Synthesis of Azido block copolymers for Targeting and Labeled Micelle

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Background

- Polymeric micelles have emerged as promising drug delivery vehicles for tumor due to the enhanced permeability and retention (EPR) phenomenon.
- The polymers are composed by hydrophobic blocks and hydrophilic blocks, enabling them to self-assemble in aqueous solutions and encapsulate drugs.
- An azido group was introduced to the polymer to enables the polymer to conjugate with other functional ligands, such as targeting peptides and radio-labeling ligands.
- The conjugation process was achieved through copper-free click chemistry, ensuring efficient and precise attachment of the ligands to the micellar surface.

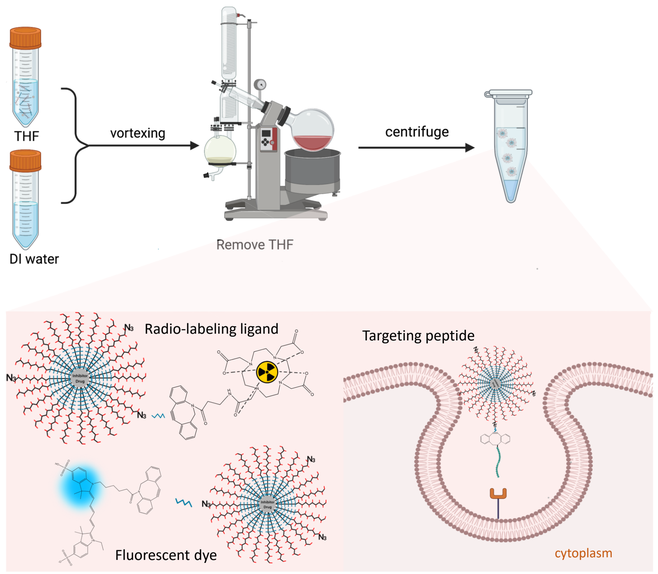
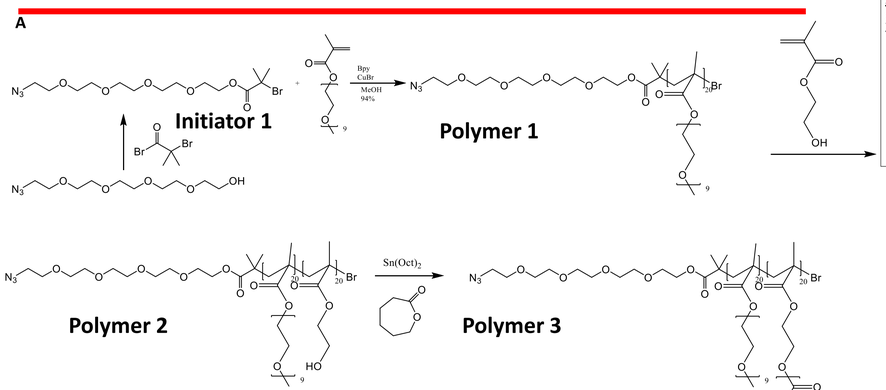


Figure 1. Schematic illustration of polymeric micelle formation and conjugation with targeting peptides and radio-labeling ligand.

Methods



B

	Polymer 4 (mg)	Polymer3 (mg)	Inhibitor drug (mg)	DI water (ml)
1	50	0	2.5	1.2
2	45	5	2.5	1.2
3	40	10	2.5	1.2

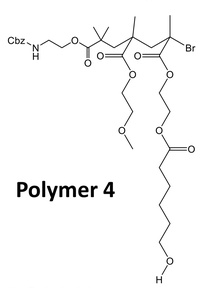


Figure 2. A. The synthesis of Azido-poly $(PEGMA)_{20}$ – b – poly $[HEMA–g–(ε–caprolactone)_7]_{20}$ (polymer 3). B. Formulation of micelles. C. Structure of poly $(PEGMA)_{20}$ – b – poly $[HEMA–g–(ε–caprolactone)_7]_{20}$ (polymer 4).

