The Fabrication of Photo-Deformable Polymer Nanostructures Using Biocompatible Molecules

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Abstract

Polymer nanospheres are useful drug delivery techniques. The nanospheres are formed by molecular self-assembly, which is a processes where molecules spontaneously assemble into stable structures. The ability for a nanosphere to undergo conformational changes is a beneficial characteristic for drug delivery techniques. Recently, a special type of polymer nanosphere was developed by Xiao et al. The particles were able to transform from a spherical conformation to an oblong conformation due to the photo-deformability of azo-dyes.[1] The azo-dye component is toxic to the human body and could not be used in drug delivery. Retinoic acid is a biocompatible molecule and shows similar *cis-* and *trans-* conformational changes as the azo-dyes, which suggests a photo-deformable characteristic. The polymer PAN-stat-P4VP was synthesized and coupled with retinoic acid (RA). Also, a complex was formed between PAN-stat-P4VP and the azo-dye metanil yellow (MY) to use as a comparison to the PAN-stat-P4VP/RA complex. The nanospheres were exposed to a polarized laser and characterized using Fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR) analysis, and scanning electron microscopy (SEM). The data from this experiment shows that the PAN-stat-P4VP/RA complex forms an interesting spaghetti shape instead of spheres. Also, the IR spectra indicate the presence of retinoic acid in the self-assembly and little signal of the polymer. But, the carbon-13 NMR of the self-assembly suggests indeed the presence of polymer and retinoic acid. Furthermore, the fact that the complex did not self assemble into a sphere is an indication that the molecular weight of the polymer may have been too small, or the polymer chain itself was too short. The SEM images of the PAN-stat-P4VP/MY self-assembly post laser treatment (figure 8) shows that the particles are slightly deformed. We expect the more apparent deformation will be observed with the increase of exposure time.

Results

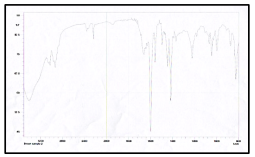

Figure 4: Polymer infrared spectrum.

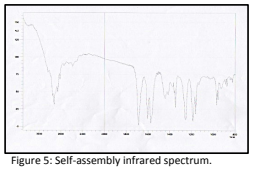

Figure 5: Self-assembly infrared spectrum.

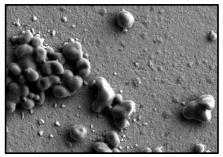

Figure 8: Self-assembly with metanil yellow in DMF post laser treatment.

Figure 9: Self-assembly with retinoic acid in DMF.

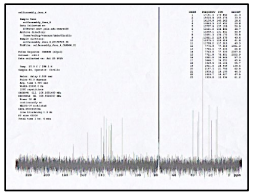

Figure 6: Self-assembly Carbon-13 NMR.

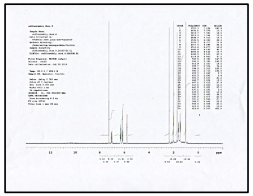

Figure 7: Self-assembly proton NMR.

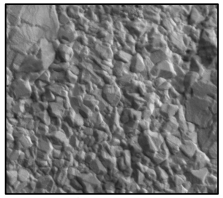

Figure 10: Self-assembly with retinoic acid in DMF post laser treatment.

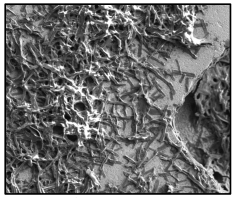

Figure 11: Self-assembly with retinoic acid in ethanol.

Discussion

The data suggests that a complex between the PAN-stat-P4VP polymer and the retinoic acid was formed. However, the complex self assemble into a spaghetti shape instead of the spherical conformation. The IR spectrum of the self-assembly shown in figure 5 provides evidence for the presence of retinoic acid in the complex but no evidence of polymer in the complex. This could suggest that the molecular weight of polymer was too small to be accurately detected by the IR instrument. The carbon-13 NMR spectrum of the complex does show evidence for the presence of retinoic acid and polymer in the complex. Since the NMR instrument was able to detect the presence of polymer in the complex, it could be a more sensitive instrument.

