Carbohydrate Polymers 101 (2014) 650–655

Contents lists available at ScienceDirect

Carbohydrate Polymers

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

Designing nanoemulsion templates for fabrication of dextrin nanoparticles via emulsion cross-linking technique

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ARTICLE INFO

Article history:
Received 10 July 2013
Received in revised form 22 August 2013
Accepted 14 September 2013
Available online xxx

Keywords:
Dextrin
Nanoparticles
Emulsion crosslinking technique
Ultrasonication

ABSTRACT

The aim of this study was to prepare dextrin nanoparticles by emulsion cross-linking technique. The nanoparticles were prepared from nanoemulsion templates produced by high power ultrasonication. The influence of hydrophilic–lipophilic balance (HLB), surfactant type and concentration, water content, and sonication time on the template size were examined in order to find optimal conditions for preparing dextrin nanoparticles. Nano-scaled templates were achieved when mixed surfactants (Span80/Tween80 and Span80/Brij30) at HLB 6 were used while using Span80 or other HLB values resulted in micron-sized templates. The smallest emulsion templates were achieved when using 7% (w/w) mixture of Span80/Tween80 at HLB 6, 15% (w/w) water, and sonication time of 30 min. The spherical dextrin nanoparticles possessed a slight negative charge on the surface. FTIR spectra confirmed that dextrin was cross-linked by glyoxal. This study developed a novel way of formulating dextrin nanoparticles, which may prove to be useful in future for drug delivery.

1. Introduction

Currently, nanoparticles have been used in a wide number of applications, for example, as drug carriers, biosensors, and in the nanoelectronic field (Jiang, 2012; Qureshi, Kang, Davidson, & Gurbuz, 2009; Xie, Lee, & Chen, 2010). Due to their submicron size, nanoparticles possess a high surface-to-volume ratio, improved dispersibility and adaptability for multiple functions (Singh & Lillard, 2009). Both synthetic and natural materials have been investigated for fabrication of nanoparticles with different characteristics. Several natural biopolymers such as chitosan, alginate, pectin, polylactic acid, shellac, gelatin, starch and dextrin have received growing attention as nanocarriers for pharmaceutical applications. Dextrin, a saccharide-based polymer containing D-glucose units linked by α-(1 → 4) glycosidic bonds, is produced by partial hydrolysis of starch. It has a same general structure as starch but is smaller and thereby less complex (Carvalho, Gonçalves, Gil, & Gama, 2007). Dextrin is a widely used material with a variety of applications, from adhesives to food additives and textiles (Carvalho et al., 2007). Due to the biocompatibility and degradability attributes of dextrin, this biopolymer is used to prepare biodegradable drug carriers, especially hydrogels, with applications in a large number of areas such as medicine and pharmacy (Carvalho et al., 2007; Ferguson & Duncan, 2009).

Various techniques have been explored for the production of polysaccharide nanoparticles, including free radical graft polymerization, cross-linking by chemical reactions, radiation-induced polymerization and cross-linking, and self-assembly processes (Motornov, Roiter, Tokarev, & Minko, 2010). The emulsion (water-in-oil) cross-linking technique provides broad capabilities for variations in the structure that involves dispersion of an aqueous phase in an oil phase, in the presence of an effective surfactant system to produce nanoscale droplets or nanoemulsions (Burapapadh, Takeuchi, & Sriamornsak, 2012). The droplets of nanoemulsions can maintain the shape and size of the particles within the dispersed phase while generating starch particles through a cross-linking reaction (Ethirajan, Schoeller, Musyanovych, Ziener, & Landfester, 2008). Since the nanoemulsion is a non-equilibrium system, energy input from chemical potential or mechanical devices is required (Antonietti & Landfester, 2002; Landfester, 2001). Nanoemulsion can be prepared by high-energy emulsification methods or by low-energy emulsification methods (Noor El-Din & Al-Sabagh, 2012). Low-energy emulsification methods create chemical

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http://dx.doi.org/10.1016/j.carbpol.2013.09.049

potential through the use of surfactants. However, this method requires a large quantity of surfactants compared to the nanoemulsion which is obtained by the high-energy method (Liu, Sun, Li, Liu, & Xu, 2006). High-energy emulsification requires large mechanical energy generated by rotor–stator equipments such as ultrasound generator or high-pressure homogenizer to produce fine droplets (Lin & Chen, 2006; Burapapadh et al., 2012). The high-energy input provides forces that are able to deform and break off drops into smaller ones, provided the Laplace pressure is overcome. Adsorption of surfactant at the drop interface reduces the Laplace pressure (Solans et al., 2003), however, the smaller the droplet size, the higher the energy required for further drop break-off (Shi, Li, Wang, Li, & Adhikari, 2011).

