Iranian Polymer Journal (2019) 28:957–967
https://doi.org/10.1007/s13726-019-00758-8

ORIGINAL RESEARCH

Multi-stimuli-responsive poly(hydroxyethyl methacrylate-*co*-*N*-vinyl pyrrolidone-*co*-methacrylic acid-*co*-*N*-isopropylacryl amide) hydrogel: synthesis, characterization and application in drug release

Xiaoli Yang[1] · Kunyan Wang[1] · Lei Yan[1] · QiNing Yu[1] · Hongxia Xia[1] · Yanbo Liu[1] · Chengjun Yan[1]

Received: 14 April 2019 / Accepted: 5 October 2019 / Published online: 22 October 2019

Abstract

Multi-stimuli-responsive hydrogels are being increasingly studied due to their sensitive response to small stimuli and wide applications in biosensors and drug delivery. In this study, a multi-stimuli-responsive hydrogel, poly(hydroxyethyl methacrylate-*co*-*N*-vinyl pyrrolidone-*co*-methacrylic acid-*co*-*N*-isopropylacryl amide) [poly(HEMA-*co*-NVP-*co*-MAA-*co*-NIPA)], was synthesized by radical polymerization and characterized by Fourier transform infrared (FTIR) and ^{13}C NMR spectroscopy techniques. With the aids of scanning electron microscopy (SEM) characterization, it was confirmed that the sensitive stimuli-responsive behavior of the hydrogel stemmed from its microstructure variation with those external stimulus. Rheological study showed that the hydrogel had rheological feature of typical elastomer. Compression tests revealed that the poly(hydroxyethyl methacrylate-*co*-*N*-vinyl pyrrolidone) [poly(HEMA-*co*-NVP)] played an important role in enhancing the compressive modulus of such hydrogel. More interestingly, the equilibrium swelling ratio (ESR) studies further confirmed that the composite hydrogel displayed response sensitively to the stimulus of temperature, pH, and ionic strength. Herein, theophylline as a drug model was adopted due to the multi-stimulus properties of hydrogels, which were a potential candidate for drug loading and delivering. Releasing drug continuously in a given period was dependent on the characteristics of solution and loading time. The mechanisms for drug release from the hydrogels were studied by Ritger–Peppas model.

Keywords Stimuli-responsive · Hydrogel · Thermo-response · pH-response · Drug release

Introduction

Hydrogels are generally considered as three-dimensional (3D) networks of linear hydrophilic polymers that can swell and retain large amounts of water in aqueous media [1]. Over the past few years, hydrogels have attracted much research interests due to their high mechanical strength [2], good biocompatibility [3], optical properties [4], stimuli-response [5], and oxygen permeability [6].

Stimuli-response is one of the most fascinating properties of hydrogels, namely, the hydrogels can respond sensitively to a variety of external stimuli, such as pH [7], temperature [8], ionic strength [9], light [10], etc. For instance, poly(*N*-isopropylacryl amide) (PNIPA) gel is a famous thermo-responsive polymer, which exhibits a sharp phase transition (lower critical solution temperature, LCST) of around 32–33 °C in water [11]. Functionalized by hydrophilic or hydrophobic groups, PNIPA chains exhibit a hydrated coiled conformation below LCST as their hydrophilic amide groups, form large amounts of hydrogen bonds with surrounding water molecules, while transforming to a globular conformation above LCST by exposing their hydrophobic isopropyl groups to the surrounding water [12]. Poly(methacrylic acid) (PMAA) polymer, a well-known pH-response hydrogel, is functionalized by carboxylic acid and methacrylate groups [13]. At low pH value, carboxylic acid groups are protonated and engaged in hydrogen bond to maintain the PMAA hydrogel in a collapsed configuration. While at high pH value, the carboxylic acid groups are deprotonated to become anions, which repel each other to minimize the

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s13726-019-00758-8) contains supplementary material, which is available to authorized users.

✉ Xiaoli Yang
yangxljit@163.com

[1] College of Material Engineering, Jinling Institute of Technology, Nanjing 211169, People's Republic of China