

The Fabrication of Photo-Deformable Polymer Nanostructures Using Biocompatible Molecules

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Abstract

Polymer nanospheres created by the process of molecular self-assembly could be used for drug delivery. In fact, it has been shown that nanoparticles that undergo conformational changes have an increased ability to deliver a drug effectively. In this study, retinoic acid (RA) is used for synthesizing photo-deformable nanospheres. Based on the conditions (e.g., organic solvents and polymer molecular weights) used in this experiment, the PAN-stat-P4VP/RA self-assembly deposited on copper surface was not observed as spheres, but interestingly, flakes or stripes. Also, the infrared spectra indicate the presence of retinoic acid in the self-assembly but not the presence of a nitrile group that is characteristic of the polymer. However, the carbon-13 NMR of the self-assembly suggests the presence of polymer and retinoic acid. Therefore, the complex was formed but polymer IR signals were embedded in the RA IR signals. The SEM images of the PAN-stat-P4VP/MY self-assembly post laser treatment (figure 7) shows that the particles are only slightly deformed. Therefore, the laser parameters need to be adjusted to enable apparent photo-deformation, which needs to happen before the polymer can be tested for photo-deformable characteristics.

Introduction

The process of molecular self-assembly is characterized by the molecules' ability to form stable structural formations without the influence of outside forces. The molecules self-organize and are held together by non-covalent forces. This is a spontaneous process that is common in many biological systems, and it is used to create nanoparticles for specific uses. [1]

Nanoparticles are increasingly being used as drug delivery techniques. A study performed by Fei et al. involved the development of a nanoparticle that underwent conformation changes to form a bacillus shape. The nanoparticle was tested in its ability to effectively deliver an anticancer drug both in vivo and in vitro. The nanobacillus particles showed better penetration and, thus, better tumor treatment than the traditional nanosphere. [2] The experiment performed by Fei et. al. showed that the shape of a nanoparticle plays an important role in the effectiveness of drug delivery.

Photo-induced deformation is a unique behavior in which some compounds undergo conformational changes when exposed to polarized light, which has a potential application in drug deliver. Recently, a special type of polymer nanosphere was developed by Xiao et al. The nanoparticles could transform from spheres to oliver shapes due to the photo-deformability of azo-dyes. The azo-dye is the key component for the photo-deformation property because azo-dyes can undergo isomerization between cis-configuration and trans-configuration in response to light. [3] In order to use the photo-deformable polymer nanospheres in biomedical applications such as drug delivery, the biocompatibility needs to be improved. Retinoic acid, a molecule that is found in the human body, has high biocompatibility. The chromophore of retinoic acid is an important part of the vision system in human body because it can change from cis-configuration to trans-configuration in response to light. Thus, using retinoic acid

can potentially obtain photo-deformable polymer nanospheres with better biocompatibility.

Materials and Methods

Preparation of PAN-stat-PV4P polymers

RAFT of 4-vinylpyridine and acrylonitrile was performed using 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. 0.407mL of CDB macro-RAFT agent was added to the flask. 6mL of DMF was used to dissolve 0.069 grams of AIBN, and the solution was added to the addition funnel. In a 10mL graduated cylinder 0.0741mL of acrylonitrile and 1.436mL of 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. After heating, the solution the addition funnel was slowly added



Figure 1: Polymer Synthesis Setup

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.

Fabrication of hollow polymer nanospheres

PAN-stat-P4VP was neutralized with concentrated hydrochloric acid. A 10⁻³M solution was prepared using a 75% ethanol. A 10⁻³M 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. The remaining solution



Figure 2: PAN-stat-P4VP/RA precipitate

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.

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 Setup

Results and Discussion

The polymer, retinoic acid, and self assembly were characterized using FTIR spectroscopy, carbon-13 NMR and proton NMR.

The FTIR of the polymer (figure 4) shows a small spike around 2200 1/cm, which is an indication of the presence of a nitrile group. Also, the spikes shown between 1500 and 1600 1/cm are evidence of aromatic, double-bonded carbons. The nitrile group and the aromatic ring are groups that are present in the compounds that were used to synthesize the polymer, which suggests that the two compounds did successfully react to create a polymer.

The FTIR of the self assembly (figure 5) shows evidence of an -OH from the carboxylic acid group of retinoic acid at about 2900 1/cm, which is clear evidence of the retinoic acid in the self assembly. However, there are no spikes indicating the presence of a nitrile group or aromatic group present in polymer as shown in figure one.