Furthermore, the SEM images show that DMF was too effective of a solvent to properly form a colloid. As shown in figures 9 and 10, one sample formed a crystal and the other formed a coating on the grate. Figure 11 shows that dissolving the complex in ethanol allowed for the complex to make a colloid; however, the complex did not self assemble into a sphere. The lack of a spherical conformation is further evidence that the molecular weight of the polymer may have been too low. It is also possible that the polymer chain is not long enough to form the proper conformation. The polymer needs to be synthesized with varying CDB-RAFT to AIBN ratios and analyzed again for colloid formation in ethanol.

The SEM images also show that the polymers with metanil yellow are only slightly deformed, which suggests that the laser parameters need to be adjusted for future testing.

Methods

Preparation of PAN-stat-PV4P polymers

RAFT of 4-vinylpyridine and acrylonitrile was performed using cumyl dithiobenzoatte (CDB) as a macro-RAFT agent and 2,2'-azobisisobutyronitrile (AIBN) as an initiator. The molar ratio was [CDB-RAFT] : [AIBN] = 4 : 1. A dry three-neck flask was filled with 15mL of dimethylformamide (DMF) and purged with nitrogen gas for 15 minutes. The CDB macro-RAFT agent was added to the flask. DMF was used to dissolve the AIBN, and the solution was added to the addition funnel. In a 10mL graduated cylinder the acrylonitrile and 4-vinylpyridine were mixed, and five drops of the solution was added to the solution in the addition flask. The solution in the three-neck flask was heated to 60°C, and the solution in the addition funnel was slowly added drop-wise to the three-neck flask. The solution was reacted at 70°C for 30 minutes. After 30 minutes, the 4-vinylpyridine and acrylonitrile solution was put into the addition funnel and added very slowly drop wise to the three-neck flask. The solution was reacted at 70°C overnight. The DMF was evaporated using the Rotavapor® and the remaining solution was poured into copious amounts of deionized water. The precipitate was filtered and dried for two days at 60°C in a vacuum oven.

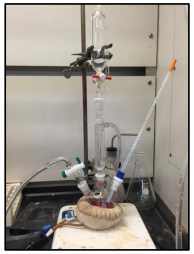

Figure 1: Polymer synthesis set up.

Fabrication of hollow polymer nanospheres

PAN-stat-P4VP was neutralized with concentrated hydrochloric acid. A 10^{-3}M solution was prepared using a 75% ethanol. A 10^{-3}M solution of retinoic acid was prepared by neutralizing the retinoic acid with 0.1M NaOH and dissolving it in 75% ethanol. The retinoic acid solution was added drop-wise to the polymer solution. The Rotavapor® was used to evaporate the ethanol, and the remaining solution was cooled to room temperature and filtered via vacuum filtration. The filtrate was left to air-dry overnight and then dried at 60°C in a vacuum oven. The polymer/retinoic acid precipitate was dissolved in a couple drops of DMF. A few drops of deionized water were then added to the DMF mixture to form the colloid. Ethanol was also used as a solvent to prepare the colloid

Figure 2: PAN-stat-P4VP/ RA precipitate.

Characterization and conformational change of polymer nanospheres

The particles were exposed to a polarized laser light of 800nm and 1.35watts of power for five minutes. The polymer nanospheres were characterized using Fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR) analysis, and scanning electron microscopy (SEM).

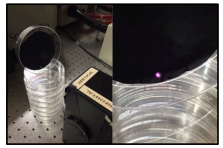

Figure 3: Laser treatment set up.

References

[1] Jin, Cheng, Taoran Zhang, Fangzhuan Liu, Lingyu Wang, Qinjian Yin, and Dequan Xiao. "Fabrication of Size Controllable Polymeric Hollow Nanospheres Containing Azo Functional Groups via Ionic Self-assembly." *RCS Advances* 4.16 (2014): 8216. Print.

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