Results

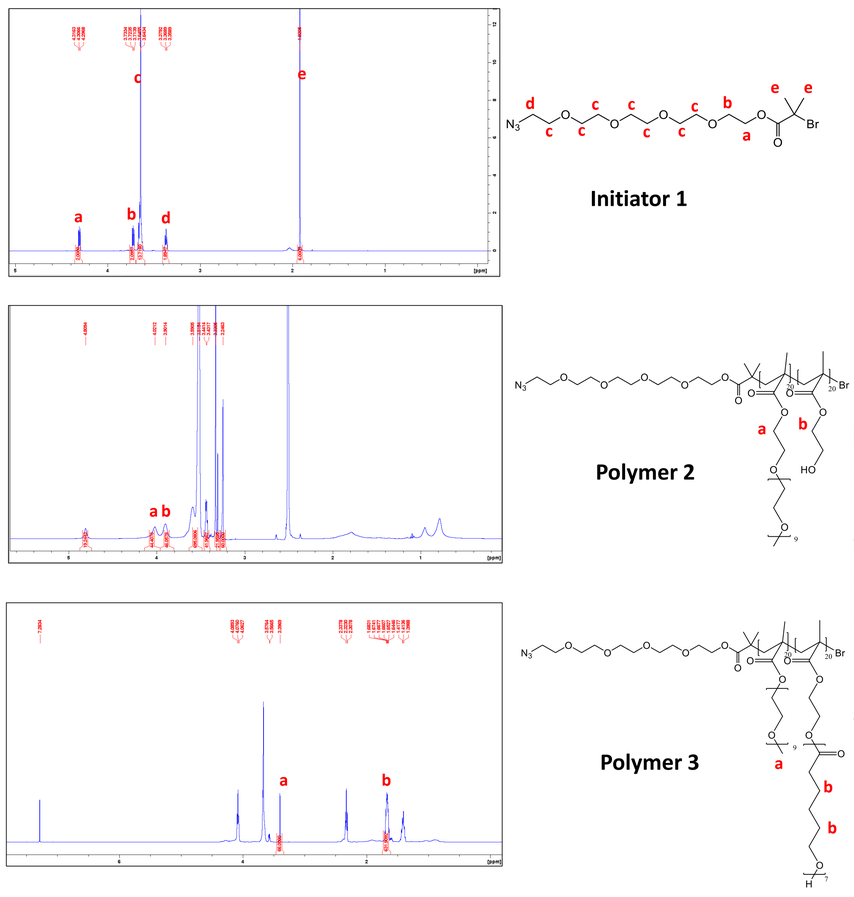


Figure 2. ^1H NMR Spectra of Initiator 1, polymer2, and polymer 3. Their structure are consistent with our design.

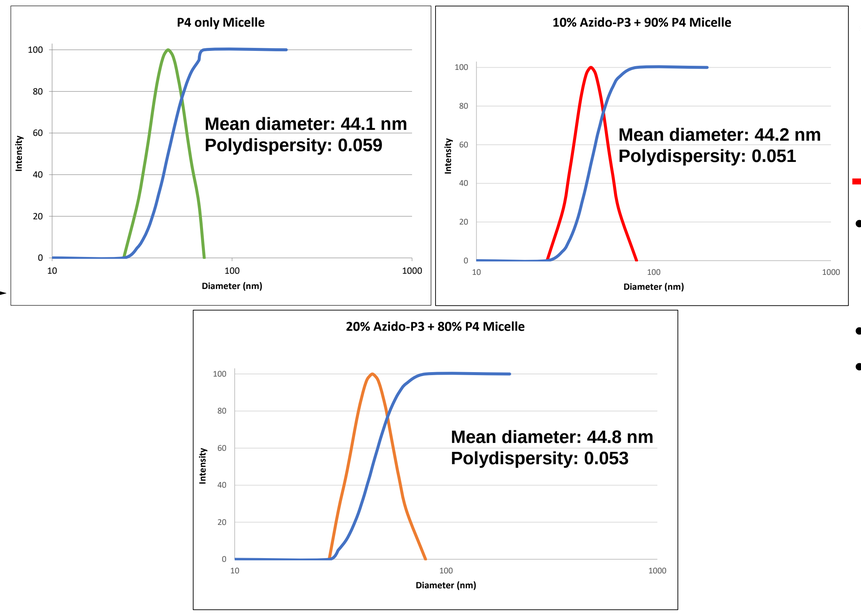


Figure 3. Lognormal chart of Micelles size. Nanoparticle size of micelles composed by P4 only, 10% P3 + 90% P4, and 20% P3 + 80% P4 were measured by Dynamic Light Scattering (DLS.) They all have relatively small mean diameter and polydispersity index(PDI) value. A significant difference on diameters and PDI value between micelle batches is not observed, which suggest the introduction of Azido polymer into the micelle does not have large influence on size and homogeneity of micelle.

Results

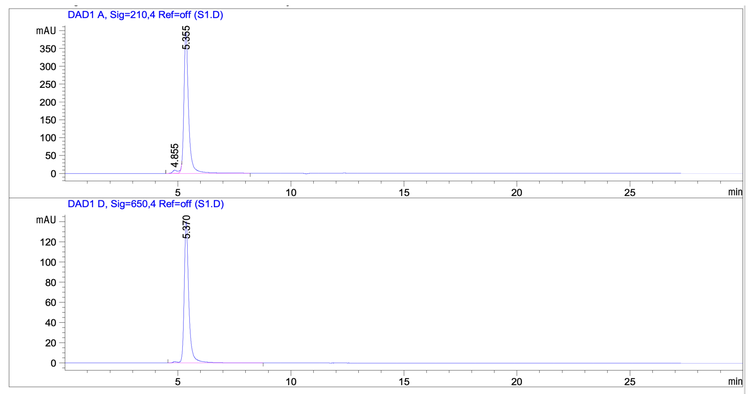


Figure 4. HPLC analysis of micelle that conjugate with sulfo-cy5-DBCO (ab wavelength 650nm, Lumiprobe, Maryland). The micelle product was purified using PD-10 column before the analysis. The HPLC analysis was performed using a GPC column (Viscoteck A4000) with dual wavelength detection at 210nm and 650nm. The detection of consistent absorbance peaks for both the micelle (210nm) and the sulfo-Cy5 (650nm) indicates successful conjugation of the fluorescent dye to the nanoscale micelles.

Conclusions

- Azido-Poly$(PEGMA)_{20}$-b-poly$[HEMA-g-(ε-caprolactone)_7]_{20}$ was successfully synthesized.
- They were able to self-assembly to nanoscale micelles with Poly$(PEGMA)_{20}$-b-poly$[HEMA-g-(ε-caprolactone)_7]_{20}$ and encapsulate drug .
- The Azido group on the polymer enables copper-free click chemistry conjugation with DBCO.

Future Direction

- Evaluation of encapsulation efficiency (EE) and micelle stability. The EE will be assessed using HPLC, and the stability of the micelles will be analyzed using DLS.
- Investigation of diverse drug encapsulation.
- Conjugation of targeting peptides and radio-labeling ligands. The targeting and labeled polymeric micelles will be subjected to in vitro studies and in vivo studies to evaluate the micelle's cytotoxicity, targeting efficiency, and therapeutic efficacy.

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References

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