Supporting Information

Hyperbranched Polyphosphates for Drug Delivery Application: Design, Synthesis and In Vitro Evaluation

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**Preparation of HPHEEP.** The self-condensation ring opening polymerization of HEEP in bulk was performed in a glove box with the water content less than 0.1 ppm. HEEP (5.00 g, 23.6 mmol) was introduced into a 10 mL flask and stirred by a magnetic bar in an oil-bath at 25 °C for 48 h. The resulting product was dissolved in 30 mL deionized water, enclosed in dialysis membrane (MWCO 1.0 kDa), and then purified by dialyzing in 1000 mL deionized water for 72 h and exchanged at appropriate intervals. After dialysis, the polymer solution was frozen and lyophilized by a freeze-dryer system (Martin Christ, α1-4, Germany) at -20 °C for 48 h.

**NMR Characterization.** Typical $^1$H, $^{13}$C and $^{31}$P NMR spectra of HPHEEP are shown in Figure S1. According to $^1$H NMR spectrum in Figure S1A, the resonances at 3.56, 3.49, 4.13 and 3.64 ppm are assigned to the methylene protons of -OCH$_2$CH$_2$OCH$_2$CH$_2$OH, -OCH$_2$CH$_2$OCH$_2$CH$_2$OH, -POCH$_2$CH$_2$OCH$_2$CH$_2$O- and -POCH$_2$CH$_2$OCH$_2$CH$_2$O- respectively. The peaks at 3.65 and 4.04 ppm are assigned to the methylene protons of -POCH$_2$CH$_2$OH and -POCH$_2$CH$_2$OH respectively. The resonance at 4.21 ppm is the characteristic absorptions from methylene protons (-POCH$_2$CH$_2$OP-). Furthermore, the corresponding signals of carbon atoms of HPHEEP are labeled in Figure S1B. However, the signals of methylene protons and carbons in various structural units such as dendritic, linear or terminal units can not be distinguished in $^1$H and $^{13}$C NMR spectra. Fortunately, the assignment of phosphorus atoms signals in dendritic (-0.41 ppm), linear (0.01, -0.18 ppm) and terminal (0.25 ppm) units of HPHEEP can be identified by $^{31}$P NMR spectrum (Figure S1C). The degree of branching is determined by the quantitative $^{31}$P NMR spectrum of HPHEEP.
Figure S1. NMR spectra of HPHEEP in D$_2$O: (A) $^1$H, (B) $^{13}$C and (C) $^{31}$P spectra.
**GPC Measurement.** As shown in Figure S2, the number-average molecular weight of HPHEEP is 4250 g/mol with PDI of 2.48.

![Figure S2. GPC chromatogram of HPHEEP.](image)