The carbon-13 NMR (figure 6) of the self assembly does indicate the presence of polymer in the self assembly along with the retinoic acid. There is a carboxylic acid shift around 175ppm and a nitrile shift around 120ppm.

The SEM images, figures 7-9, show the various images of the self assembly in different solvents as well as pre and post laser treatment. Figure 7 shows the polymer and metanil yellow complex post laser treatment. The particles appear to be only slightly deformed. Figures 8 and 9 show the self assembly dissolved in DMF, which did not properly form the colloid. Instead the complex formed a crystalline pattern. Figure 10 shows the self assembly colloid that formed when dissolved in ethanol. The colloid did not form in the shape of a sphere.

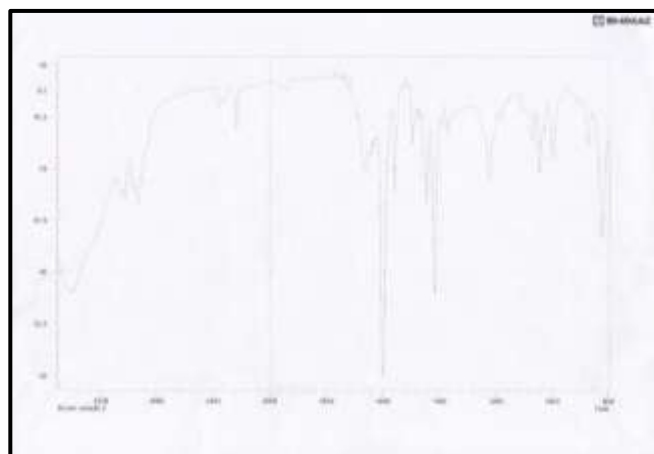


Figure 4: Polymer Infrared Spectrum

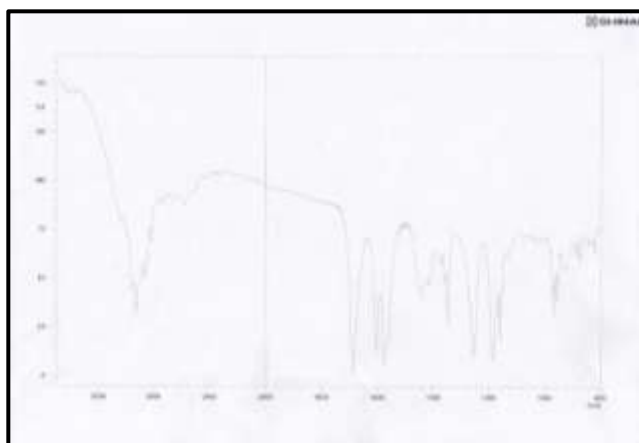


Figure 5: Self-assembly Infrared Spectrum

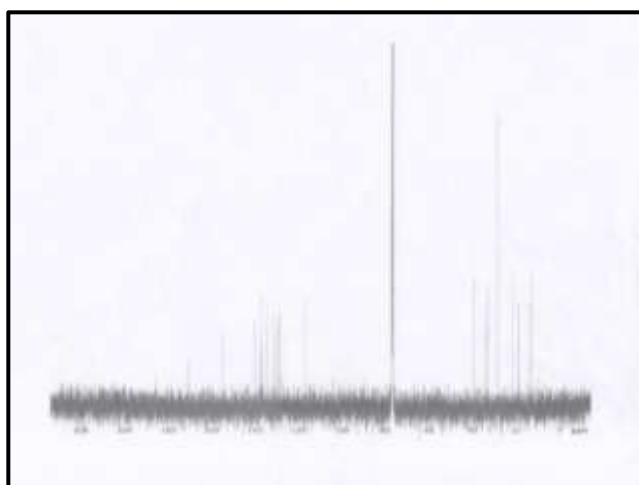


Figure 6: Self-assembly Carbon-13 NMR

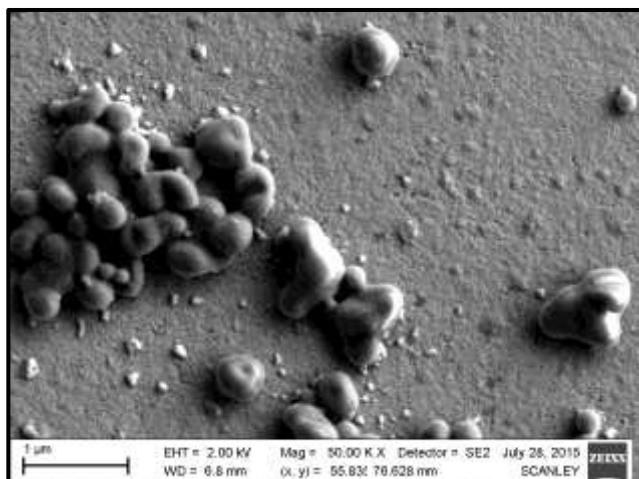


Figure 7: Self-assembly with metanil yellow in DMF post laser treatment

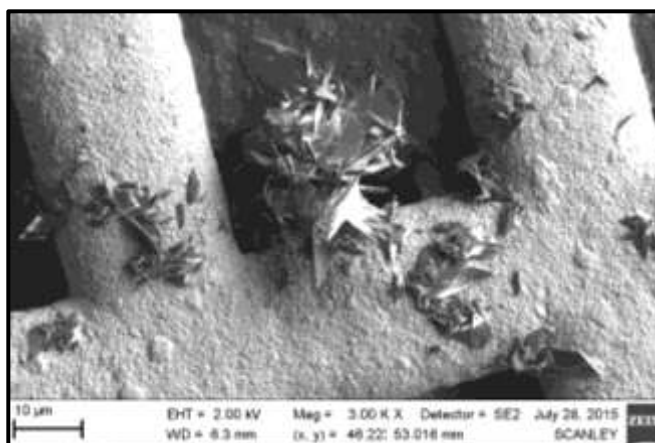


Figure 8: Self-assembly with retinoic acid in DMF

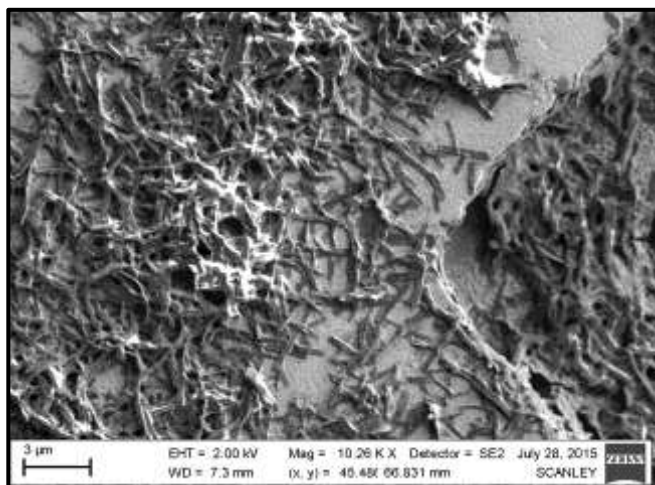


Figure 9: Self-assembly with retinoic acid in ethanol

Conclusion

The result suggests that a self-assembly complex between the PAN-stat-P4VP polymer and the retinoic acid was formed. The IR spectrum of the self-assembly shown in figure 5 provides evidence for the presence of retinoic acid in the complex but no signals of polymer in the complex. This could suggest that characteristic IR peaks of the polymer were embedded in the IR signals of retinoic acids. However, the carbon-13 NMR spectrum of the complex does show evidence for the presence of retinoic acid and polymer in the complex.

