Materials Science and Engineering C xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Materials Science and Engineering C

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

On spray drying of oxidized corn starch cross-linked gelatin microcapsules for drug release

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ARTICLE INFO

Article history:
Received 28 August 2016
Received in revised form 30 October 2016
Accepted 11 December 2016
Available online xxxx

Keywords:
Gelatin
Oxidized corn starch
Microcapsules

ABSTRACT

Spray-dried gelatin/oxidized corn starch (G/OCS) microcapsules were produced for drug release application. The prepared microcapsules were characterized through a scanning electron microscope (SEM) picture and thermogravimetric analysis (TGA). The swelling characteristics of the G/OCS microcapsules and release properties of vitamin C were then investigated. The results from structural analysis indicated that the presence of miscibility and compatibility between oxidized corn starch and gelatin, and exhibits high thermal stability up to 326 °C. The swelling of G/OCS microcapsules increased with increasing pH and reduced with decreasing ionic strength, attributed to the cross-linking between gelatin and oxidized corn starch, ionization of functional groups. Vitamin C release characteristic revealed controlled release behavior in the first 3 h of contact with an aqueous medium. This release behavior was independent of the swelling behavior indicating the potential of the encapsulating matrix to produce controlled release across a spectrum of pH environment.

1. Introduction

Spray drying is the most common technology used in the microcapsules industry due to its low cost and availability [1]. It is an attractive process for obtaining particulate pharmaceutical products containing gelatin, because of the short heating time involved in spite of the high thermal and high humidity shear stressed [2]. In recent years, the use of microcapsules have been proposed for the treatment of many diseases, because it can maintain drug concentration in the blood or deliver targeting drug to specific cells and organs [3,4]. Natural polymers such as albumin and gelatin are good candidates for the preparation of microcapsules, to decrease toxicity or biodegradability problems possibly related to the use of synthetic materials [5]. In particular, gelatin represents a good raw material since it easily forms film and can gelatinize into particles. In addition, gelatin is cheap and available with desirable biocompatible and bio-adhesive properties [6], which open new application opportunities in drug delivery systems. According to previous research [3–6,7], the gelatin has many sources and uses, however, there are few reports on gelatin and oxidized corn starch microencapsulation which can be applied to drug controlled release for a model therapeutic ingredient. In this study, gelatin was used for the preparation of microcapsules to achieve the drug release application, which was based primarily on our previous research in the broad application of gelatin [5,7]. The research results indicated that gelatin has good biological compatibility, biodegradable properties, water-retention, etc., and it is good candidates for the preparation of microcapsules, to decrease toxicity or biodegradability problems possibly related to the use of synthetic materials. In addition, vitamin C (Vc) is used as an essential nutrients in most organisms, including humans, pigs, and birds. To achieve the excellent release properties of Vc, the gelatin need be modified to use for the preparation of microcapsules. Because a main drawback of gelatin is the rapid solubility in aqueous system [8] which could introduce a fast drug release. Cross-linking the gelatin can be used to control the release speed. The cross-linking process (e.g. glutaraldehyde and formaldehyde treatment) between gelatin and other materials could reduce the dissolution rate of the polymer and drug release by the formation of partially soluble polymers [9]. However, the use of cross linkers can lead to toxic side effects due to the residual of the cross-linking agent or unwanted reactions with the drugs. It had been reported that oxidized dextran could be an interesting means to cross-link gelatin microspheres allowing the use of this delivery formulation for controlled release of drugs [10]. In this respect, oxidized corn starch with a large

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http://dx.doi.org/10.1016/j.msec.2016.12.047
0928-4931/

number of carboxyl and carbonyl groups can be used as a potential of crosslinker with gelatin, to adjust the drug release behavior by manipulating the cross linking density. Therefore, oxidized starch cross-linked gelatin microcapsule production with conventional technology and without the shortcomings of pure gelatin have both scientific and commercial importance. This work explores the potential to use oxidized starch cross-linked gelatin as microencapsulation material in providing controlled release for a model therapeutic ingredient.

2. Materials and methods

2.1. Materials

Corn starch (CS), gelatin (G, type A), hydrogen peroxide (H_2O_2) and L-ascorbic acid (99%) were purchased from Sigma Aldrich (Australia). Ascorbic acid, also known as vitamin C (Vc), is a water-soluble vitamin necessary for normal growth, development and repair of damaged tissues in the body. Human and other animals lack the ability to produce it and therefore require it as a dietary supplement [11]. In our work, Vc was used as a model of water soluble drug. Buffer solutions (pH 4.0, 7.4 and 10.0) were bought from Sigma Aldrich in Australia. The dialysis sacks (Avg. flat width 25 mm) were obtained from Sigma Aldrich (Australia). 0.1 mol/L sodium hydroxide (NaOH, Sigma Aldrich) and 0.1 mol/L hydrochloric acid (HCl, Sigma Aldrich) were used to adjust the solution to the desired pH.

