J Polym Res (2014) 21:580
DOI 10.1007/s10965-014-0580-7

ORIGINAL PAPER

Synthesis and characterization of thermosensitive poly(N-isopropylacrylamide-co-hydroxyethylacrylamide) microgels as potential carriers for drug delivery

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Received: 7 May 2014 / Accepted: 30 September 2014 / Published online: 12 October 2014

Abstract Thermoresponsive colloidal microgels were prepared by precipitation copolymerization of N-isopropylacrylamide (NIPAM) and N-hydroxyethylacrylamide (HEAM) with various concentrations of a cross-linker in the presence of an anionic surfactant, sodium dodecylsulphate (SDS). The volume phase transition temperature (VPTT) of the prepared microgels was studied by dynamic light scattering (DLS), ultraviolet–visible spectroscopy (UV–vis) and proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. In addition, atomic force microscopy (AFM) was used to characterize the polydispersity and morphology of the microgels. Results indicated that poly(NIPAM-co-HEAM) microgels are spherical and monodisperse. VPTTs of microgels determined by DLS and UV–vis methods are almost the same and very close to the human body temperature, presenting the microgels as candidates for biomedical application. The temperature at which the phase transition occurred is nearly independent of the cross-linking density, whereas the transition range is deeply influenced by temperature. Also, the SDS concentration was increased to decrease the average hydrodynamic size of the microgels, due to the electrostatic repulsion between the charged particles during the polymerization process. ^{1}H-NMR spectra of the microgels show a decrease in peak intensity with an increased temperature due to a reduction in molecular mobility of the polymer segments. Release rates of propranolol from microgels are deeply influenced by temperature; below the VPTT at 25 °C, the drug is rapidly released at a rate comparable to that of a free drug, whereas above the VPTT (37 and 42 °C), a fraction of the drug is mechanically expulsed in the first five min, followed by a prolonged release.

Keywords poly(N-isopropylacrylamide) · Microgel · Smart network · Drug delivery

Introduction

The field of microgels research is marked by some important milestones, such as the preparation of the first microgel in 1935, represented by poly(divinylbenzene) particles [1], the synthesis of the first thermally sensitive microgel based on poly(N-isopropylacrylamide) (poly(NIPAM)) in 1986 [2], the consequent discovery of the importance of surfactants [3], and copolymerization [4, 5].

Microgels can be defined as cross-linked three-dimensional networks able to absorb a solvent to a high degree without dissolution [6], with the average particle diameter ranging between 50 nm and 100 μm. Microgels show clear unique advantages in comparison with other polymer systems: a fast response rate to external stimuli due to their colloidal particle nature; suitability for subcutaneous administration [7]; good biocompatibility since they contain mostly water in the swollen state [8]; a large surface area for multivalent bioconjugation; an internal network for the incorporation of therapeutic drugs; adjustable chemical and mechanical properties [3]; and soft architecture enabling them to flatten themselves onto vascular surfaces, thus simultaneously anchoring in multiple points [9].

Paper dedicated to the 65th anniversary of "Petru Poni" Institute of Macromolecular Chemistry of the Romanian Academy, Iasi, Romania.

Electronic supplementary material The online version of this article (doi:10.1007/s10965-014-0580-7) contains supplementary material available to authorized users.

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