Poly(aspartic acid) hydrogels showing reversible volume change upon redox stimulus

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The shortcomings of conventional solid drug formulations – e.g. non-effective or toxic blood levels of drug – might be overcome by the use of formulations providing controlled delivery. Responsive hydrogels can be developed to such formulations because they are able to control the release of their payload by changing their physical properties upon environmental stimuli [1]. Redox sensitive hydrogels have gained particular attention in targeted delivery, since they respond to the redox gradient in the body caused by the different glutathione concentrations in the cytosol (0.5–10 mM) and in the extracellular matrix (2–20 µM) [2]. Most of the reported hydrogels exhibited only a one-way response and disintegrated upon reduction [3]. Redox-responsive gels with a reversible volume change [4] would have a large advantage: a modulated release controlled by the pathological state of the patient could be achieved similarly to the glucose dependent release of insulin from certain nanogels [5].

Redox and pH sensitive poly(aspartic acid) (PASP) based hydrogels were prepared by cross-linking cysteamine-modified PASP with a non-cleavable (permanent) cross-linker, poly(ethyleneglycol)diglicidyl ether. The volume of the hydrogels increased upon reduction and decreased upon oxidation (Fig 1) due to the reversible cleavage of disulphide linkages inside the matrix as proven by infrared spectroscopy. The degree of swelling was highly dependent on the thiol-content and the cross-linking ratio. Mechanical stiffness of hydrogels was characterized by their elastic modulus, which was also strongly affected by the composition and oxidation state. To explore the possible biomedical use of the hydrogels, hydrogel loaded with model drug was prepared. Drug release measurement showed that the drug release was remarkably faster in reducing environment, which indicates the potential use of the synthesized hydrogels for redox-modulated drug delivery.

Figure 1 Degree of swelling of redox-sensitive poly(aspartic acid) hydrogels upon repeated oxidation/reduction.