

Novel Self-forming Nanosized DDS Particles for BNCT: Utilizing A Hydrophobic Boron Cluster and its Molecular Glue Effect

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Boron neutron capture therapy (BNCT) is a novel nuclear therapeutic modality that can induce apoptosis in targeted cells, such as malignant cancer cells. Boronophenylalanine and sodium borocaptate are well-known as the first boron compounds clinically approved for BNCT, however, these boron compounds have limited application, particularly in combination with drug delivery systems (DDS). To address the issues, we designed self-assembling nanoparticles composed of polymeric micelles, namely “AB-type lactosome (AB-Lac)” loaded with boron compounds. The particles consist of amphipathic polydepsipeptide linked to a hydrophilic polysarcosine and a hydrophobic poly-L-lactic acid, and this polymer assembly forms micellar-like particles with an average diameter of 36 nm [1]. Moreover, the AB-Lac particles show promising prospects for solid tumor accumulation via the enhanced permeability and retention effect. Three carborane isomers (*o*-, *m*-, and *p*-carborane) and three alkylated *o*-carborane derivatives are 1,2-dimethyl-*o*-carborane (diC1-Carb), 1,2-dihexyl-*o*-carborane (diC6-Carb), and 1,2-didodecyl-*o*-carborane (diC12-Carb), were separately loaded with AB-Lac. diC6-Carb was highly loaded with AB-Lac particles, and their stability indicated the “molecular glue” effect. The efficiency of *in vitro* B uptake of diC6-Carb for BNCT was confirmed at non-cytotoxic concentrations in several cancer cell lines. *In vivo/ex vivo* biodistribution studies showed that the AB-Lac particles were remarkably accumulated within 72 h post-injection in the tumor lesions of mice bearing syngeneic breast cancer 4T1 cells, but reached the maximum accumulation at 12 h post-injection. *In ex vivo* boron biodistribution, the ratios of tumor/normal tissue and tumor/blood of the diC6-Carb-loaded particles remained stably high up to 72 h. Therefore, we propose the diC6-Carb-loaded AB-Lac particles as a promising drug for BNCT [2].

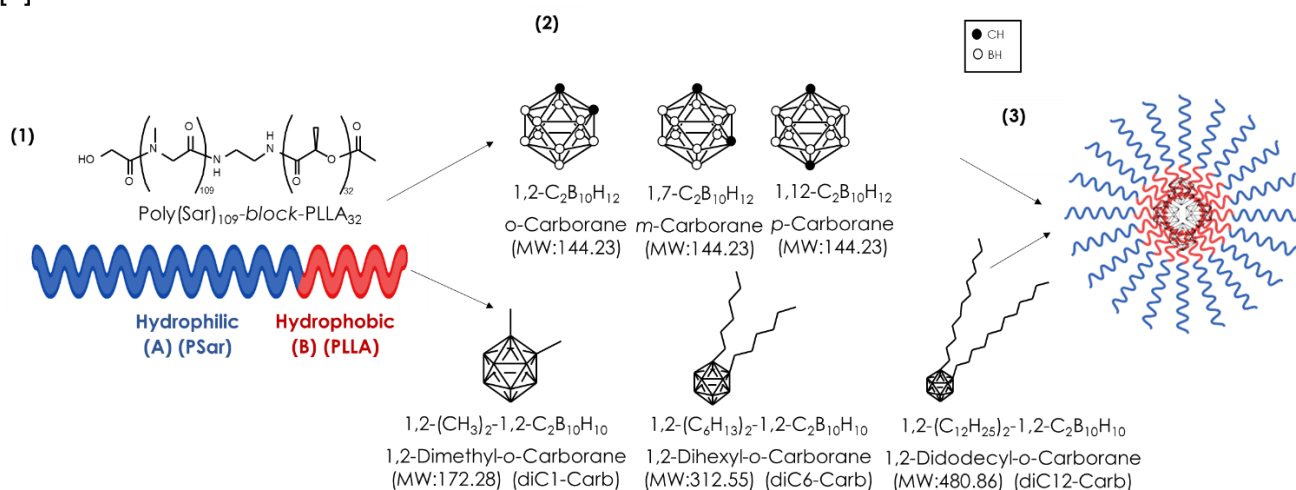


Figure 1. The structural concept of a novel DDS for BNCT.

References

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