Preparation of Polyamino Acid Self-Healing Hydrogels Based on 2-Ureido-4[1*H*]-Pyrimidinone

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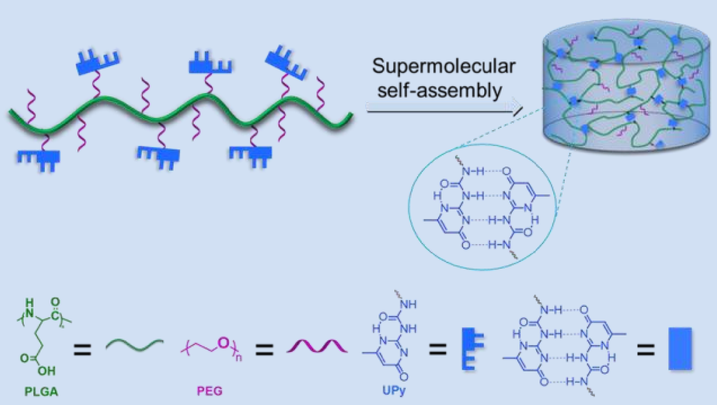
Introduction

Hydrogen bonding is a driving force of great significance in nature life self-assembly. 2-Ureido-4[1*H*]-pyrimidinone (UPy), as a self-complementary quadruple hydrogen bonding, is the most widely studied hydrogen bonding motif, which has a favorable dimerization constant in methylbenzene. Self-healing hydrogels can be devised for stem cell delivery and therapy as an injectable cell carrier, getting more and more attention from researchers. Currently, self-healing hydrogels have been extensively reported, but few reports are focused on the development of self-healing hydrogels using UPy motifs as cross-linking points, especially for tissue engineering applications. The reason is that most self-healing hydrogels employ non-degradable polymers, such as polyethylene glycol (PEG), polyacrylates, dextran, for the substrates. Poly(l-glutamic acid) (PLGA) is a biodegradable and biocompatible polypeptide, which has been successfully used in a variety of tissue reconstructions.

Results

The reversible nature of UPy dimers endows the hydrogel with characteristics of self-healing and shear-thinning properties as well as the cross-linked network. At the microscopic level, when the strain applied increases, the hydrogel's cross-linked network begins to break down. When the strain reaches a certain degree, the gel network is completely broken down and transformed into sol. In the strain-modulus curve, as shown in Fig.2a, when the strain was 200%, the storage modulus G' was the same as the loss modulus G'', where was the gel-sol conversion point. Cyclic alternate strain test was conducted on the hydrogels, as shown in Fig.2b, indicating that the hydrogels had good self-healing performance. Through the determination of viscosity-shear rate, as shown in Fig.2c, showing the characteristics of shear-thinning. At high-speed shear, the crosslinking network was damaged, with the corresponding viscosity decreased. When the shear force was removed, the UPy dimers were recombined to form a new crosslink point and realize the healing of the hydrogels. The shear-thinning property of hydrogels made it convenient to deliver from outside to inside of the vials during injection (Fig.2d-f).

All the dynamic characteristics of the self-healing hydrogels showed the great potential in tissue engineering application.



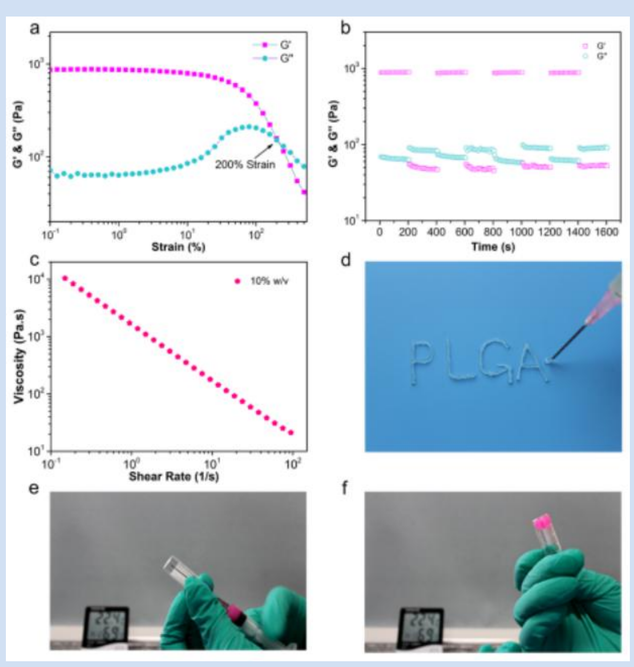


Fig.1 Preparation of the self-healing hydrogels

Fig.2 Dynamic characteristics of the self-healing hydrogels: (a)(b) self-healing ability (c)shear-shinning ability (d)(e)(f) injectability

Experimental

UPy moieties were grafted on the PLGA backbone, employing α-hydroxy-ω-amino poly(ethylene oxide) (HAPEO) as the connection agent. Self-healing hydrogels were developed through UPy units as crosslinked blocks. Self-healing and shear-thinning behaviors of the hydrogels were performed at 37° C by oscillatory mode on a rheometer. The injectable test was verified with an 18G needle (outside diameter=1.20 mm, injection speed=1 mL/min).

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