Industrial Crops and Products 93 (2016) 227–234

Contents lists available at ScienceDirect

Industrial Crops and Products

journal homepage: www.elsevier.com/locate/indcrop

Cellulose nanocrystals extracted from rice husks as a reinforcing material in gelatin hydrogels for use in controlled drug delivery systems

Shok Yin Ooi[a], Ishak Ahmad[a,*], Mohd. Cairul Iqbal Mohd Amin[b]

[a] Faculty of Science and Technology, University Kebangsaan Malaysia, 43600, Bangi, Selangor, Malaysia
[b] Faculty of Pharmacy, University Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia

ARTICLE INFO

Article history:
Received 10 October 2015
Received in revised form
17 November 2015
Accepted 29 November 2015
Available online 14 December 2015

Keywords:
Gelatin
Cellulose nanocrystal
Hydrogel
Cross-linking
Swelling behavior
Drug carrier

ABSTRACT

Hydrogels with remarkable sensitivity toward changes in pH were prepared using gelatin reinforced with cellulose nanocrystals (CNCs). Glutaraldehyde was used as a crosslinker because of its high chemical reactivity toward the NH_2 group on gelatin. CNC ratios of 0%, 5%, 10%, 15%, 20%, and 25% were chosen to study the effects of CNCs on the dynamic mechanical properties and swelling behavior of gelatin-based hydrogels. Crosslinking between gelatin monomers was confirmed by the presence of a C═N stretching group at 1630 cm^{-1} in the FTIR spectrum of gelatin hydrogels. The overall crystallinity and dynamic mechanical properties of gelatin hydrogels increased as the CNC content increased. The increase in the overall crystallinity improved the storage modulus of the CNC-gelatin hydrogel from 122 Pa to 468 Pa by the addition of 25% CNC. From the swelling test, CNC-gelatin hydrogels showed excellent pH sensitivity with a maximum swelling ratio at pH 3. The ability of the CNC-gelatin hydrogel to respond to different pH values along with its high dynamic mechanical stability suggested that CNC-gelatin hydrogels are promising candidates as drug carriers. Theophylline was used in this research as a model drug to further evaluate the potential of these CNC-gelatin hydrogels to act as drug carriers. Drug loading efficiency and drug release profiles of the CNC-gelatin hydrogels were studied. The findings suggest that gelatin hydrogels reinforced with 15% CNC are the best potential candidates for controlled drug delivery system.

1. Introduction

Hydrogels are polymeric materials with capability to swell and retain large amounts of water without dissolving in water (Iqbal et al., 2011). Hydrogels can be produced from both natural and synthetic polymers by physical or chemical crosslinking. Recently, attention has been focused on finding materials that are non-toxic and biocompatible for applications in pharmaceutical, medical, and nutritional fields (Muhamad et al., 2011). Examples of some specific uses of hydrogels include drug carrier systems (Kim and Park, 2011), wound dressings (Balakrishnan et al., 2005), gene transfection (Gojgini et al., 2011), tissue engineering scaffolds (Hou et al., 2010), sensors (Frisk et al., 2007), and dye removal materials (Abdel-Halim, 2013).

Gelatin is one of the biopolymers used to produce hydrogels owing to its advantages such as non-toxicity, high water absorption, biodegradability, and biocompatibility. These features make gelatin an excellent candidate for use in drug delivery systems. The principal benefit of using hydrogels in drug delivery systems is their ability to deliver drugs locally and with a time-release capability. This benefit can reduce drug dosages, costs, and side effects, and, therefore, can enhance the efficacy of their use (Kim and Park, 2011). Hydrogels act as drug delivery systems by entrapping drug molecules within the confines of crosslinked polymer networks. When inserted into a recipient, contact with water will cause the hydrogel to swell. Swelling increases the distance between the crosslinked polymer chains, which allows the drug to be released and absorbed into the bloodstream (Tada et al., 2005).

Recently, other natural materials such as polysaccharides have been used as reinforcement materials in the production of polymer hydrogels (Vakili and Rahneshin, 2013). Cellulose, one of the most common naturally occurring polysaccharides, is attractive to researchers because it is readily available, biodegradable, and bio-

* Corresponding author. Fax: +60 3 89215410.
E-mail addresses: gading@ukm.edu.my, gading_99@yahoo.com (I. Ahmad).

