Synthesis of Block Copolymers to Deliver Ortho-Carborane for Proton Capture Therapy

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Background

- Ortho-carborane is utilized for proton capture therapy.
- To ensure the ortho-carborane to be delivered to the target site, the block copolymers could be utilized as nanocarrier.
- Poly $(PEGMA)_n$ – b – poly $[HEMA–g–(\varepsilon–caprolactone)_7]_m$ has been proven as an effective delivery vehicle for therapeutic drug.

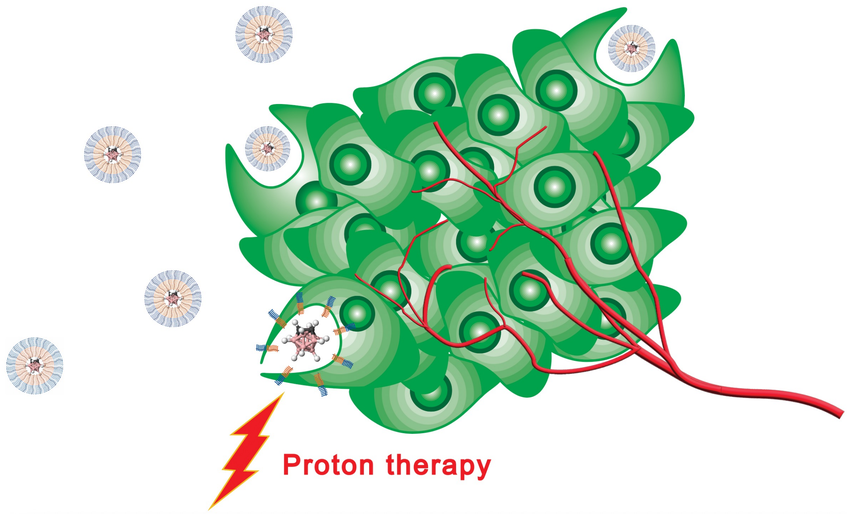
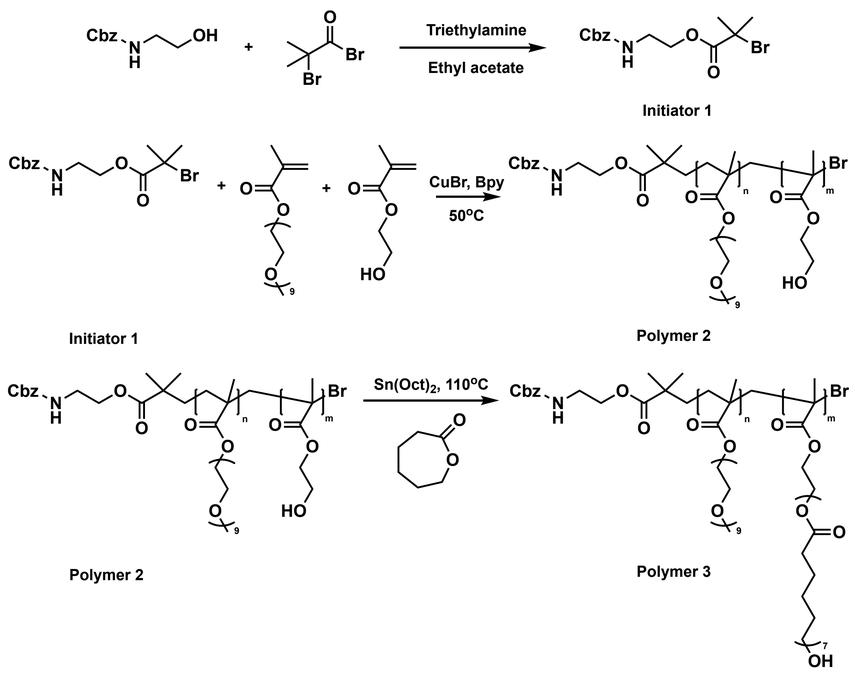


Figure 1. The overview of ortho-carborane delivery via polymer micelles for proton capture therapy.

Methods



Scheme 1. The synthesis of poly $(PEGMA)_n$ – b – poly $[HEMA–g–(\varepsilon–caprolactone)_7]_m$ (polymer 3).

