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Preparation and characterization of quercetin/dietary fiber nanoformulations

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ABSTRACT

Quercetin is well known for its beneficial health effects on the human body. However, the slow dissolution rate leading to poor bioavailability constitutes a barrier to being further developed for nutritional products. In this work, quercetin was co-precipitated with dietary fibers into a fast-dissolving nanoformulation via antisolvent precipitation, followed by spray drying. With the help of cellulose fiber, resistant starch or resistant maltodextrin, a high dissolution rate and good storage stability was achieved for quercetin nanoformulations. In addition, nanoformulations exhibited higher level of antioxidant activities in contrast to raw quercetin. The developed quercetin/dietary fiber nanoformulations could be used as supplements or functional ingredients for food development.

1. Introduction

Antioxidant dietary fiber (ADF) is described as a product containing significant amounts of antioxidants associated with the fiber matrix. It has the attractive dual property of an antioxidant and a nutritional fiber in one single material (Daou & Zhang, 2011; Eskicioglu, Kamiloglu, & Nilufer-Erdil, 2015; Pérez-Jiménez & Sáyago-Ayerdi, 2009; Quiros-Sauceda et al., 2014; Saura-Calixto, 1998). For example, ADF is able to promote the health of circulatory and digestive systems through regulation of bowel flow, reduction of bile acids resorption and carbohydrate absorption and the production of health beneficial short-chain fatty acids in the large intestine (Brown, Rosner, Willett, & Sacks, 1999; Drzikova, Dongowski, Gebhardt, & Habel, 2005; Kim et al., 2009; Lattimer & Haub, 2010; Qureshi, Sami, & Khan, 2002; Roehrig, 1988). These beneficial health effects are conferred by water-soluble or insoluble fibers (Elleuch et al., 2011; Mudgil & Barak, 2013). Meanwhile, the presence of antioxidants provides antioxidative, antiproliferative, anticancer activities, etc (Hooper & Cassidy, 2006). Most ADFs come from plant processing by-products including red grape pomace (Pérez-Jiménez & Sáyago-Ayerdi, 2009), apple pulp (Bravo, Saura-Calixto, & Goni, 1992), cocoa fiber (Lecumberri et al., 2007), and carrot peel (Chantaro, Devahastin, & Chiewchan, 2008).

Quercetin is well known for its antioxidant, anti-cancer, anti-obesity, anti-inflammatory and anti-microbial properties (Boots, Haenen, & Bast, 2008; Middleton, Kandaswami, & Theoharides, 2000). Like other water-insoluble plant-derived polyphenols, quercetin is predisposed with a poor dissolution rate that resulted in low and inconsistent bioavailability in the gastrointestinal tract. A number of formulation approaches have been reported to improve the solubility/dissolution rate of quercetin in the endeavor to enhance its bioavailability, such as particle size reduction, cyclodextrin complexation, nanoencapsulation, solid dispersion and cocrystallization (Cai, Fang, Dou, Yu, & Zhai, 2013; Fujimori et al., 2015; Goncalves et al., 2015; Li et al., 2013; Pool, Mendoza, Xiao, & McClements, 2013; Smith, Kavuru, Wojtas, Zaworotko, & Shytle, 2011; Tran, Guo, Song, Bruno, & Lu, 2014; Zheng, Haworth, Zuo, Chiw, & Chow, 2005). Nanosizing, i.e. reduction of the compound particles size to the submicron range, is among them a most direct and effective strategy (Kesisoglou, Panmai, & Wu, 2007). According to the Noyes-Whitney equation, dissolution rate is proportional to the surface area of the particles exposed to the medium. Therefore, the significantly-enlarged surface area of the particles from nanosizing is in favour of a considerably-expedited dissolution. In literature, quercetin nanoparticles has been produced by "bottom-up" (i.e. antisolvent precipitation) (Kakran, Sahoo, & Li, 2011; Kakran, Sahoo, Li, & Judeh, 2012; Neethu, Kavitha, Krishnakumar, Anish, & Dineshkumar, 2015) and "top-down" (Karadag, Ozcelik, & Huang, 2014; Lai et al., 2015; Sahoo et al., 2011) method. Antisolvent precipitation is a facile technique