2.2. The preparation of oxidized corn starch

The oxidized corn starch (OCS) was prepared as follows: one known concentration (30% wt) of slurry was prepared by mixing CS and distilled water with the pH adjusted to 4.0. The reactants were heated at 80 °C for 1 h with gentle stirring followed by cooling the solution to 50 °C and maintaining at this temperature till required. Hydrogen peroxide (0.1 M) was then added to the reactants with an amount equivalent to 30% of the weight of the corn starch. After 6 h, the slurry was immediately separated by high speed centrifugation at 5000 rpm for 10 min [12]. The oxidized corn starch was then dried at 50 °C for 24 h using a vacuum oven. The carboxyl group content was estimated based on one chemical titration method [13] without modification with 10% carboxyl group. It was determined by titrating a sample solution with a standard NaOH solution. While the carbonyl group content was determined by reacting carbonyl groups with hydroxylamine reagent and then back-titrating with an HCl solution [14] containing 50% carbonyl group. And the total degree of oxidation of oxidized corn starch was obtained 38.5% according to one simple method [15].

2.3. The preparation of precursor solution

The compositions of precursors for spray drying are showed in Table 1. In a typical procedure, 100 g of a 3% (wt) G/OCS (60:40) [12] solution was prepared by mixing distilled water at 80 °C for an initial 30 min at a 100 rpm stirring speed then for a further 30 min at 500 rpm stirring speed. Calculated amounts of Vc as the model drug were added into the solution based on the percentage of the G/OCS solid mass. Therefore, the final solution will have a higher %wt solute depending on the amount (g) of Vc added.

2.4. Spray drying

Spray drying process was performed in a laboratory spray Labplant SD-05 (Huddersfield, England) with a 1.5 diameter nozzle in the RMIT University. The prepared precursor solutions were obtained with a 1.5Ø pressure nozzle assisted with a vibration generated by the piezoceramic material surrounding the nozzle. From preliminary trials, we found that free flowing powders were obtained with a feed flow rate (10 mL/min) and an atomization pressure of 0.06 MPa. The dryer inlet temperatures were adjusted at 120 °C, 150 °C and 180 °C. The obtained dried powders were collected and kept in sealed reagent bottle.

Table 1
Gelatin/oxidized corn starch microcapsules characteristic under different compositions of precursors.

Number of runs	Model drug (w/w)	Inlet temperature (°C)	Outlet temperature (°C)	Moisture content (%)	Particle color
1	0	120	71	8.2	White
2	0	150	80	7.0	White
3	0	180	90	6.4	White
4	20	120	70	8.5	White
5	20	150	80	7.5	White
6	20	180	90	6.0	Light red
7	40	120	71	8.7	White
8	40	150	81	7.5	White
9	40	180	90	6.4	Light red
10	60	120	70	8.5	White
11	60	150	80	7.0	White
12	60	180	90	6.3	Light red

Note: the particle shapes were consistently spherical with wrinkled surface in all 12 runs.

2.5. Characterization of samples

In order to reveal the microstructure of the G/OCS microcapsules which were obtained by using the method of spraying-dried. Then the microstructure of the microcapsules was investigated by using Hitachi S-4800 scanning electron microscope (SEM, Hitachi Co., Japan); Thermogravimetric analyses of the G/OCS microcapsules were carried out by a TG209F1 thermal analyzer (NETZSCH-Gertebau GmbH, Germany) under nitrogen atmosphere. Thermostability of the samples was inferred from the decomposition profile in the TGA thermogram.

2.6. Moisture content

The moisture content of the powder was determined gravimetrically by drying in a vacuum oven at 60 °C until constant weight about 48 h [16].

2.7. Swelling analysis under different parameters

The swelling behavior of the G/OCS microcapsules was studied by determining the increase in the weight of the swollen microcapsules at increasing time intervals of 5, 10, 30 and 120 min. At different time intervals, data points were obtained for the last time interval. The dried microcapsules (250 mg) were put into a dialysis sack and were kept in an aqueous solution under 37 °C with 50 rpm stirring speed in a shaking incubator. At each time interval, the swollen microcapsules were taken out and wiped with a filter paper to remove the surface water, weighed and then put back into the same bath [17]. The mass determination was continued until the weight of microcapsules remained constant. All the experiments were carried out with three duplicates and an average of six values were reported in this work.

When a typical polymer is placed in a solvent, the solvent diffuses into the polymer matrix, forming a swollen gel phase in the wetted region, which is defined as swelling process [18]. At the same time, if the polymer is cross-linked, the polymer would swell to some equilibrium state, limiting the amount of water penetration and controlling the release of the loaded drug. The diffusion procedure involves transport of water into pre-existing or dynamically formed spaces between the macromolecular chains [19]. Assuming a spherical particle, the initial

Please cite this article as: X. Dang, et al., On spray drying of oxidized corn starch cross-linked gelatin microcapsules for drug release, Mater. Sci. Eng., C (2016), http://dx.doi.org/10.1016/j.msec.2016.12.047