Materials Science and Engineering C 75 (2017) 478–486

Contents lists available at ScienceDirect

Materials Science and Engineering C

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

Ultrasound stimulated release of gallic acid from chitin hydrogel matrix

Huixin Jiang, Takaomi Kobayashi *

Department of Materials Science and Technology, Nagaoka University of Technology, 1603-1 Kamitomioka, Nagaoka, Niigata 940-2188, Japan

ARTICLE INFO

Article history:
Received 10 August 2016
Received in revised form 14 February 2017
Accepted 15 February 2017
Available online 20 February 2017

Keywords:
Chitin hydrogel
Gallic acid
Ultrasound
Drug delivery

ABSTRACT

Ultrasound (US) stimulated drug release was examined in this study using a chitin hydrogel matrix loaded with gallic acid (GA), a drug used for wound healing and anticancer. Using phase inversion, GA-chitin hydrogels were prepared from chitin-dimethylacetamide (DMAc)/lithium chloride (LiCl) solution in the presence of GA, with 24 h exposure of the solution to water vapor. The GA release from the GA-chitin hydrogel was examined under different US powers of 0–30 W at 43 kHz. The effects of GA loading amounts in the hydrogels (0.54, 0.43, and 0.25 mg/cm^3) and chitin concentrations (0.1, 0.5, and 1 wt%) on the release behaviors were recorded under 43 kHz US exposure at 30 W. Results show that US accelerated the release efficiencies for all samples. Furthermore, the release efficiency increased concomitantly with increasing US power, GA loading amount, and decrease of the chitin concentration. The highest release rate of 0.74 μg/mL·min was obtained from 0.54 mg/cm^3 of GA-loaded hydrogel fabricated from a 0.1 wt% chitin mixture solution under 43 kHz US exposure at 30 W: nine times higher than that of the sample without US exposure. The hydrogel viscoelasticity demonstrated that the US irradiation rigidified the material. FT-IR showed that US can break the hydrogen bonds in the GA-chitin hydrogels.

© 2017 Elsevier B.V. All rights reserved.

1. Introduction

Recently, smart drug delivery systems (SDDS) have attracted greater attention because of their higher drug-release efficiency and more-controllable properties than those of DDS without external stimuli [1]. Generally speaking, SDDS are controllable systems in which the drug is loaded into a certain carrier. The drug is later released under control of external stimuli. Therefore, three important SDDS components are the carrier, drug, and external stimuli. Usually, polymeric carriers are effective when external stimuli of magnetic [2], pH [3], temperature [4], light [5], and ultrasound (US) [6] are used to improve the SDDS release efficiency.

Because of its safe, non-invasive, and painless properties, US technique has become noteworthy [7]. One US process, known as a sonoprocess, has been applied widely in material chemistry [8], organic synthesis [9], separation processes [10] for food production industries [11], and in medical areas [12] because US can strongly accelerate chemical and physical processes. Actually, US waves are known to be transduced in water medium and to cause cavitation effects. Oscillatory US can strongly promote the release of a drug from its carrier [7]. The application of US to drug delivery has proven to be useful for enhancing the drug release efficiency relative to commonly applied diffusion process [13]. Moreover, soft US therapy has been used in the treatment of carpal tunnel syndrome [14], musculoskeletal disorders [15], chronic wounds [16], and some other therapeutic applications.

Among the carrier materials used for SDDS, hydrogel matrix plays an important role in medical therapy [17]. Biomass polymers such as cellulose, chitin, and chitosan, and other polysaccharides are favorable to prepare hydrogels that are suitable for application to the human body [18,19]. Hydrogels produced from biomass polymers can retain large amounts of water and provide excellent biocompatibility. Actually, the use of chitin is known to provide several advantages over other natural polymers such as cellulose, dextran, starch, and carrageenan for wound healing ability and antibacterial activity [20]. In tissue engineering, drug delivery applications have become especially meaningful for wound healing. Through combined healing ability of the drug support matrix, drug delivery systems should be addressed much more effectively. Therefore, investigation of chitin is necessary for drug delivery systems. Chitin (Fig. 1(a)), an abundant natural material, derives mainly from crab and shrimp shells, presents benefits of nontoxicity, biocompatibility, and biodegradability, making chitin a useful biomaterial [21]. Actually, chitin has been used widely in biomedical applications such as tissue engineering [22], wood dressing [23], drug delivery [24], and cancer treatment [25]. These biomedical applications make chitin a good candidate for use as an implantable material [26]. Unfortunately, most common solvents show difficulty dissolving chitin because interaction of OH groups gives it a highly crystallized structure. This shortcoming hinders the chitin hydrogel process. Applications of chitin hydrogels are therefore severely constrained, especially for non-functionalized chitin as a raw material to form a chitin hydrogel matrix.