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to make nanoparticles with ease of scaling-up. However, the precipitated nanoparticles in the suspension are mostly metastable and prone to agglomerate/grow leading to an increased overall size and decreased surface area (Liu, Kathan, Saad, & Prud'homme, 2007; Verma, Kumar, Gokhale, & Burgess, 2011). Immediate conversion of the freshly precipitated nanosuspensions into dried powders therefore seems an ideal solution to alleviate this undesirable phenomenon. Drying, however, can also cause agglomeration of the nanoparticles upon dehydration, leading to a diminishment of the full dissolution benefits brought by nanosizing (Cerdeira, Mazzotti, & Gander, 2013; Chaubal & Popescu, 2008; Van Eerdenbrugh et al., 2008a). To minimize the drying-caused agglomeration, water-soluble or insoluble matrix formers are generally used in the drying process (Dong, Ng, Hu, Shen, & Tan, 2014; Van Eerdenbrugh et al., 2008b).

The purpose of this work is to prepare rapidly-dissolved quercetin nanoparticles by antisolvent precipitation technique followed by conversion of the nanosuspensions using spray drying with the dietary fibers as novel matrix formers to minimize the drying-caused agglomeration. To our knowledge, this innovative quercetin/dietary fiber nanoformulation has not been reported in the literature. The dietary fibers used in this work included water-insoluble cellulose fiber (CF) and resistant starch (RS), and water-soluble resistant maltodextrin (RM). Cellulose fiber comes from the leaves, stem, bark and roots of plants constituting a major component of plant cells. Due to water insolubility, cellulose fiber holds water to increase fecal mass. This fiber also goes through fermentation in the colon to produce short-chain fatty acids (Lattimer & Haub, 2010; Mudgil & Barak, 2013). Resistant starch is fiber-like material that escapes digestion and absorption in the small intestine adopting granular structure such that digestive juices cannot easily access. The reported beneficial health effects of resistant starch include prevention of colonic cancer, reducing blood glucose, increasing satiety and act as a prebiotic for the growth of good bacteria (Cassidy, Bingham, & Cummings, 1994; Englyst, Kingman, & Cummings, 1992; Fuentes-Zaragoza, Riquelme-Navarrete, Sánchez-Zapata, & Pérez-Álvarez, 2010; Nilsson, Ostman, Hoist, & Bjorck, 2008; Quílez, Bulló, & Salas-Salvadó, 2007; Sajilata, Singhal, Kulkarni, 2006; Topping, Fukushima, & Bird, 2003; Willis, Eldridge, Beiseigel, Thomas, & Slavin, 2009). Resistant starch also bears favorable physicochemical properties that make it more appetizing compared to traditional sources of fiber. Resistant maltodextrin is a soluble fiber generally processed from starch. It has the ability to raise satiety level, produce short chain fatty acids, and increase good bacteria populations in the colon (Fastinger et al., 2008; Guérin-Deremaux et al., 2011; Lefranc-Millot et al., 2012; Miyazato, Nakagawa, Kishimoto, Tagami, & Hara, 2010; Ohkuma, Matsuda, Katta, & Hanno, 1990). The circumvention of nanoparticles agglomeration is illustrated mechanistically in Fig. 1. For water-soluble resistant maltodextrin, nanoparticles would be individually embedded and immobilized in the solidified matrix of the fibers, alleviating the dehydration-caused agglomeration (matrix-embedding). In terms of water-insoluble cellulose fiber and resistant starch, the nanoparticles are deposited and immobilized onto their surfaces upon dehydration, leading to an unfavorable environment for the particle–particle interaction or agglomeration. In addition, water-insoluble matrix former can also act as physical barriers in the suspension to prevent agglomeration and growth of the nanoparticles prior to drying (Dong et al., 2014). In this work, quercetin nanoparticles were prepared by antisolvent precipitation in the presence of dietary fibers and converted into dried quercetin/dietary fiber nanoformulation powders by spray-drying. The achieved powders were characterized by field emission scanning electronic microscopy (FESEM), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FTIR) for morphology, physical state and chemical structure, respectively. Finally, the dissolution rate of the nanoformulations was measured and their antioxidant activities were assessed by 2, 2-Diphenyl-1-picrylhydrazyl (DPPH) method. The developed unprecedented quercetin/dietary fiber nanoformulations could be used as supplements or novel functional ingredients for food development.

