SUPPORTING INFORMATION

Materials

Propargyl alcohol (PA-OH), fluorescein isothiocyanate dextran (FITC-dextran; Mw~150 & 2000 kDa), 1,1'-carbonyldiimidazole (CDI), 3-chloropropanol, sodium azide, dextran (M_w~40 kDa), dimethyl sulfoxide (DMSO), ethyl acetate were purchased from Sigma-Aldrich-Fluka. Sodium ascorbate and tetrabutylammoniumhydrogen sulfate were purchased from Acros. Polyethylene glycol (20 kDa), dichloromethane, ether, copper sulfate ($CuSO_4$), magnesium sulfate and sodium sulfate were purchased from Merck. Phosphate buffered saline (PBS) was purchased from Dulbecco's.

Synthesis propargyl carbonylimidazole (PA-CI)

A dry round bottomed flask was charged with 29.19 g (180 mmol) CDI and 200 ml dichloromethane yielding a turbid suspension. 5.82 ml (100 mmol) propargyl alcohol was added under vigorous stirring yielding a clear solution upon dissolution of the propargyl alcohol. After 1 h reaction at room temperature the to mixture was extracted three times with 35 ml water. The organic layer was dried over magnesium sulfate. After filtering off the magnesium sulfate the liquid was evaporated by rotary evaporation and propargyl carbonylimidazole (PA-CI; 11.86 g; 79 % yield) was obtained as a dry powder. ^{1}H-NMR in $CDCl_3$ recorded with a Bruker AVANCE 500 MHz spectrometer: δ (ppm) 2.6 (t, 1H, HC≡C-), 5.0 (d, 2H, CH_2-O), 7.0 (s, 1H, C=CH-N), 7.4 (s, 1H, N-CH=C), 8.1 (s, 1H, N-CH=N).

Synthesis of dextran-propargylcarbonate (dex-C≡C)

In a dry round bottomed flask 1 g dextran (corresponding to 6.167 mmol glucopyranose repeating units) was dissolved in 20 ml anhydrous DMSO. To this mixture 280 mg (1.86 mmol) PA-CI was added and the reaction was stirred overnight at 50°C under a nitrogen atmosphere. Subsequently the reaction mixture was put in dialysis bags (M_w cut off 3.5 kDa; Spectra Por) and

dialysed against pure water for 5 days. After lyophilisation dextran-propargylcarbonate was obtained as a white fluffy powder.[1]H-NMR in D_2O recorded with a Bruker AVANCE 500 MHz spectrometer: δ (ppm): 5.01 ($1H_{dextran}$, O-C(C<u>H</u>)-O), 4.88 (2H, C≡C-C<u>H_2</u>), 3.5-4.3 (6H, dextran).

Synthesis of 3-azidopropanol

3-azidopropanol was synthesized according to literature.[1] 3-Chloropropanol (30 ml; 33.9 g; 0.358 mol), sodium azide (47 g; 0.716 mol) and tetrabutylammoniumhydrogen sulfate (1g) were dissolved in ml water and stirred at 80°C for 24h followed by overnight stirring at room temperature. The solution was three times extracted with 100 ml ether and dried over sodium sulfate. The ether was removed by rotary evaporation and 3-azidopropanol was obtained as a liquid and purified by vacuum distillation (boiling point 62°C at 3-4 mbar). Yield was 71 %. [1]H-NMR in $CDCl_3$ recorded with a Bruker AVANCE 500 MHz spectrometer: δ (ppm) 1.84 (m, 2H, C-C<u>H_2</u>-C), 3.46 (t, 2H, C<u>H_2</u>-N_3), 3.76 (t, 2H, C<u>H_2</u>-O).

Synthesis of 3-azidopropyl carbonylimidazole (AP-CI)

A dry round bottomed flask was charged with with 18.24 g (112.5 mmol) CDI and 200 ml ethyl acetate yielding a turbid suspension. Ethyl acetate was used as solvent instead of dichloromethane to avoid the formation of diazomethane which is prone to detonation. 6.96 ml (75 mmol, 7.58 g) 3-azidopropanol was added dropwise under vigorous stirring while the reaction mixture turned into a clear solution. After 2 h reaction at room temperature the solution was three times extracted with 200 ml water The organic layer was dried over magnesium sulfate. After filtering off the magnesium sulfate the solvent was evaporated by rotary evaporation and 3-azidopropyl carbonylimidazole (AP-CI) was obtained as a liquid. Yield was 52 %. [1]H-NMR in $CDCl_3$ recorded with a Bruker AVANCE 500 MHz spectrometer: δ (ppm) 2.03 (m, 2H, CH_2-C<u>H_2</u>-CH_2), 3.45 (t, 2H, N_3-C<u>H_2</u>), 4.47 (t, 2H, C<u>H_2</u>-O), 7.0 (s, 1H, C=C<u>H</u>-N), 7.4 (s, 1H, N-C<u>H</u>=C), 8.1 (s, 1H, N-C<u>H</u>=N).

