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Development of a gallic acid-loaded chitosan and polyvinyl alcohol hydrogel composite: Release characteristics and antioxidant activity

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ABSTRACT

The physico-chemical properties of a chitosan and polyvinyl alcohol (CS/PVA)-based hydrogel composite were investigated. Tetraethyl orthosilicate (TEOS) was employed as a crosslinking agent. The results indicated that the chitosan-based composite presented a thermal resistance up to 200 °C. The structural properties, which were evaluated using FTIR and DSC, showed good miscibility between chitosan and polyvinyl alcohol. SEM presented a compact and homogeneous structure. The release profile of the chitosan-based hydrogel composite was investigated using gallic acid (GA). It showed high antioxidant activities, which were monitored using DPPH radical scavenging. Diffusion of water into the chitosan-based hydrogel was assumed to be pseudo-Fickian in PBS solution. The CS/PVA-based hydrogel composite exhibited good properties as a drug delivery system.

1. Introduction

With the exponential growth of the worldwide population, the development of industrial technology was researched to fulfill the requirement of human welfare. The role of industrial technology was developed from lab-scale research to the industrial sector. From the fundamental point of view, numerous technology approaches are versatile and are used in the food and beverage, medical research, infrastructure, electronic devices and automotive industries. Although, the existence of technology offers many benefits for quality of life and welfare, it may result in waste and hazardous products, which are difficult to manage. Therefore, to solve this issue, many environmental policies are strictly encouraged. The concept of policy may involve the utilization of chemical reagents and hazardous products on a controllable scale. This concept was employed in many research studies and product lines. However, the concept of green technology is very challenging. It is considered an alternative technique for solving environmental issues [1–4]. Moreover, it is remarkable to note that the properties of biomaterials have gained significant interest. Biomaterials offer high mechanical properties, high chemical resistance, high thermal stability and good optical properties. Utilization of biomaterials was strongly considered as the most efficient technique for sustainable development. Up to now, many biomaterials have been developed such as cellulose and its derivatives, chitin and chitosan, poly lactic acid, and starch.

To our knowledge, chitosan (CS) was considered a naturally occurring biopolymer. It was commercially produced via deacetylation of chitin. From the structural point of view, chitosan was described as a linear polysaccharide composed of randomly distributed β-(1→4) linked D-glucosamine and *N*-acetyl-D-glucosamine [5–9]. It was produced by treating the chitin shells of shrimp and other crustaceans with an alkaline substance. Utilization of chitosan provided many advantages such as low toxicity, a high level of biocompatibility and assistance in cell attachment, proliferation and non-antigenicity. Currently, due to many benefits, the use of chitosan has gained significant interest for development in food technology, medical and pharmaceutical research. One of the most challenging research aspects for chitosan was focused on hydrogel formation [10–13]. From the fundamental point of view, a hydrogel's physicochemical properties can be altered in response to external stimuli. Due to the existence of certain functional groups along the polymeric chain, a hydrogel can be changed by temperature, pH, enzyme and even ionic strength. Subsequently, this resulted in the utilization of hydrogels in many diverse applications such as drug delivery systems, artificial muscle, gene delivery systems, immobilization of enzyme, food technology and cosmetic applications [14–16]. To form a

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hydrogel composite, polyvinyl alcohol (PVA) was considered as the matrix phase. The water absorbing capacity of polyvinyl alcohol is 5–10 times its weight. It was commonly employed in the food, medicine and chemical industries. It provided many excellent properties such as gel properties, water holding capacity, film formation and foaming ability [17]. Chitosan and polyvinyl alcohol crosslink with TEOS, which is a non-toxic and biocompatible crosslinker that easily binds via condensation reactions in comparison with previously reported crosslinkers (glutaraldehyde, epichlorohydrin, borate and tripolyphosphate) [18]. Islam et al. have reported the use of TEOS for synthesizing a pH sensitive chitosan and polyvinyl alcohol blend for controlled drug delivery application [19]. TEOS or a silane crosslinker are suitable for enhanced interfacial adhesion and improved mechanical properties of composite materials due to the reaction of Si-O bonds in TEOS, which reacted with an amino group in a chitosan polymer.

Therefore, to evaluate the chitosan-based hydrogel as a controlled-release material, gallic acid (GA, 3, 4, 5-trihydroxybenzoic acid) was employed as a bioactive compound. It is considered an antioxidant and is commonly found in a variety of fruits and vegetables, for example, in tea leaves, grapes, cherries, and longan seeds. From the structural point of view, GA is considered as a trihydroxybenzoic acid, which is commonly employed in health science research [20]. It is a natural phenolic antioxidant, which is extractable from natural products. It has been reported that GA has anti-allergic, anti-inflammatory, anti-mutagenic and anti-carcinogenic activity [21]. Furthermore, de Rosa et al. prepared chitosan-containing GA via the lyophilization method to enhance antioxidant activities [22]. Chitin hydrogel-loaded GA provided wound healing, and anticancer activity was studied [23]. To integrate chitin into a CS/PVA-based hydrogel composite, chitosan was conjugated with GA to provide water solubility, water swelling property, and antioxidant activity to the chitosan hydrogel using a crosslinking agent [24].

