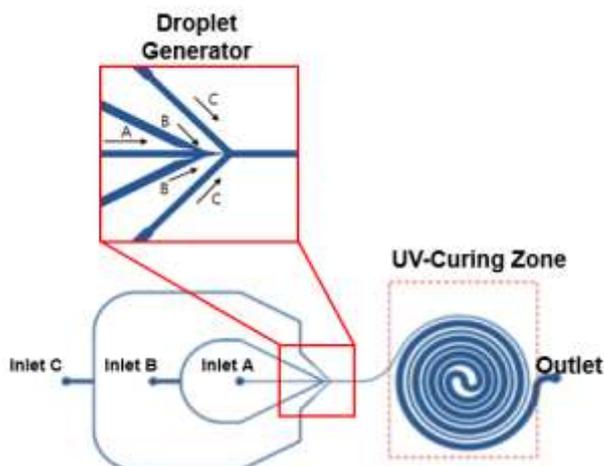


Fig. 2. Schematic design of the microfluidic chip for the preparation of the core-shell particles

2.2. Fabrication of core-shell generator

The flow rates of input through the inlet A, B and C were controlled using a syringe pump, respectively. The continuous phase (Input C, Hexadecane) flow rate was 15–40 $\mu\text{L}/\text{min}$. shell phase (Input B, PEGDA) flow rate was 3–6 $\mu\text{L}/\text{min}$. and the core phase (Input A, Prussian blue) flow rate was 0.5–2 $\mu\text{L}/\text{min}$. The preparation the core-shell in the microfluidic could be observed as shown in the Fig. 3 and Fig. 4.

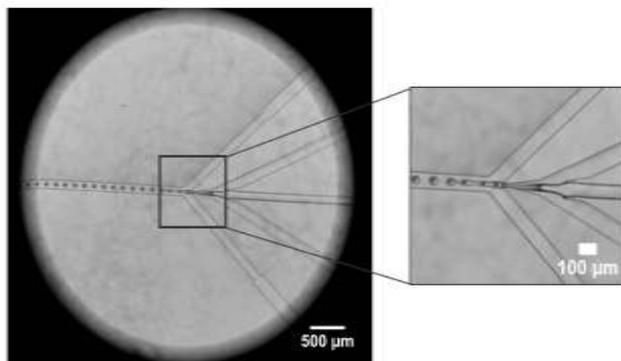


Fig. 3. Microscope image of the manufactured core-shell at the droplet generator.

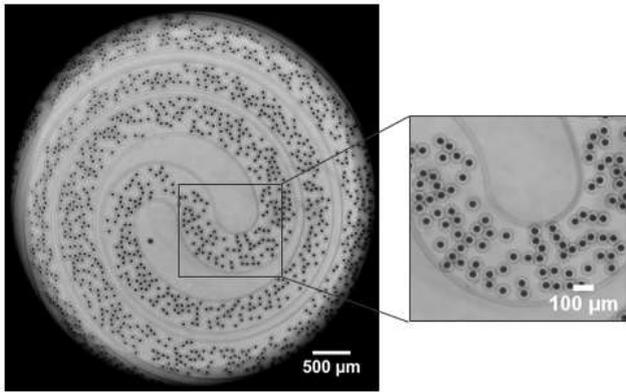
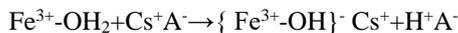


Fig. 4. Microscope images of core-shell particles at the UV-Curing Zone.

3. Results and discussion

Prussian blue has physical and chemical interaction with cesium ions. The physical adsorption mechanism is related to the magnitude of hydration of alkali metal ions: $Cs^+ \gg K^+ \geq Na^+$. Radius of alkali metal ions are Cs^+ (1.19 Å) < K^+ (1.25 Å) < Na^+ (1.84 Å). Among those ions size of the cesium ion fits to the lattice structure of Prussian blue.

The chemical adsorption mechanism is adsorption in the hydrophilic space inside the Prussian blue molecules. When cesium ions are trapped inside the Prussian blue, Fe^{3+} ions are coordinated and cesium is adsorbed by proton exchange of water molecules [3].



Equation 1. Adsorption mechanism of cesium ions via proton exchange [3].

For the aforementioned reason, Prussian blue was chosen as a cesium carrier in the core of the particles. To confirm the leakage of the Prussian blue from the PEGDA into the water phase, we observed UV-visible spectra of Prussian blue solutions as shown in the Fig. 6. Maximum absorption peaks of the Prussian blue in water were observed at 695 nm from the standard samples (sample 1, 2 and 3). PEGDA doped with Prussian blue was then immersed in the water to measure leakage of the Prussian blue. Fig. 6 shows the UV-visible spectra of the Prussian blue leaked from the PEGDA, according to the time. Prussian blue concentrations from the leakage were similar to the blank sample taken from the distilled water as a background. Therefore, we can confirm the stability of Prussian blue in the PEGDA with negligible leakage.

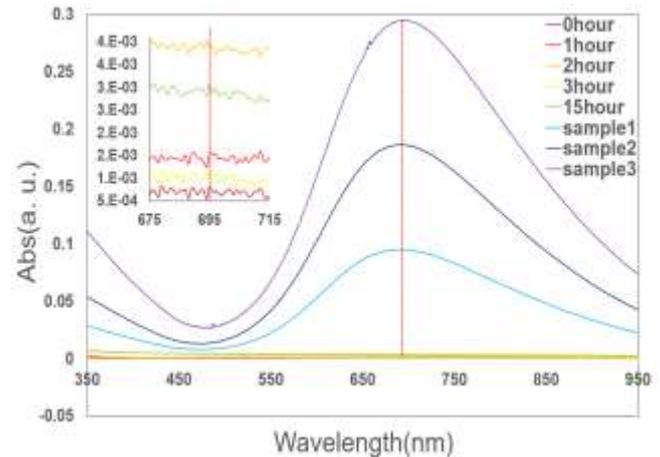


Fig. 5. UV-vis spectra of Prussian blue in the water.

4. Conclusions

In this study, we confirmed that Prussian blue can be embedded in the PEGDA core-shell particles without leakage. As a future work, amount of cesium leakage will be characterized through cesium adsorption experiments. In addition, it is expected to manufacture multifunctional core-shell particles for various purposes by introducing different functional materials, such as magnetic nanoparticles, gold nanoparticles and fluorescence.

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