http://dx.doi.org/10.1016/j.indcrop.2015.11.082
0926-6690/

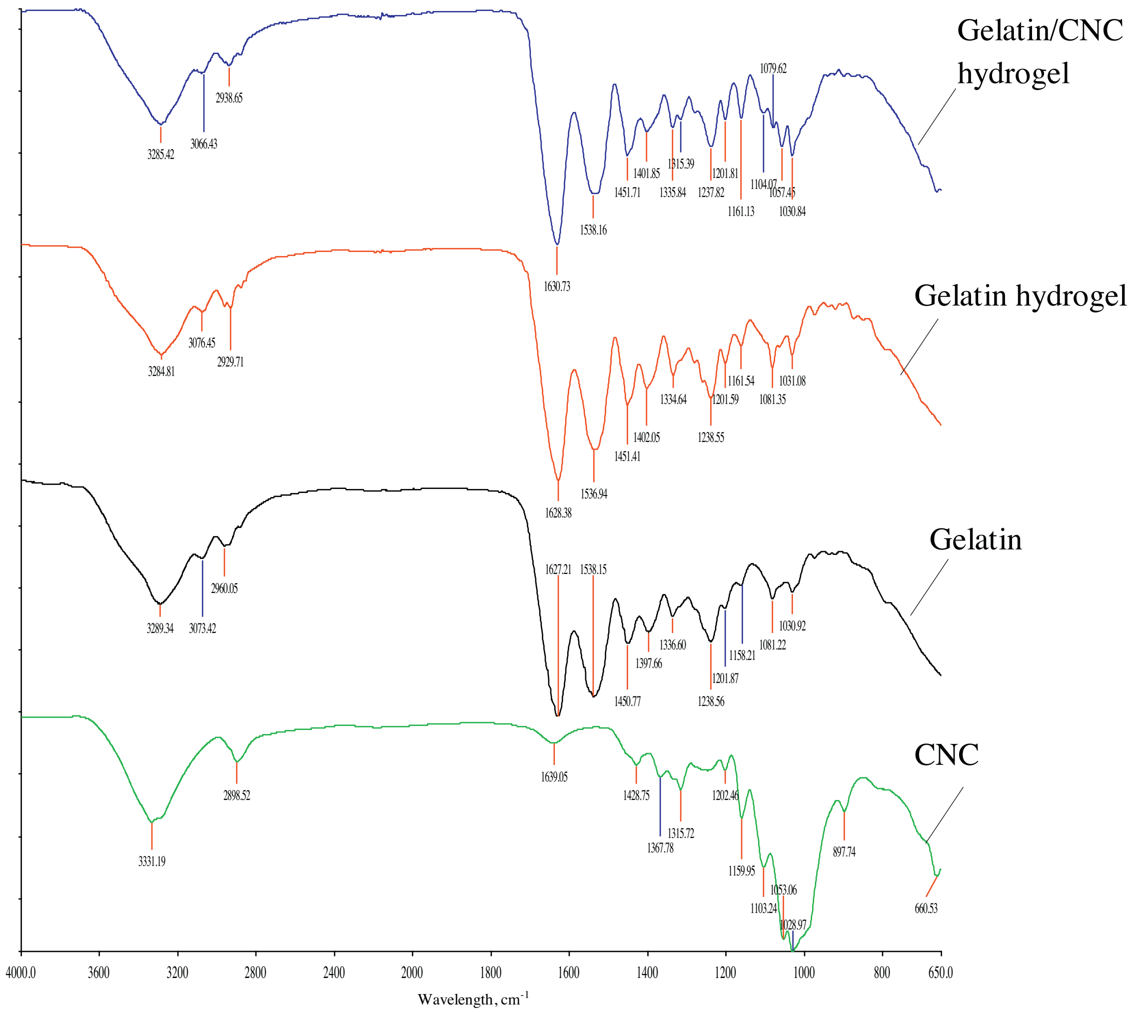

Fig. 1. FTIR spectra recorded for gelatin and cellulose nanocrystal (CNC)-gelatin hydrogels.

compatible (Wang and Wang, 2010). Rice husks, which are the byproducts of grain crops, are one of the largest waste products in crop production today. Rice husks contain a high cellulose content and can be easily modified chemically, which make them suitable for the extraction of cellulose nanocrystals (CNCs) (Xie et al., 2011). CNCs exist in a needle-like form with dimensions less than 100 nm in length with a high degree of crystallinity (Peng et al., 2011). The main features that make CNCs attractive as a reinforcement material in polymers are their large surface area, high mechanical strength, high aspect ratio, hydrophilicity, non-toxicity, low bulk density, biocompatibility, and biodegradability (Dufresne, 2003). Despite much researches on cellulose based hydrogels for different applications, the use of CNC as reinforced materials in hydrogels from gelatin for drug delivery system has not been reported previously.

In the research presented in this paper, gelatin is used in the production of hydrogels for potential use in drug delivery systems. However, due to gelatin's poor mechanical properties, gelatin hydrogels are reinforced with CNCs that form semi-interpenetrating polymer networks (semi-IPNs). Semi-IPNs improve a hydrogel's mechanical properties, control its swelling ratio, and improve its drug release behavior. Typically, a high amount of crosslinking agent is required to control a hydrogel's mechanical properties and swelling ratio. By using CNCs in this research, we were able to reduce the amount of chemical crosslinking agent used while achieving the same desired results.

2. Materials and methods

2.1. Materials

Pharmaceutical-grade gelatin was purchased from Halagel (M) Sdn. Bhd. Glutaraldehyde, acetone, and theophylline were obtained from System ChemAR and Sigma–Aldrich.

2.2. Preparation of gelatin-CNC hydrogels

CNCs were extracted from rice husk fibers by acid hydrolysis using sulfuric acid. We followed the preparation and characterization of CNCs reported in a previously published study (Ooi et al., 2015). CNCs were first homogenized using homogenizer Ultra Turrax model T25 Digital, Ika to ensure that they are dispersed uniformly. Gelatin was added to the CNC suspension, and then heated and stirred on a hot plate at 55 °C for 1 hour. Once a uniform viscous mixture was obtained, 3 wt% glutaraldehyde was added dropwise. The mixture was then gently stirred for 4 h to prevent bubble formation before casting onto a Petri dish. The resulting hydrogel was placed in an oven at 45 °C until it became dry. After removing from the oven, the hydrogels in the form of thin films were removed