Controlled release systems maintain the drug concentration in the blood or in target tissues at a desired value as long as possible. Normally, initially, the controlled release system rapidly releases a drug. Then, the drug release kinetics follows a release behavior to supply the maintenance dose, which enables the attainment of a desired drug concentration. The Higuchi and Korsmeyer-Peppas model was used to detect the mechanism of drug release. This model is represented by the equation $M_t/M_\infty = Kt^n$, where M_t/M_∞ is the fraction of drug release at time t, K is the release rate constant, and n is the release exponent. The n value is used to predict the release mechanism of the drug. A value of $0.45 \leq n$ corresponds to the Fickian diffusion mechanism, that of $0.45 < n < 0.89$ to non-Fickian transport, $n = 0.89$ to case II transport, and n □ 0.89 to super case II transport.

The objective of this research work is to encapsulate GA, as a model phenolic compound, in a CS/PVA-based hydrogel composite using a conventional synthetic route. The physicochemical properties of the hydrogel were investigated. In addition, the antioxidant capacities and release characteristics of the encapsulated GA were measured.

2. Experimental

2.1. Materials

Chitosan (medium molecular weight, 75–85% degree of deacetylation) and polyvinyl alcohol (molecular weight 4000 g/mole) were purchased from Sigma Aldrich, Co, ltd. They were employed as starting chemical reagents. Tetraethyl orthosilicate (TEOS) was purchased from Sigma Aldrich, Co, ltd. Phosphate buffered saline (PBS) was purchased from VWR Cief Science Amresco, LLC. These compounds were employed as a crosslinking agent and a buffer solution, respectively. Acetic acid was purchased from Labscan Asia Co., ltd. All chemical reagents were used as received without further purification.

2.2. Methods

2.2.1. Preparation of a chitosan and polyvinyl alcohol-based hydrogel composite

A chitosan and polyvinyl alcohol (CS/PVA)-based hydrogel composite was prepared via wet conventional synthesis. The amount of chitosan that was added to the CS/PVA hydrogel (9:1 to 5:5 ratios) was coded as CS/PVA 9:1, CS/PVA 8:2, CS/PVA 7:3, CS/PVA 6:4 and CS/PVA 5:5. Briefly, chitosan was dissolved in acetic acid (1% v/v) at room temperature for 3 h to ensure solubility. In parallel, polyvinyl alcohol was dissolved in DI water (10% w/v). Then, the chitosan solution was poured into the polyvinyl alcohol solution. In total, 2 ml of TEOS was added to the mixture. The solution was stirred at 70 °C for 3 h to obtain a homogeneous gel. After that, the gel was casted onto a petri dish and dried in an oven at 70 °C. To load GA into the CS/PVA composite hydrogel, which is coded as GA-CS/PVA, GA was loaded into a CS/PVA solution in the amount of 20%wt based on the polymer solution, coded as GA-CS/PVA 9:1, GA-CS/PVA 8:2, GA-CS/PVA 7:3, GA-CS/PVA 6:4 and GA-CS/PVA 5:5. The solution was stirred at 70 °C for 3 h to obtain a homogeneous gel. Then, the gel was casted onto a petri dish and dried in an oven at 70 °C.

2.2.2. Swelling properties of the hydrogel composite

The CS/PVA-based composite was investigated for swelling behavior. In this study, the gravimetric technique was employed to determine the swelling and equilibrium data of the hydrogel. It was immersed in DI water for 48 h. After an appropriate time interval, specimens were removed from the solution, dried with a filter paper to remove excess water, and were measured. Five samples were investigated, and the data were reported as the statistical average and standard deviation. The swelling ratio was determined as follows [Eq. (1)]:

$$Q(g/g) = (W_{wet} - W_{dry})/W_{dry} \quad (1)$$

where W_{wet} is the weight of a swollen hydrogel at submersion time, and W_{dry} is the initial weight of the dry hydrogel.

2.2.3. DPPH radical scavenging activity of gallic acid-loaded chitosan/PVA hydrogels

The DPPH radical scavenging activity of GA-CS/PVA hydrogels was determined using the method developed by Chuysinuan et al. [26]. Briefly, each specimen with a 2.5-cm diameter round shape was first extracted in 10 ml of methanol and then shaken in a water bath for 1 h. An aliquot of the sample was diluted with 10 ml of methanol. The reaction mixture consisted of 1.0 ml of the sample and 3.0 ml of the DPPH radical solution (0.1 mM in methanol). The absorbance of the reaction mixture, which was protected from light, was measured after 30 min. The mixture was incubated for 30 min in the dark at ambient temperature. The absorbance was measured using a microplate reader at 517 nm. The % scavenging activity was calculated according to the following equation [Eq. (2)]:

$$\%\text{scavenging} = [(\text{Abs.Blank} - \text{Abs.Sample})/\text{Abs.Blank}] \times 100 \quad (2)$$

2.2.4. In vitro release study

The cumulative amount of released GA from GA-CS/PVA hydrogels was measured using immersion methods. The specimens (2.5 cm in diameter, circular shape) were individually immersed in 30 ml of a phosphate buffer solution (PBS buffer) at 37 °C for 4320 min. The sample solution (1 ml) was withdrawn at submersion time intervals, and an equal amount of fresh release medium