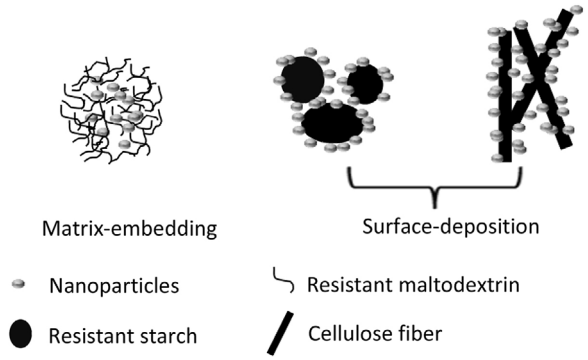

Fig. 1. Mechanism illustration of circumvention of nanoparticles agglomeration upon dehydration by dietary fibers.

2. Materials and methods

2.1. Materials

Quercetin was purchased from Hunan Kang Biotech Co. Ltd (Changsha, China). Cellulose fiber (Unicell® PF 200) was a gift from InterFiber (Warsaw, Poland). HI-MAIZE® 260 resistant starch was kindly provided by Ingredion Singapore Pte Ltd, an affiliate of Ingredion Incorporated. Resistant maltodextrin (Promitor 85™) was obtained from Tate & Lyle Co. (Decatur, IL, USA). 2, 2-Diphenyl-1-picrylhydrazyl (DPPH), 37% hydrochloric acid, Tween 80, sodium acetate and acetic acid were from Sigma-Aldrich (Steinheim, Germany). HPLC grade methanol and absolute ethanol were from Avantor (J.T Baker®, PA, USA) and VWR Chemicals (Fontenay-sous-Bois, France), respectively. Deionized water was used throughout the work.

2.2. Preparation of quercetin/dietary fibre nanoformulation

Quercetin nanoparticles were prepared by antisolvent precipitation technique. In brief, 1 mL quercetin solution in ethanol at 10 mg/mL was mixed with 5 mL water containing 90, 40, 23.3 or 0 mg of dietary fiber. The quercetin nanoparticles were precipitated immediately and spray-dried with BUCHI Mini Spray Dryer B-290 (BÜCHI Labortechnik AG, Switzerland) with the following parameters: inlet temperature 140 °C, feed rate 20%, aspiration rate 100%, and nitrogen flow rate 40 mm. The obtained quercetin/dietary fiber nanoformulations were collected and stored in capped bottles for further analysis. The nanoformulation powders were denoted as, for example, CF10 and RS20, which represented quercetin/cellulose fiber nanoformulation with 10% quercetin and quercetin/resistant starch nanoformulation with 20% quercetin, respectively. The spray-dried quercetin nanoformulation without dietary fiber was denoted as SDQ.

2.3. SEM

Morphology and size of raw quercetin, quercetin/dietary fiber nanoformulation powders and nanosuspensions were visualized by FESEM (JEOL JSM-6700F, JEOL Ltd., Japan). Raw quercetin or nanoformulation powders were deposited onto double-sided carbon tape and sputtered with gold (Cressington 208HR, High Res-