Polymer 141 (2018) 21–33

Contents lists available at ScienceDirect

Polymer

journal homepage: www.elsevier.com/locate/polymer

Stimuli responsive microgels decorated with oligoglycidol macromonomers: Synthesis, characterization and properties in aqueous solution

Christian Willems [a, b], Sascha Pargen [a], Andreea Balaceanu [c], Helmut Keul [a, b], Martin Möller [a, b], Andrij Pich [a, b, *]

[a] Functional and Interactive Polymers, Institute of Technical and Macromolecular Chemistry, RWTH Aachen University and DWI Leibniz Institute for Interactive Materials, Forckenbeckstraße 50, D-52056 Aachen, Germany
[b] Institute of Technical and Macromolecular Chemistry, RWTH Aachen University, Worringerweg 1, 52074 Aachen, Germany
[c] Institute for Research in Biomedicine Barcelona, Carrer de Baldiri Reixac, 08028, Barcelona, Spain

ARTICLE INFO

Article history:
Received 18 December 2017
Received in revised form
20 February 2018
Accepted 21 February 2018
Available online 26 February 2018

Keywords:
Polyglycidol
Macromonomer
Precipitation polymerization
Microgel

ABSTRACT

In this work we focused on synthesis and characterization of aqueous poly(*N*-vinylcaprolactam) (PVCL) microgels decorated with oligoglycidol-macromonomers. Oligoglycidol macromonomers with styrene or acrylate polymerisable group and tunable length of the oligoglycidol chain (6, 12 and 50 glycidol units) were synthesized. The microgels were synthesized by aqueous precipitation copolymerization of *N*-vinylcaprolactam and oligoglycidol macromonomers in presence of crosslinking agent. The length of the oligoglycidol chain and the concentration of macromonomer in the reaction mixture were varied to investigate a direct influence on the polymerization rate and microgel properties. Synthesized microgels exhibit radii from 50 to 350 nm and show temperature-responsive properties. We demonstrate that oligoglycidol macromonomers are localized predominantly on the microgel surface. This ensures excellent colloidal stabilisation of oligoglycidol-decorated microgels in aqueous solutions and functionalization of microgels with hydroxyl groups, which can be potentially used for further post-modification reactions.

1. Introduction

Microgels are soft polymer colloids, which consist of crosslinked polymer chains with a size ranging from a hundreds of nanometers to several micrometers [1]. Microgels exhibit highly porous structure and subsequently contain large quantities of solvent.

Since microgels exhibit exceptional properties like tunable swelling, stimuli-responsiveness and good colloidal stability in aqueous solutions they are of interest for applications in biotechnology, medicine, cosmetics, etc. [2] Poly(*N*-vinylcaprolactam) (PVCL) or poly(*N*-isopropylacrylamide) (PNIPAM) are suitable building blocks for aqueous microgels [3,4]. Microgels based on PVCL and PNIPAM can change reversibly their size and density with temperature. Furthermore, the incorporation of functional groups may induce a change of the microgel properties through changes of the pH, the intensity and wavelength of incoming light, the strength of a magnetic field or the ion concentration in the solvent [5–10]. For example the incorporation of imidazole groups causes a pH-sensitivity by which the particle swells or shrinks depending on the pH of the surrounding environment [11]. Functional microgels can be obtained by (i) post polymerization modification, (ii) by using a two-step polymerization to create core-shell particles or (iii) by directly incorporating functional monomers or macromonomers during the microgel synthesis [12–17]. Surface functionalization is also used to enhance the colloidal stability of dispersion and to incorporate reactive groups for further modification.

