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Core–shell biopolymer nanoparticle delivery systems: Synthesis and characterization of curcumin fortified zein–pectin nanoparticles

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ABSTRACT

Biopolymer core–shell nanoparticles were fabricated using a hydrophobic protein (zein) as the core and a hydrophilic polysaccharide (pectin) as the shell. Particles were prepared by coating cationic zein nanoparticles with anionic pectin molecules using electrostatic deposition (pH 4). The core–shell nanoparticles were fortified with curcumin (a hydrophobic bioactive molecule) at a high loading efficiency (>86%). The resulting nanoparticles were spherical, relatively small (diameter ≈ 250 nm), and had a narrow size distribution (polydispersity index ≈ 0.24). The encapsulated curcumin was in an amorphous (rather than crystalline form) as detected by differential scanning calorimetry (DSC). Fourier transform infrared (FTIR) and Raman spectra indicated that the encapsulated curcumin interacted with zein mainly through hydrophobic interactions. The nanoparticles were converted into a powdered form that had good water-dispersibility. These core–shell biopolymer nanoparticles could be useful for incorporating curcumin into functional foods and beverages, as well as dietary supplements and pharmaceutical products.

1. Introduction

Curcumin is a natural lipophilic polyphenol found in the rhizomes of turmeric (*Curcuma longa*) (Kumar, Mahesh, Mahadevan, & Mandal, 2014). It has been used as a traditional medicine and as a food pigment in India and China for centuries. Recent research suggests that it may possess a broad range of pharmacological activities such as antioxidant, anti-inflammatory, antimicrobial, antiviral, antirheumatic, and neuroprotective properties (Anand, Kunnumakkara, Newman, & Aggarwal, 2007; Bhawana et al., 2011; Duvoix et al., 2005). Curcumin has also been shown to inhibit the viability and proliferation of a variety of human cancer cell lines including skin, gastrointestinal, genitourinary, breast, ovarian, and lung cancers (Anand et al., 2008; Jambhrunkar, Karmakar, Popat, Yu, & Yu, 2014). Despite its potential health benefits, curcumin has found limited use as a pharmacological or nutraceutical agent, which can be partly attributed to its low water-solubility and poor oral bioavailability.

Many efforts have been made to increase the water-dispersibility and bioavailability of curcumin, including encapsulation in liposomes (Dhule et al., 2012), cyclodextrins (Mohan et al., 2012), emulsions (Ahmed et al., 2012; Li, Ma, & Cui, 2014; Lin et al., 2009), solid lipid nanoparticles (Sun et al., 2013), polymer nanoparticles (Simion et al., 2013; Verderio et al., 2013), and inorganic nanoparticles (Gangwar et al., 2013; Jambhrunkar et al., 2014; Singh et al., 2013). Recently, there has been interest in utilizing biopolymer nanoparticles fabricated from proteins or polysaccharides to encapsulate curcumin, such as casein (Esmaili et al., 2011; Pan, Zhong, & Baek, 2013), chitosan (Yadav et al., 2012), and starch (Chin et al., 2014). The advantage of using food-grade biopolymers to fabricate delivery systems is that they can be incorporated into a wide range of commercial products, and they are biodegradable, natural, and label friendly.

Zein is the major storage protein in corn and consists of four major constituents: α-, β-, γ-, and δ-zein (Rishi & Munir, 2001). More than 50% of the amino acid residues in zein are hydrophobic, which makes it one of the few proteins that can be solubilized in concentrated aqueous ethanol (60–90%) solutions but not in pure water (Dong, Padua, & Wang, 2013; Zhang, Luo, & Wang, 2011). This property makes zein a suitable material for development of colloidal delivery systems to encapsulate hydrophobic bioactive molecules, such as curcumin (Chen & Zhong, 2014; Patel et al., 2010, 2013; Zhong & Jin, 2009). However, zein particles often have poor stability to aggregation when exposed to environmental conditions commonly encountered in food and pharmaceutical products, such as certain pH ranges, high salt contents, and

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thermal processing. Researchers have shown that food biopolymers (such as sodium caseinate) can be used to coat zein nanoparticles and thereby improve their stability to aggregation under certain conditions (Patel et al., 2010).

Zein-biopolymer nanoparticles have already been used to encapsulate a variety of lipophilic bioactives, including α-tocopherol (Luo et al., 2011), vitamin D_3 (Luo, Teng, & Wang, 2012), and thymol (Zhang et al., 2014). In this study, we focus on the utilization of an anionic polysaccharide to coat and stabilize zein nanoparticles since this type of biopolymer is already widely used as a functional ingredient in the food industry. Previously, we have shown that alginate can be used to form core–shell zein-biopolymer nanoparticles with relatively small sizes (diameter = 150 nm), which had good stability over a range of temperatures, pH values, and ionic strengths (Hu & McClements, 2015). In the current study, we investigated the ability of citrus pectin to form and stabilize curcumin-loaded zein nanoparticles that might be suitable for use as delivery systems in the food and pharmaceutical industries.