When colloidal solution of the PAN-stat-P4VP/MY self-assembly was formed, depositing the colloids on copper grid surface lead to the formation of polymer nanospheres, as observed by SEM images (see Figure 7). By observation, a colloidal solution of PAN-stat-P4VP/RA was formed. Interestingly, deposition of the colloids on the copper grid surface leads to the formation of strip shapes, instead of spherical shapes. The reason for the formation of such nest-like strips will be subjected to further investigations.

We also found that the use of different organic solvents during the formation of colloidal solutions can influence the morphology slightly on the copper surface. Using DMF as the organic solvent, we found that the

deposited colloids grew into flake shapes (see Figure 8). While using ethanol as the organic solvent, the deposited colloids grew into long strip shapes (see Figure 9). We anticipate that spherical shapes of PAN-stat-P4VP/RA on copper spheres can be observed by adjusting the organic solvent types and the molecular weights of the polymers, as the colloidal solution of PAN-stat-P4VP/RA was formed.

By exposing the deposited self-assembly on copper surfaces under polarized laser light, we found that the nanospheres of the PAN-stat-P4VP/MY are slightly deformed, which suggests that longer exposure time can be used for the future tests of the PAN-stat-P4VP/RA self-assemblies.

References

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Biography

Jessica Damon is currently a senior at the University of New Haven majoring in chemistry. After graduation, Jessica plans to attend pharmacy school to obtain a Pharm. D. degree. She is also a member of the University New Haven chapter of Health

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