Characterization of UV-Responsive Expansile Nanoparticles

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Statement of Purpose: Nanoparticles (NPs) offer promise as drug delivery vehicles for their ability to alter the pharmacokinetics, solubility, and distribution of systemically administered drugs, and, in so doing, minimize systemic side effects while maximizing drug efficacy.[1-2] Of particular interest to our research group are stimuli-responsive NPs due to their increased spatiotemporal control over drug release as compared to non-responsive particles. We have previously developed pH-responsive expansile nanoparticles (eNPs) that expand upon a pH trigger to release drug intracellularly.[3] Here, we developed light-responsive eNPs possessing photo-caging functional groups sensitive to irradiation with 365 nm ultraviolet (UV) light. By switching from an environmental to and external trigger for eNP swelling, a greater degree of control is engineered into the delivery system. Photo-decaging of the eNP monomer results in a structural change that leads them to swell with water and expand in size; thus these are termed UV-eNPs. Here we characterize UV-eNP swelling using a number of traditional particle characterization techniques.

Methods: UV-eNPs monomer was prepared from commercially available chemicals in a three-step synthesis with all structures confirmed by NMR. To synthesize particles, a sonication probe was used to create a mini-emulsion with dichloromethane and water, followed by a base catalyzed polymerization using ammonium peroxydisulfate. UV-eNPs were cleaned of excess surfactant and salts by dializing for 24 h. Liquid-chromatography mass-spectrometry (LCMS) was used to confirm photo-decaging of the photo-labile moieties when polymerized into nanoparticles. To investigate UV-eNP swelling, particles were diluted 1000X in de-ionized water and exposed to UV-irradiation (365 nm) for up to 10 minutes using a hand-held UV-lamp. Aliquots of UV-eNPs were removed at time points and sized using dynamic light scattering (DLS) with a Malvern 360 DLS. To examine morphological changes during swelling, aliquots of UV-eNPs were transferred to silica wafers at each time point. Particles were air dried and sputter coated with Au/Pd and examined using scanning electron microscopy (SEM).

Results: Results demonstrate that UV-eNPs are readily synthesized and that the photo-labile functional groups de-protect upon UV-irradiation. De-protection is a rapid process with over 50% occurring in less than 5 minutes. Furthermore, irradiation causes UV-eNPs to swell and expand in aqueous environments. SEM images of UV-eNPs without UV-irradiation reveal smooth, spherical particles of approximately 100-500 nm in diameter (Fig. 1). Following 10 minutes of UV-irradiation, particles have increased to over 1 um in diameter and the surface morphology has changed from uniformly smooth to apparently porous, rough, and broken. UV-eNP swelling mirrors the photo-decaging of the monomer unit with most swelling occurring within 5 minutes of irradiation.

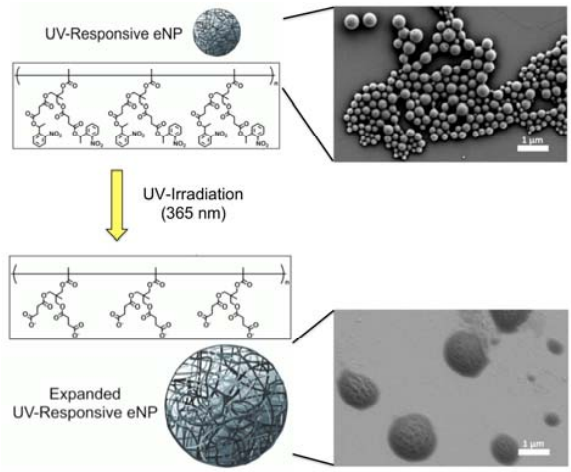

Figure 1: (left) Schematic depiction of UV-eNP mechanism of swelling. The initially hydrophobic UV-eNP (top), contains photo-labile protecting groups on carboxylic acid moieties (box). Upon irradiation with UV (365 nm) light, the protecting group cleaves off leaving the carboxylic acids behind and transforming the particle into a more hydrophilic structure which, in an aqueous environment, swells with water. (right) UV-eNPs exposed to zero (top) and 10 min (bottom) of UV irradiation are visualized using scanning electron microscopy (SEM). Irradiated UV-eNPs have increase in diameter and apparent porosity.

Conclusions: The results demonstrate the UV-responsive eNPs can be readily synthesized using facile techniques. Furthermore, the UV-eNP monomer maintains its photo-labile functionality when polymerized into a nanoparticle and this can be triggered using a relatively rapid (< 5 min) exposure to UV light (365 nm). Lastly, UV-eNPs swell rapidly upon exposure to UV-irradiation, increasing in diameter at least two-fold. These data suggest that UV-eNPs may provide a useful, responsive delivery platform for further development in a therapeutic application.

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