2. Materials and methods

2.1. Materials

Zein (Lot SLBD5665V) was purchased from Sigma–Aldrich (St. Louis, MO, USA). Curcumin (>98%) was obtained from Acros Organics (New Jersey, USA). Pectin (Genu® pectin from *citrus*, type USP/100) was a gift from CP Kelco US Inc. (Atlanta, USA). Other chemicals, such as sodium chloride, sodium hydroxide, hydrochloric acid, HPLC grade ethanol alcohol, and dimethyl sulfoxide (DMSO), were obtained from Fisher Scientific (Fairlawn, NJ, USA).

2.2. Solution preparation

2.2.1. Curcumin–zein solution

1.7 g zein was added to 100.0 ml 85% (v/v) aqueous ethanol solution with magnetic stirring at 500 rpm (IKA R05) for 1 h, then curcumin powder was added and the mixture was stirred continuously for another hour.

2.2.2. Pectin solution

Pectin powder was dispersed in double distilled water at a concentration of 0.1% (w/v), and stirred for 3 h, then filtered through filter paper (Fisher Science, P5) to remove any insoluble components.

2.3. Preparation of curcumin loaded zein–pectin nanoparticles

5.88 ml of curcumin–zein ethanol solution was rapidly dropped into 25.00 ml of pH 4.0 adjusted water using a syringe with constant stirring at 900 rpm (IKA R05, USA). The resulting dispersion was then stirred for another 5 min, and then the ethanol was evaporated using a rotary evaporator (Rotavapor R110, Büchi Crop., Switzerland). Water (adjusted to pH 4.0) was added to compensate for the lost ethanol, so that the final volume of the dispersion was 25.00 ml. The dispersion was then filtered and poured into a 31.25 ml pectin solution with continuous stirring at 600 rpm for 30 min.

2.4. Nanoparticle characterization

2.4.1. Particle size and zeta potential measurements

The particle size distribution of the colloidal dispersions formed was measured by dynamic light scattering (DLS), Nano-ZS (Malvern Instruments, Worcestershire, UK). The Z-average diameter and polydispersity index (PDI) were calculated from the light scattering measurements. The electrical characteristics (ζ-potential) of the particles in the colloidal dispersions were determined using a micro-electrophoresis device (Nano-ZS, Malvern Instruments, Worcestershire, UK). Samples were diluted with water (adjusted to pH 4.0) prior to measurements to avoid multiple scattering effects.

2.4.2. Particle yield and curcumin loading efficiency (LE)

Freshly prepared colloidal dispersions were centrifuged at 3000 rpm for 10 min (Sorvall® RC-6 Plus, Thermo Electron Corporation, USA) to separate any large particles, and then the nanoparticles in the serum phase were freeze dried and weighed, and the curcumin content in the dried nanoparticles was determined. The particle yield and the curcumin loading efficiency were calculated as follows:

$$\text{Particle yield } (\%) = \frac{\text{the weight of the freeze dried particles}}{\text{total weight of curcumin, zein and pectin}} \times 100\% \quad (1)$$

$$\text{Loading efficiency } (\%) = \frac{\text{curcumin in nanoparticles}}{\text{total curcumin input}} \times 100\% \quad (2)$$

2.4.3. Curcumin loading determination

10 mg of freeze-dried nanoparticles were solubilized in 10 ml DMSO and then stirred overnight in the dark. The resulting solution was then centrifuged at 15,000 rpm for 30 min. The supernatant was diluted 10 times with DMSO, and the absorbance at $\lambda_{435\ nm}$ was measured using a UV-spectrophotometer (Ultrospec® 3000 Pro, Biochrom Ltd, England) to determine the curcumin concentration on the basis of a calibration curve which was previously established using standard solutions (0–10 μg/ml free curcumin in DMSO).

2.4.4. Transmission electron microscopy (TEM)

Freshly prepared colloid dispersions were diluted with water (adjusted to pH 4.0), then dropped onto a plasma-treated (glow-discharged) carbon-filmed grid and allowed to dry in the air. TEM experiments were performed on a JEM-2200FS microscope (JEOL Ltd, Japan) with an acceleration voltage of 200 kV. The image was taken on film at 20,000 × magnification.

2.5. Differential scanning calorimetry (DSC)

The thermal behavior of the dried nanoparticle sample was characterized using a differential scanning calorimeter (Q100, TA Instruments, USA). Ten milligrams of powdered sample were sealed in a hermetic aluminum pan and heated from 30 to 200 °C at a rate of 5 °C/min. Nitrogen was used as the transfer gas at a flow rate of 50 ml/min. Curcumin, zein, and pectin were also analyzed for comparison.

2.6. Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of curcumin, zein, pectin, curcumin encapsulated nanoparticles, and curcumin–zein–pectin physical mixtures were recorded on a FTIR spectrophotometer (IR Prestige 21®, Shimadzu Corporation, Kyoto, Japan). The scanning range used was 600–1800 cm^{-1} with 32 scans and the resolution was set at 4 cm^{-1}.

2.7. Raman spectroscopy

A Raman microscope with spectroscopy capabilities (DXR Raman, Thermo Fisher Scientific, Madison, WI) was used to measure the spectra of curcumin, curcumin-encapsulated nanoparticles, and curcumin–zein–pectin physical mixtures. This instrument used