Synthesis of dextran-azidopropylcarbonate (dex-N_3)

In a dry round bottomed flask 1 g dextran (corresponding to 6.167 mmol glucopyranose repeating units) was dissolved in 20 ml anhydrous DMSO. To this mixture 0.301 g (1.54 mmol) or 1.204 g (6.16 mmol) AP-CI was added and the reaction was stirred overnight at 50°C under a nitrogen atmosphere. Subsequently the reaction mixture was put in dialysis bags (M_w cut off 3.5 kDa; Spectra Por) and dialysed against pure water for 5 days. After lyophilisation dextran-azidopropylcarbonate was obtained as a white fluffy powder.^{1}H-NMR in D_2O recorded with a Bruker AVANCE 500 MHz spectrometer. δ 2.02 (2H, C≡C-C$\underline{H}_2$), 3.5-4.3 (6H, dextran), 4.36 (2H, CH_2-C$\underline{H}_2$-O), 5.02 (1$H_{dextran}$, O-C(C$\underline{H}$)-O)

Fabrication of microgels

Microgels (with a predicted water content (according to Stenekes *et al.*[2]) of 50 % (w/w)) were fabricated using a microemulsion method based on the immiscibility between an aqueous dextran and polyethylene glycol phase described by Franssen et al. [3] 12.5 mg dex-N_3 and 12.5 mg dex-C≡C were dissolved in 420 µl pure water. This solution was added to 536 µl of a 50 % (w/w in pure water) polyethylene glycol solution and vortexed for 60 s. $CuSO_4$ (17 µl of a 50 mg/ml stock solution) and sodium ascorbate (17 µl of a 50 mg/ml) were added followed each addition followed by briefly vortexing. The reaction was allowed to proceed for 30 min followed by the addition of water (10 ml) and 3 centriufation (1000 g / 3 min)/washing steps with 10 ml water. Finally the obtained microgels were stored in 5ml water. FITC-dextran was encapsulated in the microgels by addition of 2.5 mg FITC-dextran before the emulsification step.

IR spectroscopy

IR was obtained by attenuated total reflectance IR (Biorad 930C apparatus) using the Golden Gate accessory (diamond crystal). 32 scans were performed at a resolution of 4 cm^{-1}

Release experiment

Directly after the synthesis and washing steps the microcapsules are put in a 15 ml conical centrifugation tube, dispersed in 10 ml PBS and put at 37°C under continuous shaking. At regular time intervals the tubes are centrifuged (1000 g/ 10 min) and 1 ml of the supernatant is withdrawn and replaced by fresh PBS. The tubes are then vortexed to redisperse the microcapsules and the tubes are placed back at 37°C under continuous shaking. The withdrawn samples are stored in the dark at -20 °C. The time point of complete microcapsule degradation is determined visually when no pellet remains after centrifugation of the tubes. The samples are then measured in a Wallac Victor 2 (Perkin Elmer) plate reader and the cumulative release curve is constituted.

Microscopic characterisation

Optical microscopy images were recorded in transmission mode using a Nikon EZC1-si confocal laser scanning microscope equipped with a 60x water immersion objective.

For scanning electron microscopy (SEM), a drop of microcapsule suspension was deposited on a silicon wafer and dried under a nitrogen stream followed by sputtering with gold. SEM images were recorded with a Quanta 200 FEG FEI scanning electron microscope operated at an acceleration voltage of 5 kV.

References

1. Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K., Highly efficient "click" functionalization of poly(3-azidopropyl methacrylate) prepared by ATRP. *Macromolecules* **2005,** 38, 7540-7545.
2. Stenekes, R. J. H.; Franssen, O.; van Bommel, E. M. G.; Crommelin, D. J. A.; Hennick, W. E., The use of aqueous PEG dextran phase separation for the preparation of dextran microspheres. *International Journal of Pharmaceutics* **1999,** 183, 29-32.
3. Franssen, O.; Hennink, W. E., A novel preparation method for polymeric microparticles without the use of organic solvents. *International Journal of Pharmaceutics* **1998,** 168, 1-7.