* Corresponding author.
E-mail addresses: takaomi@nagaokaut.ac.jp, takaomi@vos.nagaokaut.ac.jp (T. Kobayashi).

http://dx.doi.org/10.1016/j.msec.2017.02.082
0928-4931/© 2017 Elsevier B.V. All rights reserved.

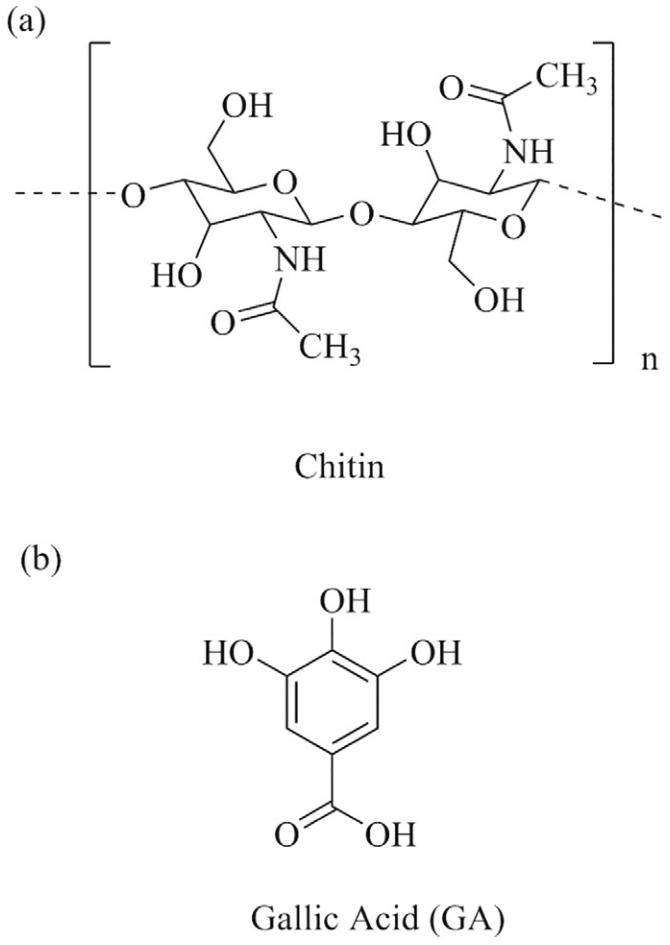

Fig. 1. Chemical structures of chitin (a) and GA (b).

Hydrogels composed of biomass polymers for tissue engineering can be prepared using chemical cross-linking [27] and physical effects achieved through freezing-thawing [28] and phase inversion processing [29]. More recently, phase-inversion hydrogels of cellulose have exhibited excellent biocompatibility [30] and less cytotoxicity [31]. Such cellulosic hydrogels loaded with drugs have been applied as a US trigger for drug release [32].

Therefore, in this study, to produce raw chitin that can accommodate more applications, chitin hydrogels from crab shells loaded with drugs were prepared using phase inversion processing. They were then applied for US SDDS. To complement the biocompatibility and wound healing capabilities of the chitin hydrogel matrix, gallic acid (GA, 3, 4, 5-trihydroxybenzoic acid, Fig. 1(b)) loaded into the chitin hydrogel provided excellent wound healing, anticancer, antibacterial, anti-inflammatory, and antioxidant capabilities [33,34]. This study examined GA release properties under US exposure from the raw chitin hydrogel. The US power, experiment conditions, GA loading amount, and chitin concentration for the hydrogel matrix were used as variable parameters to investigate GA release behavior. The viscoelasticity and FT-IR of hydrogels were compared before and after US exposure to elucidate the hydrogel properties.