Ultrasonic emulsification is a type of mechanical homogenizing technique that has been used for emulsion preparation by ultrasonic vibrating waves. Powerful ultrasonic waves with a high frequency can generate a continuous cycle of production and collapse of air bubbles, causing a phenomenon called cavitation. Large amounts of energy are released by this process and are transferred to the liquid solution, thereby creating a mechanical dispersion effect, which can result in homogeneous emulsification (Lin & Chen, 2006). It was found that the ultrasonic homogenizer creates emulsions with smaller droplet size and better stability than a simple homogenizer (Abismaïl, Canselier, Wilhelm, Delmas, & Gourdon, 1999). Moreover, the ultrasonic emulsification technique has been used to prepare emulsions for various applications including the food (Koocheki & Kadkhodaee, 2011) and fuel (Lin & Chen, 2006) industries.

The present study aimed to prepare dextrin nanoparticles using a two-step process. Firstly, nanoemulsion templates were prepared by high power ultrasonication. The effects of various parameters such as HLB, concentration of surfactant, water content and sonication time were investigated to optimize conditions that provide the smallest droplet size for fabrication of dextrin nanoparticles. Secondly, dextrin nanoparticles were produced using the emulsion cross-linking technique in the nanoemulsion templates. The physicochemical properties of the obtained dextrin nanoparticles were characterized.

2. Materials and methods

2.1. Materials

Dextrins (MW of 1400 and 1000, referred as D2 and D4, respectively) were donated by the Siam Modified Starch Co., Ltd. (Pathumthani, Thailand). Glyoxal and ethanol were obtained from Sigma–Aldrich Chemie (Steinheim, Germany). Hydrochloric acid and *n*-hexane were purchased from RCI Labscan (Bangkok, Thailand). Tween® 80, Brij® 30 and Span® 80 were purchased from PC Drug Center Co., Ltd. (Bangkok, Thailand) and are hereafter referred to as Tween80, Brij30 and Span80, respectively. All reagents were of analytical grade or pharmaceutical grade and used as supplied without further purification. Deionized water was used throughout the study.

2.2. Preparation of nanoemulsion templates

Nanoemulsion templates were prepared by a high energy emulsification method using high power ultrasonicator (400 W, 24 KHz) with constant amplitude (100%). A water bath was also used to maintain the temperature of the mixture at $30 \pm 2\,^{\circ}C$. In this method, different amounts of water were added to the *n*-hexane phase containing a mixture of Span80 and Tween80 or Brij30 at various ratios.

2.3. Preparation of dextrin nanoparticles

To prepare dextrin nanoparticles, dextrin was dissolved in the water phase to obtain the final concentration of 5% (w/w) and then added to the emulsions obtained from Section 2.2. The mixture was ultrasonicated for 1 min to form nanoemulsions. After the nanoemulsion was formed, glyoxal (as a cross-linker) was added immediately and ultasonicated for 30 min. The obtained mixtures were then stirred with a magnetic stirrer for 12 h to continue the cross-linking reaction. The dextrin nanoparticles were precipitated from the nanoemulsion by adding 99% ethanol and washed 3 times with ethanol and finally rinsed with deionized water. Subsequently, the nanoparticles were dried by lyophilization for 24 h. The dry nanoparticles obtained from the lyophilization process was kept in a plastic bag and stored in the refrigerator (4–5 °C) until further use.

2.4. Droplet size and surface charge (zeta potential)

The mean droplet size and surface charge of the prepared nanoemulsions were determined using a laser scattering particle size distribution analyzer (model LA-950, Horiba, Japan) and zeta potential analyzer (Zeta Plus, Brookhaven, USA), respectively. The measurement of particle size and surface charge was performed in triplicate.

2.5. Morphology

Surface morphology of dextrin nanoparticles was observed using scanning electron microscope (SEM; model Maxim-2000, Camscan Analytical, England) and transmission electron microscopy (TEM; model JEM-1230, JOEL Corp., Japan). SEM samples were sputter-coated with gold to increase their conductance. The samples are then viewed and photographed using SEM. TEM analyses were performed by sample mounting on a copper glider grid of 3.5 mm with a single aperture.

2.6. FT-IR spectroscopic analysis

The prepared nanoparticles were blended with KBr and compressed at a pressure of 5 tons for 30 s. The KBr discs were scanned by FTIR spectrophotometer (Nicolet 4700, USA) in a range of 4000–400 cm^{-1}.

2.7. Statistical analysis

Analysis of variance (ANOVA) was performed using SPSS version 11.5 for Windows (SPSS Inc., USA). *Post hoc* testing ($p < 0.05$) of the multiple comparisons was performed by either the Scheffé or Games-Howell test depending on whether Levene's test was insignificant or significant, respectively.

3. Results and discussion

3.1. Formation of nanoemulsion templates

In this study, water-in-hexane emulsions were formed by high energy emulsification technique using high power (400 W, 24 KHz) ultrasonication. Generally, the emulsion droplet formed by high energy emulsification method is controlled by the interplay between droplet break up and droplet coalescence (Dickinson, 2003; McClements, 2004). Moreover, droplet break up is controlled by the type and amount of shear applied to the droplets as well as the droplets' resistance to deformation which is determined by the surfactant. The rate of droplet coalescence is determined by the ability of the surfactant to adsorb on to the surface of newly formed droplets; this is governed by the surfactant concentration and the