Smart Reactivity in Gelatine/PNIPAM Mixtures: Control of the Cross-Linking and Microheterogeneities

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Summary: Chemical cross-linking of gelatine was achieved by using a thermo-sensitive reactive poly(N-isopropylacrylamide) as a cross-linker. The reaction occurs only below the LCST. Controlled micro-heterogeneities were created inside the gel without macroscopic volume transition. Acceleration of the drying process indicates faster water diffusion in the micro-heterogeneous gel.

Keywords: gelatine; gels; heterogeneities; poly(N-isopropylacrylamide); stimuli-sensitive polymers

Introduction

Gelatine is a denatured, biodegradable protein that can be used for the preparation of hydrogel matrices in drug delivery applications.[1] The drug release depends, among other factors, on the cross-linking density and homogeneity of the hydrogel. Further control of the matrix properties can be achieved by combining gelatine with a thermo-sensitive polymer like, for instance, poly(N-isopropylacrylamide), PNIPAM.[2,3] PNIPAM exhibits inverse solubility behaviour (LCST, Lower Critical Solution Temperature) in aqueous solution. At the LCST (∼32 °C) the polymer chain undergoes a coil-to-globule transition and this thermo-sensitive behaviour is of interest for the development of stimuli responsive aqueous formulations, surfaces and gels.[4–8] The properties of gelatine and PNIPAM have been combined in graft copolymers[9,10] and interpenetrating networks.[2,3]

In this work we explore the possibility to control the chemical cross-linking and properties (local heterogeneity) of gelatine gels by using a NIPAM-based copolymer as a thermo-sensitive cross-linker. The copolymer bears 5 mol% acrylic acid (AA) units. The cross-linking occurs by amide bond formation between the AA groups of the NIPAM-based copolymer and the amino groups of gelatine in the presence of a water soluble carbodiimide (EDC).[11] For comparison purposes we also used a non-thermo-sensitive copolymer (LCST > 100 °C) based on dimethylacrylamide (DMAM) and containing the same fraction of AA units (5 mol%).

Experimental Methods

Gelatine (bovine, $M_w \approx 180000$ g/mol) was provided by Kodak Industrie (France). The copolymers ($M_w \approx 30000$ g/mol) were synthesized by radical copolymerization in aqueous solvent.[12] The fraction of AA units, 5 mol%, corresponds to the monomer feed composition and it was confirmed by elemental analysis and potentiometric titration of the resulting copolymers. The NIPAM and DMAM-based copolymers will be referred to as PN-5 and PD-5 respectively (Figure 1). As water-soluble carbodiimide we used 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDC) from Aldrich.