

Supplementary Information 2 - pHPMA synthesis and analysis

Chemicals

Methacryloyl chloride, 1-aminopropan-2-ol, 3-aminopropanoic acid, 4,5-dihydrothiazole-2-thiol, dimethylaminopyridine, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC), azobisisobutyronitrile (AIBN), 4-cyano-4-thiobenzoylsulfanylpentanoic acid, tert-butyl alcohol and pyridine were purchased from Sigma-Aldrich.

Synthesis of the monomers

N-(2-Hydroxypropyl)methacrylamide (HPMA) was prepared by the reaction of methacryloyl chloride with 1-aminopropan-2-ol in dichloromethane [1]. Methacrylamidopropanoic acid (Ma- β -Ala-OH) was prepared by the reaction of methacryloyl chloride with 3-aminopropanoic acid in aqueous alkaline medium [2]. 3-(3-Methacrylamidopropanoyl)thiazolidine-2-thione (Ma- β -Ala-TT) was synthesized by the reaction of Ma- β -Ala-OH with 4,5-dihydrothiazole-2-thiol in the presence of dimethylaminopyridine and EDC. [3]

Synthesis of the reactive pHPMA copolymer

Copolymer poly(HPMA-co-Ma- β -Ala-TT) (pHPMA) was prepared by reversible addition-fragmentation chain transfer (RAFT) polymerization of *N*-(2-hydroxypropyl)methacrylamide (HPMA) (92 mol %, 3 g) and 3-(3-methacrylamidopropanoyl)thiazolidine-2-thione (Ma- β -Ala-TT) (8 mol %, 471 mg) using AIBN (9.35 mg) as an initiator and 4-cyano-4-thiobenzoylsulfanylpentanoic acid (25.20 mg) as a chain transfer agent in tert-butyl alcohol as described earlier. [4] Content of reactive TT groups in the copolymer was 6.8 mol %, weight average molecular weight was $M_w = 44\ 000$ and polydispersity index was $M_w/M_n = 1.12$.

Analysis

Synthesis and purity of monomers were monitored by reversed-phase HPLC using Chromolith Performance RP-18e columns, 100×4.6 mm (Merck, Germany), with a linear gradient of water–acetonitrile (0–100% acetonitrile) in the presence of 0.1% TFA with a UV-VIS diode array detector (Shimadzu, Japan). The determination of the molecular weights and polydispersity of the copolymers was carried out by size exclusion chromatography on a HPLC system (Shimadzu, Japan) equipped with UV, differential refractive index, and multi-angle light scattering DAWN Helleos II (Wyatt Technology Corp., USA) detectors. For the analysis a TSK 3000 SWXL column (Tosoh Bioscience, Japan) (80% methanol, 20% phosphate buffer pH 6.5) at a flow rate of 0.5 mL/min was used. The content of thiazolidine-2-thione (TT) groups was determined spectrophotometrically on a Helios Alpha UV/VIS spectrophotometer (Thermospectronic, UK) using the absorption coefficients for TT in methanol ($\epsilon_{305}=10\ 800\ \text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$).

References

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