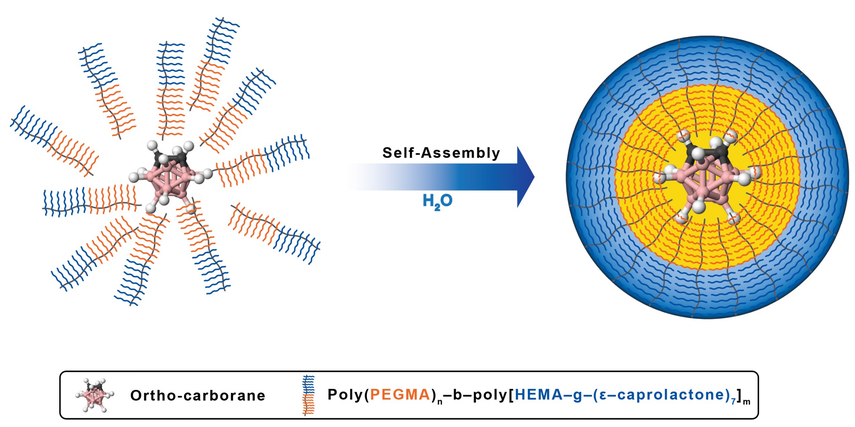
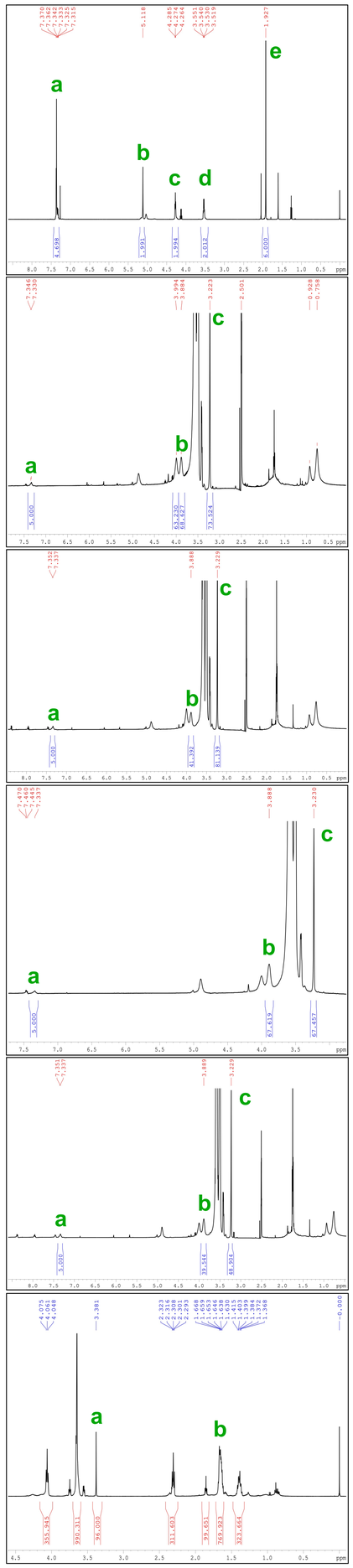
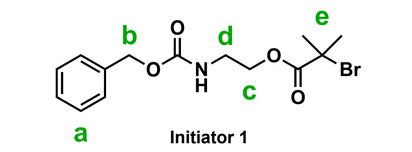
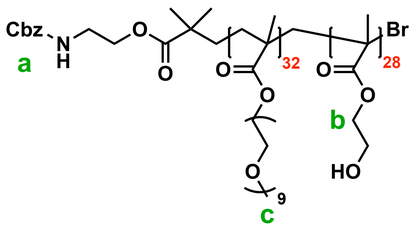


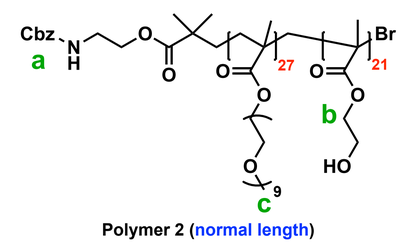
Figure 2. The ortho-carborane can be encapsulated by poly$(PEGMA)_n$–b–poly$[HEMA–g–(\varepsilon–caprolactone)_7]_n$