2. Material and methods

2.1. Materials

Crab shells were obtained from Teradomari Port (Niigata Prefecture, Japan), where *Chionoecetes opilio* were purchased. Defatted cotton was purchased from Kawamoto Corporation (Osaka, Japan). Gallic acid, lithium chloride (LiCl), potassium hydroxide (KOH), potassium bromide (KBr), hydrochloric acid (HCl, 35.0–37.0%), ethanol (C_2H_5OH) and agar were purchased from Nacalai Tesque Inc. (Japan). Carrageenan was purchased from Tokyo Kasei Kogyo Co., Ltd. (Japan). *N*,*N*-dimethylacetamide (DMAc) was a product of TCI Co., Ltd. (Japan). Before use, DMAc was dried with KOH for 5 days. LiCl was dried in vacuum at 80 °C for 24 h.

2.2. Preparation of GA-chitin hydrogel

The extraction of chitin from crab shells was conducted using methods reported by Yen [35] and Yamaguchi [36], with some modifications. Briefly, the crab shells (20 g) were washed with large amounts of water, and were treated with 1 N HCl (700 mL) at 26 °C for 24 h to remove mineral components. The resultant shells were washed with water until neutral pH and were then treated with 1 N NaOH (700 mL) at 90 °C for 5 h to eliminate protein. Subsequently, the shells were washed to neutral pH with distilled water. After that, 1000 mL of EtOH was added, and the mixture was heated at 60 °C for 12 h for decolorization. Then, extracted chitin was obtained after drying in vacuum at 50 °C for 24 h. To confirm the reproducibility of the purification process, three batches of chitin were extracted. The resultant yields were 28.8, 30.0, and 30.2%. Each molecular weight was 1.51×10^6, 1.56×10^6 and 1.47×10^6 g/mol, respectively. The degrees of acetylation were 72, 73.2, and 72% determined by FT-IR measurements. These results confirmed that the treatment method used for extracting chitin from the crab shell had reproducible results for each purification process.

As presented in Fig. 2, the obtained chitin and GA were dissolved separately in DMAc containing 6 wt% of LiCl. Then, the solutions of GA and chitin were mixed together. For the preparation of same GA loading hydrogels with different chitin contents, the GA concentrations in the mixture were fixed to 0.07, 0.09, and 0.1 wt% when the respective chitin concentrations were 0.1, 0.5, and 1 wt%. Details of GA and chitin concentrations in the mixture solution are presented in Table 1. The GA-chitin hydrogels were coagulated by exposure of the mixture solutions to water vapor at 26 °C for 24 h. Then, the hydrogels were immersed in large amounts of distilled water to remove DMAc.

To compare the drug release properties of GA-chitin hydrogels, other hydrogels of cellulose, agar and carrageenan were prepared as follows. The GA-cellulose hydrogel from defatted cotton was prepared using the same method reported before [29], except that addition of GA in the mixture solution was 0.06 wt%. For the preparation of GA-carrageenan hydrogel and GA-agar hydrogel, 1 wt% carrageenan and 1 wt% agar were dissolved separately in hot water. Then, GA was mixed with the carrageenan or agar solution and the GA concentration was adjusted to 0.02 wt%. The GA-carrageenan hydrogel and GA-agar hydrogel were obtained after the mixture solutions were gelated at 26 °C for 4 h. The obtained GA-carrageenan hydrogel and GA-agar hydrogel were used to assess the GA release property.

The extracted chitin was characterized with FT-IR spectra and gel permeation chromatography (GPC). The FT-IR spectra of the extracted chitin were recorded using a spectrometer (FTIR/4100; Jasco Inc.) in the region of 4000–400 cm^{-1} with KBr as background. The degree of acetylation (DA) was calculated using a previously reported method [37] with the following equation, $DA = (A_{1560} / A_{2875} - 0.2) / 0.0125$, where A_{1560} and A_{2875} refer to the absorbance of peak 1560 and 2875 cm^{-1} in the FT-IR spectra of chitin.

Gel permeation chromatography (GPC) was done to determine the molecular weight distribution of chitin. The GPC system was equipped with a refractive index (RI) detector (RID-10A; Shimadzu Corp., Japan), online degasser (DGU-20A; Shimadzu Corp., Japan), high-pressure pump (LC-20AD; Shimadzu Corp., Japan), manual injector (7725i; Rheodyne LLC), GPC column (KD-806 M; Shodex; Showa Denko K.K.) and a Chromatopac Integrator (CR8A; Shimadzu Corp., Japan). The column temperature and the RI detector cell were kept at 50 °C and 40 °C, respectively. A 1 wt% LiCl/DMAc solution was used as

Download English Version:

https://daneshyari.com/en/article/5434847

Download Persian Version:

https://daneshyari.com/article/5434847

Daneshyari.com