ENZYME-DEGRADABLE POLY(2-OXAZOLINE)-BASED DRUG DEPOTS

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The thiol-ene reaction is one of the most extensively investigated examples of the so-called click reactions and can be used for the crosslinking reaction of copoly(2-oxazoline)s containing C=C double bonds in their side-chains.[1] Such crosslinked poly(2-oxazoline)s can be used in biomedical applications such as cell adhesion and drug delivery.[2] Using mercapto crosslinkers that additionally contain ester bonds, polymer networks are obtained that can be degraded upon stimuli such as pH changes or the addition of enzymes.

If such poly(2-oxazoline)-based networks are synthesized from the polymeranalogous thiol-ene crosslinking reaction of dedicatedly functionalized copoly(2-oxazoline)s with glycol dimercaptoacetate, the straightforward loading of the gels with APIs present in the reaction mixture is enabled. Numerous of such gels composed of 2-ethyl- and 2-nonyl-2-oxazoline as well as 2-but-3'-enyl- and 2-dec-9'-enyl-2-oxazoline exhibit glass-transition temperatures in the range from 20 to 30 °C, which renders them stiff below and flexible at body temperature. Gels that do not contain any repetition units of 2-nonyl-2-oxazoline are hydrogels. Maximum swelling degrees of 6 in water can be observed. All other gels act as lipo- or amphigels. The degradation of the networks and concomitant release of the occluded molecules with rabbit liver esterase at pH = 8 was found to proceed very comparable with the enzyme-free degradation at pH = 10. Highest release rates were found for the degradation of the networks by porcine liver esterase at pH = 8. [3]

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