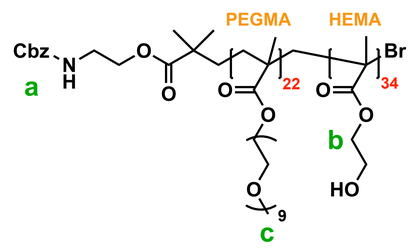
Results

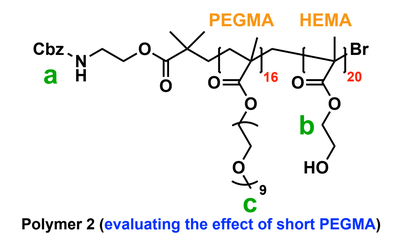












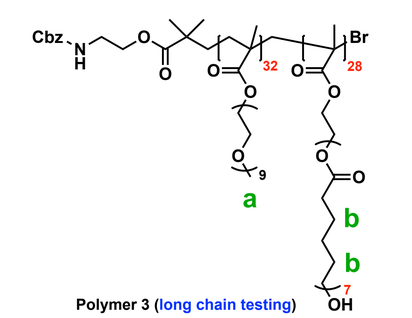


Figure 2. Polymer 3 with long PEGMA and HEMA chain was utilized as testing polymer to evaluate its capacity to form micelles in water. Normal length polymer 2, polymer 2 with long HEMA, and polymer 2 with short PEGMA were utilized to evaluate their capacity to encapsulate ortho–carborane.

Results

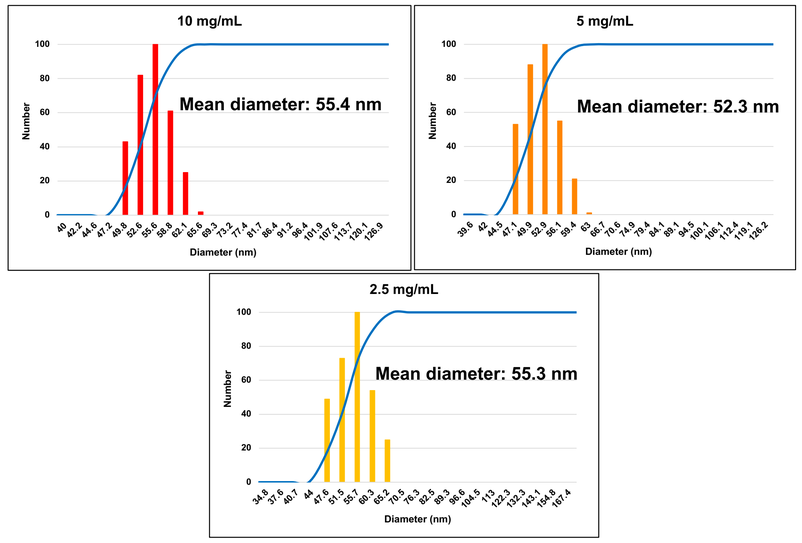


Figure 3. Duplicate of polymer 3 were dissolved in THF at three concentrations. 2 mL of each solution was added to 10 mL of water for the polymers' self-assembly to nanoparticles. The dynamic light scattering technique (above) was utilized to determine the nanoparticle sizes (number results).

Conclusions

- Poly$(PEGMA)_n$ – b – poly$[HEMA – g – (\varepsilon–caprolactone)_7]_m$ is capable of self-assembling to nanoparticles in water.
- The final polymers with different sizes are successfully synthesized and characterized.
- The dynamic light scattering results demonstrates that the concentration of the polymer does not affect the size of the nanoparticles.

Future Direction

- The testing polymer 3 will be first utilized to encapsulate the ortho-carborane using two different methods to determine the better method for this system
- Polymer with different length in PEGMA and HEMA building block will be analyzed for their capacity to encapsulate ortho-carborane using the optimal encapsulating method.
- The drug release profile of each nanoparticles will be investigated.

Acknowledgements

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References

- Zhao, J et al. Simultaneous inhibition of hedgehog signaling and tumor proliferation remodels stroma and enhances pancreatic cancer therapy. *Biomaterials* **2018**, 159, 215–228.