In previous publications it was shown, that poly(ethylene glycol) building blocks within microgels – introduced by the copolymerization of *N*-vinylcaprolactam (VCL) with PEG macromonomers – enhance their colloidal stability [17]. Additionally, the content and molecular weight of the PEG building blocks determines the

* Corresponding author. Functional and Interactive Polymers, Institute of Technical and Macromolecular Chemistry, RWTH Aachen University and DWI Leibniz Institute for Interactive Materials, Forckenbeckstraße 50, D-52056 Aachen, Germany.
E-mail address: pich@dwi.rwth-aachen.de (A. Pich).

https://doi.org/10.1016/j.polymer.2018.02.047
0032-3861/

diameter (60–220 nm) and the temperature-responsive properties of the microgels [17,18]. Their presence enhances the biocompatibility [19] and it is possible to introduce functionalities at the chain end by conversion of the hydroxyl end group [20]. Since functionalized PEG exhibits only one terminal OH group per macromonomer, the concentration of functional groups, introduced into the microgel, is rather limited. To increase the functionality of the microgel while retaining the advantages of size and stability control, which are achieved by the presence of PEG, polyglycidol (PG) macromonomers can be used as comonomers for VCL. Polyglycidol has a polyether backbone and a hydroxyl group in every repeating unit, which can be further functionalized. By incorporation of the PG macromonomer into the microgels a higher concentration of reactive hydroxyl groups compared to the same amount of PEG macromonomer could be achieved. It should be mentioned that PG based macromonomers show no cell toxicity so their usage as a comonomer will enhance the biocompatibility of microgels [21,22]. This makes the synthesized microgels desirable for usage in drug release or other medical applications.

In the present work, microgels are synthesized via precipitation polymerization of *N*-vinylcaprolactam in the presence of oligoglycidol macromonomers. We investigate the polymerization process by reaction calorimetry and microgel formation by in-situ DLS and turbidity measurements. The incorporation efficiency and localization of the macromonomers in the microgels is investigated by ^{1}H NMR spectroscopy. The experimental data indicate that macromonomers are covalently bound to the microgel surface and influence the size of the microgel and the colloidal stability of the microgel dispersions.

2. Experimental part

2.1. Materials

Ethoxy ethyl glycidyl ether (EEGE) was obtained from 2,3-epoxypropan-1-ol and ethyl vinyl ether according to Fitton et al. [23], purified by distillation and stored under a nitrogen atmosphere over molecular sieves (4 Å). Diglyme was distilled over sodium and stored under nitrogen atmosphere over molecular sieves (4 Å). 4-Vinylbenzyl alcohol (VBA) and *N*-(2-hydroxyethyl) methacrylamide (HEMAm) were obtained according to literature [24]. It was stored at 4 °C under a nitrogen atmosphere. *N*-Vinylcaprolactam (VCL) was purified by vacuum distillation. THF, hydrochloric acid, potassium *tert*-butoxide, 2, 2′-azobis (2-methylpropionamidine) dihydrochloride (AMPA) and N, N'-methylenebis (acrylamide) (BIS) were used as received. Poly(styrene) and poly(methyl methacrylate) standards for the calibration of the size exclusion chromatography were obtained from the Polymer Standard Service (PSS).

2.2. Synthesis of macromonomers

Oligoglycidol macromonomers were synthesized under a nitrogen atmosphere according to Pargen et al. [24] As a typical example the synthesis of linear oligoglycidol macromonomer VBA-PEEGE-6 with 6 glycidol repeating units is described. VBA (3.0 g, 22.4 mmol) and a small amount of hydroquinone were dissolved in diglyme (20 mL), a 1 M THF solution of potassium *tert*-butoxide (4.5 mL, 4.5 mmol) was added, and the solution was stirred for 30 min at room temperature. Then *tert*-butanol and THF were removed in vacuum. After addition of EEGE (19.65 g, 134.4 mmol) the polymerization was carried out at 80 °C overnight. The reaction was stopped by addition of a small amount of water. Afterwards, diglyme was removed and the product was dried in a vacuum.

VBA-EEGE-6: δ_H (300 MHz, $CDCl_3$) = 1.08 (t, 18 H, CH_3), 1.17 (d, 18 H, CH_3), 3.27–3.63 (m, 42 H, CH, CH_2), 4.48 (s, 2 H, CH_2), 4.64 (m, 6 H, CH), 5.35 (d, 1 H, CH_2), 5.80 (d, 1 H, CH_2), 6.68–6.76 (dd, 1 H, CH), 7.29 (d, 2 H, CH), 7.44 (d, 2 H, CH) ppm.

HEMAm-EEGE-12: δ_H (300 MHz, DMSO) = 1.11 (t, 36H, CH_3), 1.22 (d, 36H, CH_3), 1.84 (s, 3H, CH_3) 3.32–3.70 (m, 88H, CH, CH_2), 4.62 (m, 12H, CH), 5.33 (d, 1H, CH), 5.69 (d, 1H, CH) ppm.

All other oligoglycidol macromonomers were synthesized using the same procedure (The starting materials are listed in Table 1).

The digit of the sample name stands for the number of EEGE repeating units in the macromonomer with respect to the molar amount of vinyl benzyl alcohol or HEMAm.

2.3. Deprotection of Hydroxyl groups in macromonomers

VBA-EEGE-6 was dissolved in THF (30 mL per g polymer) and aqueous HCl (35–38%) was added (1.5 mL per g polymer). The solution was stirred at room temperature for 3 h. During this time an oily phase was formed. THF was decanted, and the product was washed three times with THF. After drying in vacuum the macromonomer was dissolved in water and neutralized with NaOH. After drying in vacuum, the macromonomer was dissolved in ethanol and filtrated. After removal of the solvent and drying, the product was isolated as viscous oil and characterized by NMR spectroscopy. All other oligoglycidol macromonomers were synthesized by the same procedure.

VBA-6: δ_H (300 MHz, DMSO) = 3.19–3.81 (m, 24 H, CH_2), 4.00–4.18 (m, 6 H, CH), 4.49–4.61 (br s, 2 H, CH_2), 4.92–5.01 (m, 1 H, OH), 5.25 (d, 1 H, CH_2), 5.82 (d, 1 H, CH_2), 6.73 (dd, 1 H, CH), 7.31 (d, 2 H, CH), 7.45 ppm (d, 2 H, CH).

HEMAm-12: δ_H (300 MHz, DMSO) = 1.84 (s, 3H, CH_3) 3.32–3.70 (m, 76 H, CH, CH_2), 5.33 (d, 1H, CH), 5.69 (d, 1H, CH).

The products obtained by using VBA as a starter molecule are called VBA-x with x being the number of glycidol repeating units in the macromonomer with respect to the molar amount of vinyl benzyl alcohol. The product obtained by using HEMAm as a starter molecule is called HEMAm-12 with 12 being the number of glycidol repeating units in the macromonomer with respect to the molar amount of hydroxyethyl methacrylamide.

2.4. Synthesis of microgels

2.4.1. Method A

The synthesis of the microgels was carried out in a double-wall glass reactor, equipped with a mechanical stirrer under a nitrogen atmosphere. The synthesized microgel samples are further referred to as MG-x-y-A. X stands for the number of repeating units in the macromonomer whereas y stands for the amount of macromonomer used in mol%. A stands for the synthesis method e.g. batch synthesis. For MG-6-0.5-A VCL (2.09 g, 15.05 mmol) and BIS (0.05 g, 0.32 mmol) were dissolved in distilled water (150 mL). VBA-6 (0.04 g, 0.75 mmol) was added and the temperature was raised to 70 °C. After 30 min of stirring, the initiator AMPA (0.06 g, 0.22 mmol) was added and the solution was stirred for 8 h. The obtained product was purified by dialysis. All other microgels were synthesized using the same procedure. Table 2 gives an overview of the synthesized samples.

The amount of VBA-x used is given as mol% with respect to the molar amount of the VCL monomer (15.05 mmol).

2.4.2. Method B

The synthesis of the microgels was carried out in a double-wall glass reactor, equipped with a mechanical stirrer under a nitrogen atmosphere. The synthesized microgel samples are further referred to as MG-x-y-B. X stands for the number of repeating units in the macromonomer whereas y stands for the amount of